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Dear Sir:

In the past, Xerox has submitted results of studies conducted to understand the long-term consequences of exposure to toner. These have included reports of toxicological studies (animal inhalation studies), a report of Xerox employee mortality (standardized mortality ratio analysis with follow-up through 1984), and a case-control study of employee digestive cancer mortality. The enclosed report, "**Report of an Investigation of the Health Effects of Toner Exposure**," describes the results of the Xerox employee morbidity study (cross-sectional analysis).

Results of the investigation indicated that among the employee participants, in general, health status was typical of a healthy workforce. Among Toner Exposed and Other Exposed (i.e. work exposure to solvents, acids, or other irritants) manufacturing employees, some respiratory symptoms and conditions were reported more frequently than among Never Exposed. Similarly, symptoms of irritation/injury involving the eyes and/or skin were more frequently reported by Toner Exposed and Other Exposed and by Customer Service Engineers. Pulmonary function testing results for Toner Exposed at one manufacturing location and for Customer Service engineers were comparable to non-exposed populations. Among Toner Exposed at the other two manufacturing locations, there were some reductions in pulmonary function noted.

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Study results have been communicated to the appropriate employees. Employee health data collected since 1993 through 1995 will be analyzed. The mortality study is currently being repeated with follow-up extended through 1993. As results of these studies become available, they will be forwarded to your office.

If you have any questions, please contact me at 716-422-9270.

Sincerely,

James C. MacKenzie

James C. MacKenzie
Director
Environment, Health and Safety
Xerox Corporation
800 Phillips Road, Building 105-70C
Webster, New York 14580

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REPORT OF AN INVESTIGATION
OF
THE HEALTH EFFECTS OF TONER EXPOSURE

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7/13/95

REPORT OF AN INVESTIGATION
OF
THE HEALTH EFFECTS OF TONER EXPOSURE

EXECUTIVE SUMMARY

This report describes the most recent results of employee health monitoring, part of the Xerox program of toxicological and epidemiological studies to understand the long-term consequences of exposure to toner materials. The data were collected in 1992 - 93 from manufacturing employees based in the USA (Oklahoma City and Monroe County/Rochester area, NY) and in the Netherlands (Venray), and USA-based customer service engineers attending training sessions in Leesburg, Virginia. Data included reported health history, symptoms and conditions, and results of pulmonary function testing and chest x-rays. The analyses compared health questionnaire responses and testing results of exposed groups (toner-exposed and other materials-exposed) to never exposed and to other external populations.

Results of the investigation indicated that among the employee participants, in general, health status was typical of a healthy workforce. Toner Exposed and Other Exposed employees in manufacturing and customer service engineers more frequently reported work-related irritation of eyes and skin and/or eye injury. Job tasks for each of these employee groups involve working with dusts and other potential irritants (such as solvents, acids, and metals) which could be expected to produce symptoms of eye and skin irritation.

The effects of current smoking were evaluated among manufacturing employees and found to be associated with increased risk for all respiratory symptoms. Comparing current with never smokers, there were statistically significant increases in the symptoms chronic cough (Odds Ratio Range at the three manufacturing locations/OR Range: 2.85 - 5.22), chronic phlegm (OR Range: 2.54 - 8.29), and persistent wheeze (OR Range: 2.84 - 7.70). Toner Exposed and Other Exposed employees in manufacturing reported some respiratory symptoms/conditions more frequently. The findings among Toner Exposed (Categories = *Ever* and *Current*) persisted when logistic regression models were used to control for potential confounders, such as cigarette smoking. These included statistically significant increases in the symptoms chronic phlegm (OR: 2.04 OKC - *Current* and OR: 2.78 Venray - *Ever*), wheeze and breathlessness (OR: 2.32 - 2.61 Venray - *Ever* and *Current*), dyspnea (OR: 2.15 Monroe County - *Ever*), history of pulmonary disease diagnosis (OR: 2.56 - 3.14 Venray - *Ever* and *Current*), and allergies (OR: 2.25 Venray - *Current*). There was no increase in reported respiratory symptoms/conditions among the customer service engineers.

Linear regression models produced the anticipated results for effects of cigarette smoking on pulmonary function testing; i.e. reduction in airflow measurements. At the three manufacturing locations, these included reduction in percent predicted FEV_1 of 3.27 - 4.93% and in percent predicted $FEF_{25-75\%}$ of approximately 11 - 14%. Logistic regression models demonstrated an association of smoking with an increase in proportion with percent predicted FEV_1 less than 80 (OR: 2.14) for Monroe County. The models also indicated an association of toner exposure with pulmonary function results. These included a decrease of 2.22 - 3.52% in percent predicted FVC, a measure of lung capacity, (Venray - *Ever* and Monroe County - *Ever* and *Current*),

and an increase in the proportion (OR: 1.78 - 2.39 Monroe County - *Ever* and *Current*) with percent predicted FEV_1 less than 80, a measure of airway obstruction. Pulmonary function testing results among toner manufacturing employees in Oklahoma City and among customer service engineers were comparable to those of healthy, non-smoking adults.

Results of the chest x-ray program, conducted in Monroe County and Oklahoma City, gave no chest x-ray evidence of work-related lung disease.

These results could have been influenced by a number of factors including the participation rates in these voluntary medical surveillance programs. Less than complete participation may lead to low statistical power, statistical modeling limitations, as well as potential bias. The latter would impact the results if participants (Exposed and/or Never Exposed) compared to non-participants were more or less likely to have symptoms and/or reduced pulmonary function values. Quality of measurements is always another potential limitation. Even though measures were taken to assure data quality, this could have involved both toner exposure estimates and possibly pulmonary function measurements. Differences in racial composition and other demographics between groups raised some concern of suitability of controls. To the extent possible, adjustments were made in the analysis for confounders.

To clarify whether these findings are due to toner or other workplace exposure, further investigation is needed. Among the recommendations, the highest priority must be given to further efforts to better understand the 1992 - 93 findings. The employee health programs will be offered in each location in 1995 with emphasis on improving participation and assuring that the stringent data collection procedures utilized in this program are maintained to ensure quality of the data collected and validity of the findings.

INTRODUCTION

Xerox Corporation is one of the largest manufacturers and distributors of toner materials in the world. To increase understanding of the consequences of long term exposure to toner materials, Xerox implemented in the 1980's, and has maintained, a program of toxicological and epidemiological studies. These include a mortality study comparing causes of deaths among Xerox employees to the general population, toxicological studies which examined the effects of toner inhalation on rats and hamsters, and an ongoing morbidity study of Xerox employee health. This report describes the most recent results of health monitoring of Xerox employees.

Earlier health monitoring involving health questionnaire surveys had suggested an association of respiratory, eye, and skin symptoms among Xerox employees with work exposure to toner. The results of objective testing of those employees, including pulmonary function testing and chest x-ray examination, had given no indication of adverse effect of working with toner. However, because of concerns of inadequate standardization of data collection and testing quality problems, the validity of the health monitoring results had been questioned.

Although the medical literature did not provide data that directly addressed the health effects associated with exposure to toner, information from mixed-dust exposure in other occupations suggested that exposure to occupational dusts could result in an increase in acute and chronic respiratory symptoms, and of chronic airflow obstruction.[1-5] Evidence from the general population also suggests adverse effects of inhaled particles.[6,7]

Results of Xerox-sponsored animal inhalation studies had indicated middle and high toner exposure levels could cause inflammatory changes in lung tissue and reduced lung clearance.[8] Below exposures leading to "lung overloading," these effects either did not occur or were transient in nature.[9,10] No pulmonary changes were seen at the lowest toner exposure level, the level considered most relevant to potential human exposure in toner production facilities.[8]

Based on the results of the Xerox animal studies and on other epidemiologic and pathologic evidence showing that dusts may adversely affect lung function and cause respiratory symptoms, this cross-sectional survey of employee health was undertaken in 1992 to assess potential health effects of toner exposure. The purpose of the health monitoring program was:

- To determine if workplace exposure to toner had resulted in any adverse health effects (detected through health questionnaire reporting, pulmonary function testing and/or chest x-ray examination) among specific Xerox employee categories, defined as having similar workplace exposures.

- To provide summary information to employees and management on the health status of the workforce relative to workplace exposure to toner.

- To provide information to each employee on personal health, including medical testing results and appropriate medical recommendations.

METHODS

A study protocol and procedures for data collection and entry were developed, approved by the external consultant panel, and followed to ensure standardization and to minimize bias. Data were collected between January, 1992, and May, 1993, and involved the Xerox employee groups described below, employee groups that have previously participated in the Personal Health Profile (PHP = Oklahoma City, Oklahoma, and Monroe County/Rochester area, NY; and PGP = Venray, Netherlands) and Employee Health Assessment Program (EHAP = Leesburg, VA). Each participant completed a health questionnaire and underwent pulmonary function testing. Participants at USA-based sites underwent hematologic and blood chemistry analyses, and, for certain individuals as described subsequently, chest x-rays. External quality review of pulmonary function testing was performed to ensure ongoing quality of testing data gathered.

Study Populations:

PERSONAL HEALTH PROFILE (PHP - PGP) and EMPLOYEE HEALTH ASSESSMENT PROGRAM (EHAP) were initiated in 1984 and have been offered on a voluntary basis to the following groups of employees:

- PHP: All Monroe County and Oklahoma City union employees and their first line engineers and supervisors.
- EHAP: Customer Service Engineers/Representatives from throughout the United States who attend the Xerox training center in Leesburg
- PGP: Venray employees in manufacturing and their first line engineers and supervisors.

Approximately 4,200 Monroe County and 300 Oklahoma City employees have been offered the PHP exam annually. The exams are administered by Xerox's Monroe County Medical Services staff and St. Anthony's Occupational Health Center staff respectively. Because of a low participation rate in 1992 among the Monroe County toner-exposed group, this group was offered a second opportunity to participate in early 1993. Approximately 25% of the toner-exposed group participants entered only the 1993 program. For the 58% of participants enrolled in both the 1992 and 1993 program offerings, their first examination was used in the analysis.

Customer service engineers have been offered the EHAP exam while attending training sessions in Leesburg, VA. Since not all service engineers attend training sessions in Leesburg, EHAP participants may represent some product lines more than others. In addition, service engineers participate in the EHAP exam only if their schedule at Leesburg allows time away from class. Of the approximately 14,000 USA-based service engineers employed by Xerox, 9% are scheduled to participate in the EHAP program each year. These exams are administered throughout the year by Xerox's Leesburg training center nursing staff.

The PGP exam has been offered to approximately 1,300 Venray employees annually. The exams have been administered by Xerox's Venray Medical Services staff

EXPOSURE GROUPS, identified using work histories constructed from company records, included the following:

Toner Manufacturing: Any person who ever held a job as a union employee in Monroe County or Oklahoma City (OKC), or comparable job classification in Venray, which was directly involved in the production of toner. This category has been further sub-divided into "Current" and "Past" exposed categories "Current" exposure has been defined in the data analysis as working in toner manufacturing on the day of the examination/questionnaire. Supervisors, engineers, and other salaried employees made up the category, "Salaried."

Service: Any person who ever held a position as a Customer Service Representative/Engineer (or Technical Representative).

Other Manufacturing: All other employees who were ever Monroe County or OKC union employees, or comparable job classifications in Venray. This group was further subdivided into "Other Exposed" (individuals who report working in jobs with exposure to potential respiratory hazards, such as metals, solvents, acids, other dusts and materials, and/or exposure to toner which cannot be documented in company records) and "Never Exposed." Salaried employees in OKC and Monroe County were in the category, "Salaried." Venray salaried employees were included in the "Other" and "Never Exposed" categories

TONER EXPOSURE MEASURES were derived from work histories and total dust estimates. These included the following:

Exposed (yes/no)

Total Length of Exposure (years)

Time Since First Exposure (years)

Time Since Last Exposure (years)

Cumulative Exposure Index (mg-yr/m^3 total dust)*
(*Not available for Venray or for Service employees)

Date of Hire/Dates of Exposure**
(**For Venray and Monroe County to address dust control changes)

Beginning in 1975, actual dust sampling data were available for the dust estimates. Prior to that time and for years in which no sampling data were available, dust estimates were made based on knowledge of plant conditions and engineering improvements. The dust estimates were developed by job, building, and year. When merged with the employee's work history, the employee's cumulative dust exposure (mg-yr/m^3) was determined.

There were limitations in developing the toner exposure measures. Within any job classification, a wide range of exposures was possible due to various work assignments and variation in personal work habits and use of respiratory protection. Work location by building was often missing in the work history of Webster employees from 1982 to 1986. For that time period, the difference in mean dust level between the two toner manufacturing buildings was about 50%. (Mean dust level was 1.3 mg/m^3 for one and 0.9 mg/m^3 for the second building). For those employees with unknown building, an average estimate was used. Dust exposure

was of a discontinuous nature as job changes between toner jobs and non-toner jobs were common.

The following describe toner exposure measures for each site (or group):

Customer Service Engineers (Leesburg): These toner-exposed employees can be subdivided into groups differing in length of employment. Unfortunately, since most of the differences among these groups are in variables where differences would be expected due to age (i.e. longer employment is associated with older age) and/or to smoking (i.e. older people of longer employment are more apt to have smoked and the oldest group is most apt to be ex-smokers), this measure of toner exposure was not feasible to use. Service engineers are exposed to toner during the maintenance and repair of copiers in customer facilities. Their jobs tend to be highly variable depending upon the machine problems which they encounter on a day to day basis. Dust estimates, based on sampling of individual exposures and of workplace simulations in the laboratory, have shown levels of dust exposure ranging from 0.09 to 0.94 mg/m^3.

Venray: There are three exposure groups: Toner Exposed, Other Exposed, and Never Exposed. Toner exposure information for each employee included only duration of exposure and date of hire. As shown in Figure 1, mean total dust levels were highest in Venray (estimated maximum level 16 mg/m^3 in 1978). Since 1987, mean dust level has been approximately 1 mg/m^3, lower than the Xerox exposure limit (XEL) of 2.5 mg/m^3 adopted in 1988.*

Monroe County: There are four exposure groups: Toner Exposed, Other Exposed, Never Exposed, and Salaried. Toner exposure information included each of the toner exposure measures defined on the previous page. Mean total dust levels have been reduced from levels of 6 to 9 mg/m^3 in the 1960's, to below the XEL in the early 1980's, and currently at less than 1 mg/m^3 (*See Figure 1*).*

OKC: There are three exposure groups: Toner Exposed, Other Exposed, and Salaried. Because of lack of a "Never Exposed" group, the analysis of OKC "Toner Exposed" used the Monroe County "Never Exposed" as the control group. Each of the toner exposure measures was available for Toner Exposed. As shown in Figure 1, mean total dust levels have been within the XEL at less than 1 mg/m^3 since the plant began toner production in 1976.*

*For certain work tasks, use of respiratory protection may be required to ensure dust exposure is within the XEL.

Health Data Collection:

- Health Questionnaire. Questions addressed topical areas including basic demographics, work history, personal habits, family and personal health history. The American Thoracic Society (ATS) questionnaire, validated for reporting of respiratory symptoms, formed part of the questionnaire.[11] A few questions elicited history of work exposures and outside activities involving contact with potentially toxic agents. For customer service engineers, a supplementary work history was obtained as it relates to specific product lines. A few questions were deleted from the Venray version of the questionnaire at the site's request. The questionnaire was self-administered with review for completeness by the medical personnel. The medical staff (including contract staff) participated in

interviewer training to avoid bias in data collection. An interviewer's guide was used to standardize instructions/directions to promote uniform data collection at all sites. A coding guide was followed for uniform data entry.

- Pulmonary Function Testing. Spirometry was performed by technicians/nurses who had completed a National Institute of Occupational Safety and Health approved course in pulmonary function testing. Testing was performed on an OM-P90ST Spirometry Testing System including a Sensor Medics 922 dry-rolling seal spirometer, OMI spirometry software, OMI pulmonary interpretation software, color monitor, and printer. Guidelines for spirometer calibration and for acceptability and reproducibility of testing met ATS criteria and the quality control requirements established by Mayo Pulmonary Services, Mayo Clinic.(12, 13) A sample of pulmonary function tests was sent to Mayo Clinic weekly (monthly for Leesburg) by site for external quality control review. The 1983 Knudson pulmonary function prediction equations were used for the USA-based employee analyses.(14) For the Venray employees, the 1983 prediction equations of the European Community for Coal and Steel were used.(15) Per the Mayo protocol, a reduction factor of 15% was used to adjust the prediction equations for Asians and blacks.

- Hematology and Blood Chemistry. A venous blood sample was collected from each USA participant after 8 - 12 hours of fasting and sent to MetPath Laboratory for analysis - including complete blood count with differential and a routine 24 test blood chemistry panel. Employees were advised by the medical staff of their individual test results and appropriate follow-up recommendations.

- Chest X-rays. A chest x-ray was offered to all individuals in manufacturing at USA-based sites who had not had a chest x-ray within the last five years. Films were read by a certified "B" reader following the guidelines of the International Labor Office (ILO).(16)

Data Management:

- Health questionnaire data were entered manually by computer terminal using data validation screens. Exposure data were either manually entered or directly entered via electronic feed. Blood chemistry and hematology data were provided on a magnetic tape feed from MetPath Laboratories. Spirometry data were provided on computer diskettes.

- All data are stored in the Xerox Occupational Health Information System (OHIS) data bases as medically confidential data.

Data Analysis:

Initial data analyses were descriptive. Participation rates were calculated and participants compared to non-participants on characteristics, such as, gender, age, race, length of employment, and toner exposure measures. Prevalence rates for medical conditions and symptoms among the exposed groups were compared to "Never Exposed" Xerox controls, and all groups were compared to external published reference values (when available).(4, 17 - 25) Lung function values were compared to those predicted using external population prediction equations.(14, 15)

Statistical analyses were done by site for three of the sites. Because of lack of an appropriate comparison group, no statistical analysis was possible for the customer service engineer (Leesburg) data. For the other sites, the analyses that were possible varied because of differences in sample sizes, suitability of controls, and exposure information (both in types of available exposure information and the range of observed exposures). The possible population comparisons by site are listed below:

Venray:
- Toner Exposed vs Never Exposed
- Current Toner-Exposed vs never Exposed
- within Toner Exposed, three levels of duration of exposure (low, medium, and high)
- within Toner Exposed, two levels of time of hire (pre-1980, 1980 or later)

Monroe County:
- Toner Exposed vs Never Exposed
- Current Toner-Exposed vs Never Exposed
- within Toner Exposed, three levels of cumulative total dust exposure (<1, $1 - <10$, ≥ 10 mg-yr/m^3)
- within Toner Exposed, two levels of current exposure status (current, past)
- within Toner Exposed, three levels of years since last exposure (<1, $1 - <6$, ≥ 6 yrs)
- within Toner Exposed, three levels of years since first exposure (<4, $4 - <10$, ≥ 10 yrs)
- within Toner Exposed, three levels of year of first exposure (<1975, $1975 - <1990$, ≥ 1990)

OKC:
- within Toner Exposed, three levels of cumulative total dust exposure (<1, $1 - <10$, ≥ 10 mg-yr/m^3)
- within Toner Exposed, two levels of current exposure status (current, past)
- Ever Toner-Exposed vs Monroe County Never Exposed
- Current Toner-Exposed vs Monroe County Never Exposed

The basic approach to the analysis of data for the three sites was the same.[26, 27] Most of the outcome variables were binary. Questionnaire variables categorized outcomes as present or absent, and the pulmonary function data were also classified into categories of below or above 80% of predicted value for some analyses. Each binary variable was first examined with Fisher's exact test, to determine if there was a statistically significant difference in the proportions positive across the exposure groups. Fisher's exact test, rather than the chi-squared test, was used because some of the outcome variables were positive at very low rates, which makes the chi-squared test inappropriate. Because of the known effects of smoking on respiratory function, initial analyses were repeated by smoking category (current smoker, ex-

smoker, never smoker). This procedure was followed to screen for the most important variables and thereby reduce the hundreds of outcome variables to a manageable number. However, because of the relevance of the respiratory variables to this study, they were not removed after this step, even if the results of the Fisher's exact test were not statistically significant.

The second step in the analysis of the binary data was to apply more complex modeling which included the variables identified in the screening. This step was necessary to control for the effects of possible confounding factors, such as cigarette smoking. A set of potential confounders was identified: cigarette smoking (current, past, and pack-years), gender, education, ethnicity, and age. Various combinations of these potential confounders were included as predictor variables, along with toner-exposure variables that identified the comparisons of interest, in logistic regression models. Because of the small number of females at the Venray site, this part of the analysis was restricted to males. For the OKC analysis that compared cumulative total dust exposure, the highest level group ($\geq$10 mg-yr/m^3) was omitted because it included only 11 employees.

Multiple models were examined for each outcome variable, in order to assess the need for certain adjustment variables and the adequacy of the adjustment. For example, to control for smoking, indicator variables for current- versus never-smokers and past- versus never-smokers were included to adjust for the effect of smoking on the outcome variable. Indicator variables are binary variables that code for discrete categories, such as smoking status. The findings from the model using variables for smoking status were compared with models that included alternative smoking variables, such as the cumulative measure of consumption pack-years, to assess whether or not the adjustment for smoking was sufficient with only the categories of current-, past-, and never-smoker.

Several continuous outcome measures also were examined. These variables were measures of pulmonary function, including percent predicted values for Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV_1), and Forced Mid-Expiratory Flow ($FEF_{25-75\%}$). All of these outcome variables were examined with linear regression models. The same predictor variables used in the logistic regression analysis were used in the linear regression models. Because of the relevance of these outcome variables, initial screening was not done as for the questionnaire items. The percent predicted values for these pulmonary function parameters are calculated using linear regression equations that take into account gender, age, and race. As a result, these variables were not included as predictor variables when the oucome variables were percent predicted FEV_1, FVC, and $FEF_{25-75\%}$.

RESULTS

As shown in Table 1, overall participation in the PHP/PGP programs ranged from 41% in Monroe County to 69% in Venray. Participation of the ever toner-exposed Monroe County employees was higher at 59%, but less than the 67% and 69% rates for toner-exposed employees in Oklahoma City (OKC) and Venray. Approximately 76% of eligible customer service engineers attending Leesburg (LSBG) training center participated in EHAP.

Demographic differences among the employee populations by program site included higher proportion of males in LSBG and Venray, lower proportion of blacks and Hispanics in Venray and of Asians in Monroe County, higher proportion of

Native Americans in OKC, and lower average age in OKC. Average years employed in OKC was seven years, half that in the other sites. Compared to non-participants, PHP/PGP program participants included fewer blacks and, for Monroe County, slightly older longer-term employees.

Among ever toner-exposed employees, toner exposure history differed by site. As shown in Table 2, approximately half of toner-exposed employees in Monroe County and OKC were currently exposed to toner. Sixty-eight percent of Venray and all LSBG participants were currently exposed to toner. The duration of exposure for Venray employees was 7.2 years, twice that of Monroe County and OKC employees. Level of exposure in Venray is estimated to have been higher (*See Figure 1*). Compared to Monroe County, OKC employees had slightly longer and more recent exposure, but at lower levels as indicated by the levels of cumulative exposure (mean 6.8 mg-yr/m^3 for Monroe County and 3.3 mg-yr/m^3 for OKC). LSBG participants had on average sixteen years of exposure to estimated low levels of toner.

In Monroe County and Venray, the proportion of blacks among ever toner exposed employees (25% and 3.7% respectively) was higher than that in the overall employee population at each site (15.3% and 0.9% respectively). Ever toner-exposed participants in Monroe County, compared to non-participants, were more likely to be black, to be currently exposed to toner, to have slightly longer and more recent exposure to toner, but not to differ in cumulative dust exposure, average years employed, or age. OKC participants, compared to non-participants, had slightly longer but less recent exposure with higher cumulative exposure, slightly longer employment, lower proportion of blacks, and younger average age.

Participant characteristics by exposure group, shown in Table 3, differed among the four sites and at each site. Most Toner Exposed participants in Venray and LSBG and Other Exposed participants in Venray were male. The proportion of Monroe County Toner Exposed participants who were black was significantly greater, and who were Asian was significantly lower, compared to Toner Exposed at the other sites and to all other exposure groups at the four sites. At each manufacturing site, fewer Toner Exposed participants were age 50 or older or were employed 20 or more years as compared to the other exposure groups. Only eight percent of LSBG participants were under age 30. At OKC, duration of employment was less than 20 years for most employees. Among LSBG participants, seventy five percent had attended at least some college. For Monroe County and OKC Toner Exposed participants, comparable rates were 25% and 40% respectively. LSBG participants were less likely to be current smokers, but had high pack-year history. Nearly half of OKC and Venray Toner Exposed participants were current smokers. However, pack-year history was lowest among all Venray exposure groups compared to the other sites.

Among Other Exposed participants, most were male and a high proportion employed 20 or more years and age 50 or older. There were fewer males among Never Exposed participants. Compared to Toner Exposed, a higher proportion of Venray Never Exposed were never smokers (23% and 33% respectively). Among Monroe County Never Exposed, there were fewer current but more ex-smokers. For Never Exposed and Salaried participants, the proportions age 50 or older and employed 20 or more years were higher compared to Toner Exposed. Salaried participants were most likely to have attended at least some college and to be never smokers.

Prevalence rates for reported respiratory and other potentially work-related symptoms and conditions are displayed in Tables 4 and 5 for all exposure groups, and

in Figures 2 and 3 for Toner Exposed and Never Exposed. These data are crude rates, not adjusted for demographic differences or smoking history/status. Rates for respiratory symptoms/conditions were based on positive responses to combinations of questions in order to detect potentially more serious respiratory complaints and to enable comparison with other studies in the medical literature. Prevalence rates for respiratory symptoms and conditions among Never Exposed in Venray and in Monroe County appeared to be within ranges reported in external populations.[4, 22-25] Some respiratory symptoms and/or conditions, history of work-related irritation of skin and/or eyes, and history of eye injury were more commonly reported by Toner Exposed and Other Exposed in manufacturing compared to Never Exposed and to external populations. For LSBG participants, prevalence rates for respiratory symptoms were similar to Monroe County Never Exposed, but reported history of work-related irritation of eyes and eye injury was similar to Toner and Other Exposed. No significant differences were seen between Toner or Other Exposed compared to Never Exposed or Salaried for reported prevalence of hives, migraine/tension headache, or sinus problems. Hives and sinus problems were less frequently reported in all Venray exposure groups compared to USA-based sites. Allergies and skin operations were reported more frequently by the Salaried groups.

The results of logistic regression modeling to control for confounding variables comparing symptom/condition prevalence among Toner Exposed to Never Exposed are shown in Table 6. The following highlights those odds ratios that are statistically significant ($p<0.05$). Other odds ratios were either greater than one, but did not achieve statistical significance, or were less than one. The effects of current smoking on reported respiratory symptoms were evident in a consistent pattern in the three manufacturing locations. Relative to never smoking, current smoking was associated with increased risk for all respiratory symptoms with statistically significant increases in the symptoms chronic cough (Odds Ratio Range for the three locations/OR Range: 2.85 - 5.22), chronic phlegm (OR Range: 2.54 - 8.29) and persistent wheeze (OR Range: 2.84 - 7.70). Ex-smoker history among OKC employees was associated with statistically significant increases in the symptoms dyspnea (OR: 4.26) and chronic phlegm (OR: 2.80). Toner exposure (*Ever* and *Current*) was associated with statistically significant increased odds ratios for some respiratory symptoms and conditions and for history of work-related eye and skin irritation. The respiratory symptoms and conditions included chronic phlegm (OR: 2.04 OKC - *Current* and OR: 2.78 Venray - *Ever*), wheeze and breathlessness (OR: 2.32 - 2.61 Venray - *Ever* and *Current*), dyspnea (OR: 2.15 Monroe County - *Ever*), history of pulmonary disease diagnosis (OR: 2.56 - 3.14 Venray - *Ever* and *Current*), and allergies (OR: 2.25 Venray - *Current*). The odds ratios were statistically significant for work-related skin irritation (OR: 1.68 Monroe County - *Ever*) and for work-related eye irritation (OR: 3.18 - 3.54 Monroe County - *Ever* and *Current* and OR: 2.97 - 4.83 OKC - *Ever* and *Current*).

Pulmonary function testing results, displayed in Table 7 and in Figures 4 and 5 as percent predicted (adjusted for age, race, gender, and height), suggested an increased proportion with percent predicted FEV_1 less than 80 among Monroe County and Venray Toner Exposed, with values of 13.9% and 9.2% respectively. Percent predicted values less than 80% are generally considered clinically impaired. In a healthy population, approximately 5% could be expected to have pulmonary function values less than 80% of the predicted value. Although the proportion with percent predicted FVC less than 80 appeared increased among Venray Toner Exposed compared to Never Exposed, the proportion was still less than 5%. Among OKC Toner Exposed and LSBG participants, pulmonary function results were comparable to Monroe County Never Exposed

Linear regression modeling results are shown in Table 8. This summary focuses on those results that were statistically significant. The data demonstrate an association of current smoking with reduction in percent predicted FEV_1 of 3.27 - 4.93% and in percent predicted $FEF_{25-75\%}$ of approximately 11 - 14%. For Monroe County, logistic regression modeling demonstrated an association of current smoking with an increase in proportion with percent predicted FEV_1 less than 80 (OR: 2.14). Ex-smoker history was associated with a statistically significant increase in percent predicted FVC of 4.27 - 4.47% in Venray, and a reduction in percent predicted $FEF_{25-75\%}$ of 5 - 10% in each of the three manufacturing locations. Toner exposure was associated with a statistically significant increase in proportion with percent predicted FEV_1 less than 80 (OR: 1.78 - 2.39 Monroe County - *Ever* and *Current*) and with reduction in percent predicted FVC (2.22 - 3.52% Monroe County - *Ever* and *Current* and 2.81% Venray - *Ever*). In an attempt to assess if the effect associated with exposure to toner might also interact with smoking, modeling was done within categories of smoking status (current and never). As shown in Table 9, there was a statistically significant increase in proportion with percent predicted FEV_1 less than 80 among Monroe County Toner Exposed current smokers (OR: 2.6) compared to Never Exposed current smokers. Among never smokers, the odds ratio (OR: 2.0) was of similar magnitude, but not statistically significant. No other models to evaluate potential interaction yielded statistically significant results.

Analyses of the other possible population comparisons (including levels of cumulative dust exposure, current versus past exposure, years since first and since last exposure, year of exposure, and time of hire) did not indicate statistically significant differences in reported respiratory, skin or eye symptoms, or pulmonary function. However, the categories in most of the comparisons were determined primarily by sample size requirements. Nevertheless, sample sizes in these comparison analyses limited statistical power to detect differences. In addition, for cumulative dust exposure comparisons, there was a limited range of level of exposure with most employee exposure estimates within the category less than 10 mg-yr/m^3. In the analyses, Current Exposed were not statistically different from Past Exposed, but Ever Exposed were different from Never Exposed (*See Tables 6 and 8*).

In general, there were no significant differences in prevalence of reported operations and other non-respiratory symptoms and health conditions among employees at the four sites or among the exposure groups at each site. Reported history of operations is shown in Table 10. Ear and skeletal operations were more frequently reported in Venray compared to USA-based sites manufacturing sites. In LSBG, although reported prevalence of operations increased with increasing duration of employment (which correlates with age), the rates, nevertheless, remained consistent with those in the other sites. This trend was also evident in LSBG for history of other health conditions and non-respiratory symptoms. As shown in Table 11, compared to the other sites, LSBG employees more frequently reported history of hearing loss, disc or other back problem, and knee problems. History of anemia was commonly reported by female employees at all sites. For a few conditions, reported prevalence was slightly higher compared to national rates. These included hypertension (Netherlands 7.5% : Venray 17.9%; USA 11.3% : MCO 16.2%), ulcer (USA 2.5% : MCO 6.6% / OKC 8.3% / LSBG 7.1%), hiatal hernia (USA 2.2% : MCO 7.9%), and thyroid problem (USA 1.2% : OKC 4.3%).[17, 18, 21]

Since 1984, 89% of Toner Exposed participants in Monroe County and OKC and 80% of Monroe County Never Exposed have undergone chest x-ray on one or more occasion. The prevalence of parenchymal and/or pleural abnormalities has been lowest among Toner Exposed (11 abnormalities in 441 chest x-rays). For the other

Monroe County exposure groups, the following ratios of abnormalities to total x-rays were seen: 47 : 382 Never Exposed; 110 : 682 Other Exposed; and 30 : 320 Salaried.

DISCUSSION

This investigation provided a broad array of information on the health of current Xerox employees and relationship to the workplace with focus on toner exposure. In general, there was no increase in prevalence of non-respiratory symptoms (except eye and skin symptoms), conditions, or operations among any of the employee groups at the four sites. Differences observed in prevalence of non-respiratory conditions between sites and/or exposure groups could be explained by known differences in national or regional prevalence rates, demographic differences (primarily age and gender), and/or probable differences in medical practice patterns or access to health care.

Prevalence rates of reported symptoms involving the respiratory system, eyes and/or skin were increased among some toner-exposed and other exposed employees. Toner Exposed and Other Exposed employees in manufacturing and customer service engineers more frequently reported work-related irritation of eyes and/or skin, and/or eye injury. Job tasks for each of these exposure groups involve working with dusts and other potential irritants.

Because cigarette smoking was associated with a marked increase, as much as eight-fold, in respiratory symptoms, statistical modeling was performed to control for this potential confounder. When toner exposed employees were compared to never exposed, this demonstrated a statistically significant association of toner exposure with a two- to three-fold increase in some respiratory symptoms and conditions varying by site. Toner Exposed employees in Venray reported the most symptoms, including chronic phlegm, wheeze with breathlessness, pulmonary disease diagnosis, and allergies. Chronic phlegm was also reported by OKC Toner Exposed, and dyspnea by Monroe County Toner Exposed. There was no increase in reported respiratory symptoms/conditions among the customer service engineers.

Cigarette smoking was also associated with adverse effects on pulmonary function, including reduction in percent predicted FEV_1 (3.27 - 4.93%) and $FEF_{25-75\%}$ (11 - 14%), both indicators of airflow obstruction, and in Monroe County an increase in proportion with percent predicted FEV_1 less than 80 (OR: 2.14). Modeling to control for cigarette smoking demonstrated an association of toner exposure with increased proportion with percent predicted FEV_1 less than 80 in Monroe County. Potential interaction between cigarette smoking and toner exposure could not be adequately addressed. On the other hand, the level of FEV_1 (versus the proportion having an abnormal level) in Monroe County employees was not shown to be related to exposure dose. Nor was there among Monroe County or Venray employees a clear pattern of effect of toner exposure on the $FEF_{25-75\%}$. The concomitant reduction of FVC, a measure of lung capacity, was unexpected and the explanation for this finding unclear.

Monroe County and Venray employees were considered to have higher exposures than those in OKC and the customer service engineers in LSBG. In the latter two groups of toner-exposed employees, there was no evidence of adverse respiratory effects. Interpretation of the LSBG data was made difficult by the diverse participant characteristics and lack of individual employee exposure information. Nevertheless, comparisons of respiratory symptom rates and lung function values were compatible

with other populations without respiratory problems. In OKC, a Never Exposed group was lacking and Monroe County controls used in the analyses. Respiratory symptoms tended to be more common in OKC Toner Exposed, but the increased risks were not generally statistically significant and dose-response relationships were not observed. Lung function values in OKC were higher than Monroe County controls but comparable to predicted values, providing no indication of adverse effects of workplace exposure.

Although interpretation of these analyses were constrained by the inadequacies of available information on toner exposure, sample size/statistical power limitations *(See Appendix 1)*, demographic diversity of the study populations, and the limitations of epidemiologic studies (reflective of the observational nature of the data), these issues were recognized and addressed to the extent possible. Biases of concern included selection bias, information bias and confounding bias.[28]

Selection bias could have arisen in the data if participants (Exposed and/or Never Exposed) were more or less likely to be "affected" (that is, have the respiratory symptoms/conditions and/or abnormal pulmonary function values) than non-participants. Selection bias was a concern among Monroe County Never Exposed because the participation rate was lowest for that exposure group. Review of the available demographic and work history information, however, did not indicate significant differences among Never Exposed participants compared to non-participants. Prevalence rates for symptoms, operations, and conditions, and pulmonary function values among Never Exposed participants compared to other published population data and predicted values, in general, did not suggest selection bias. Similarly among toner-exposed, for whom participant rates were highest, available information did not indicate significant differences among participants and non-participants.

The question of "healthy worker" effect, that is, whether "affected" employees had left employment such that "non-affected" remained in the current workforce, could not be addressed because sickness absence/disability information was not available. If this had involved the exposed groups, the resulting bias would have led to underestimation of effect. Of note, fewer toner-exposed employees compared to the other exposure groups had been employed more than 20 years or were over age 50 years. Similarly, although not statistically significant, the proportion of Toner Exposed in Monroe County with percent predicted FEV_1 less than 80 was lower among those with earliest year of exposure (before 1975), those with longest period since first exposure (>10 years), those with longest period since last exposure (>6 years), and those not currently exposed. This could mean "affected" had left employment, that more recent employees working in toner were more likely to report symptoms and/or have lower pulmonary function testing results, or to reflect limitations created by low participation rates, sample size and statistical power.

Information bias was minimized through careful standardization of data collection. However, the toner exposure estimates undoubtedly misclassified exposures of workers to toner, particularly by exposure level, due to the limited industrial hygiene data available and also differences in individual work habits and use of personal protective gear. This could weaken the dose-response relationship.

Predicted values for pulmonary function parameters were derived from standardized prediction equations and adjustments were made for different racial groups. As was described earlier, there were significant demographic differences among the study populations by site and by exposure group. It is possible these

adjustments, using generally accepted methods, may not be satisfactory. This could create artifactual differences between study groups of different racial composition.

A possible data quality issue was the rate of successful pulmonary function test sessions (i.e. test session data meeting ATS criteria for acceptability). In a working population, typically 90 to 95% of workers can be tested successfully. The rate of testing failure in this study ranged from 3.2 - 6.3%, a reasonable result. The rate of missing tests (i.e. tests not performed) ranged among manufacturing locations from 0.4 - 3.3%. However, at Leesburg, for nearly 20% of employees, test data were missing. The testing protocol required that testing not be performed in certain circumstances. This included, for instance, when an employee had had a recent respiratory infection or at the nurse's discretion. At Leesburg, re-scheduling for testing was not possible. Analyses of the reasons for missing test data in Leesburg indicated more than half of the tests were missing due to the employees having recent respiratory infections. Another third were missing due to the nurse stopping the testing session because of the effects of hyperventilation among the participants. The latter did not appear to be associated with poor health status

The potential for confounding was addressed using appropriate multivariate techniques. If confounding variables are not included in statistical models, estimates of risk may be biased. These analyses included the major potential confounding variables, i.e. smoking, age, and socioeconomic variables. While there is the possibility that the adjustment was not sufficient, the analysis did include adjustment factors in different forms (e.g. smoking, ex-smoking and current smoking, and pack-years) to increase the likelihood of satisfactory adjustment for the factors. When this was done, similar results were obtained in the analyses.

In summary, the data presented indicate that among these Xerox employee participants representing manufacturing employees in Oklahoma City, Monroe County (Upstate New York), and Venray, Netherlands, and customer service engineers based in the United States, in general, health status is typical of a healthy workforce. Among Toner Exposed and Other Exposed in manufacturing, some respiratory symptoms/conditions were reported more frequently than among Never Exposed. Similarly, symptoms of irritation/injury involving the eyes and/or skin were reported more frequently by Toner Exposed and Other Exposed and by customer service engineers. Job tasks for each of these employee groups involve working with dusts and other potential irritants (e.g. solvents, acids, and metals) which could be expected to produce symptoms of eye and skin irritation. Pulmonary function testing results for OKC Toner Exposed and LSBG customer service engineers were comparable to non-exposed populations. There was an increase in proportion with percent predicted FEV_1 less than 80 among Monroe County Toner Exposed, and a reduction in percent predicted FVC among Monroe County and Venray Toner Exposed. These results, however, could have been influenced by a number of factors including participation rates resulting in low statistical power, as well as potential biases described in this report. To clarify whether these findings are due to toner or other workplace exposure, further investigation is needed. Medical surveillance should be continued on a periodic basis.

RECOMMENDATIONS

- To further understanding of the 1992 - 93 program findings.

  - Although earlier cross-sectional analyses had indicated increased respiratory symptoms in some toner-exposed employees, there was no clear evidence in those analyses of reduced pulmonary function testing results. The PHP/PGP/EHAP programs will be offered in each of the four locations in 1995 to add to understanding of the recent findings. As in this investigation, the stringent requirements for equipment, training, testing procedures, and other data collection/entry methods must be maintained and monitored to ensure the quality of data collected. Efforts must be made to improve participation rates to reduce any selection bias and to increase the statistical power to detect differences.

  - As a secondary method, data collected since the 1992 - 93 programs should be analyzed (including 1993 LSBG and OKC data, and 1994 Monroe County data). It should be noted, participation in Monroe County was lower in 1994 than in the 1992- 93 program.

  - Adjust study design as indicated by validation data.

- To ensure control of dust exposure in manufacturing plants.

  - As a result of animal inhalation studies, Xerox lowered the exposure limits for toner dusts in manufacturing plants in 1988 to 2.5 mg/m^3 total dust and 0.4 mg/m^3 respirable dust, levels below applicable regulatory requirements. The program of periodic industrial hygiene sampling of the dust levels should be maintained. Exposures associated with job assignments involving potentially high exposures should be periodically re-evaluated to ensure appropriate use of engineering controls and/or personal protective equipment.

- To evaluate Healthy Worker Effect.

  - Update Xerox mortality study. The previous cohort study showed overall mortality and mortality by specific cause, in general, was lower than expected. However, the average follow-up was less than 15 years. Average age at entry into the study cohort was under 30 years of age. Update of the study at this time would increase the latency period to 23 years increasing the possibility of detecting potential workplace effects.

- To provide pulmonary evaluation for employees with low percent predicted (less than 80%) or failed pulmonary function testing.

  - Program established in Monroe County with Mark Utell, M.D., Strong Memorial Hospital, Pulmonary Medicine Department. Among 44 current employees offered the evaluation, only 9 chose to participate.

  - Program being established in Venray by Jos Valks, M.D.

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TABLE 1. MONROE COUNTY, OKLAHOMA CITY (OKC), LEESBURG (LSBG), AND VENRAY EMPLOYEE PARTICIPANTS (= Part) AND NON-PARTICIPANTS (= Non)

	MONROE COUNTY			OKC			LSBG	VENRAY		
	ALL[1]	Part	Non[1]	ALL	Part	Non	Part	ALL	Part	Non
# Employees	5274	2158	3116	371	253	118	1260	1272	884	388
% Participation	41			68			76[2]	69		
# Toner Exposed	549	324	225	259	174	85	1260	*	82	*
% Participation	59			67			76[2]	69[3]		
Male (%)	75	79	72	69	70	67	96	91	94	83
Black (%)	15.3	12.5	17.3	10.8	9.9	12.7	9	*	0.9	*
Asian (%)	0.9	0.8	0.8	4.6	5.5	2.5	4	*	4.6	*
Native Amer (%)	0.6	0.6	0.7	5.4	5.5	5.1	0	*	0	*
Hispanic (%)	2.7	2.3	3.0	5.1	5.1	5.1	5	*	0	*
Ave. Age (Yrs)	42.5	44.2	41.4	37.6	37.2	38.5	41	38.7	38.6	39
Ave. Yrs Employed	14.5	16.5	13.2	7.2	7.3	7	16	14.5	14.6	14.3

[1]Denominator does not include Salaried non-participants.
[2]Rate for those eligible to participate.
[3]Site's estimate of participation rate.

*Data not available.

TABLE 2. TONER-EXPOSED EMPLOYEE PARTICIPANTS (= Part) AND NON-PARTICIPANTS (= Non) IN MONROE COUNTY, OKLAHOMA CITY (OKC), LEESBURG (LSBG), AND VENRAY

	MONROE COUNTY			OKC			LSBG	VENRAY		
	ALL[1]	Part	Non[1]	ALL	Part	Non	Part	ALL	Part	Non
# Toner Exp.	549	324	225	259	174	85	1260	*	82	*
% Current Exp.	45	55	31	47	46	48	100	*	68	*
Exposure (Yrs)	3.2	3.3	3	3.8	3.9	3.5	16	*	7.2	*
Yrs since 1st Exp.	9 6	9.6	9.6	6.5	6.8	5.8	16	*	*	*
Yrs since last Exp.	4.5	4	5.2	2.4	2.6	2	0	*	*	*
Cumulative Exp. (mg-yr/m^3)	6.8	6.7	7	3.3	3.5	2.9	*	*	*	*
# in Cum. Exp. Group (mg-yr/m^3):										
<1	229	115	114	103	64	39	*	*	*	*
$\geq 1 - <10$	234	152	82	139	99	40	*	*	*	*
≥ 10	86	57	29	17	11	6	*	*	*	*
Ave. Yr Employed	15.3	15.3	15.3	6.7	7.0	6.1	16	*	12.8	*
Ave. Age (Yrs)	41.8	41.9	41.7	36.8	36.4	37.7	41	*	38.3	*
Black (%)	25	28.7	19.6	10.8	9.2	14.1	9	*	3.7	*

[1]Denominator does not include Salaried non-participants.

*Data not available.

TABLE 3. CHARACTERISTICS OF PARTICIPANTS BY EXPOSURE GROUP IN MONROE COUNTY (MCO), OKLAHOMA CITY (OKC), LEESBURG (LSBG), AND VENRAY (VEN)

	TONER EXPOSED				OTHER EXPOSED			NEVER EXPOSED		SALARIED	
	MCO	OKC	VEN	LSBG	MCO	OKC	VEN	MCO	VEN	MCO	OKC
# Employees	324	174	82	1260	844	17	346	475	456	515	62
Male (%)	78	70	100	96	84	82	99	70	89	79	68
Black (%)	29	9	4	9	11	12	1	10	0	8	11
Asian (%)	0	5	7	4	1	6	4	1	5	1	8
Nat. Amer. (%)	0	6	0	0	0	12	0	1	0	0	2
Age in Yrs (Mean)	42	36	38	41	45	42	40	45	38	43	38
<30 (%)	15	15	18	8	8	6	16	16	26	16	23
30 - <40 (%)	25	58	43	29	18	47	31	16	32	22	35
40 - <50 (%)	41	22	28	49	40	29	39	30	29	32	29
≥50 (%)	19	5	11	14	34	18	14	38	13	30	13
Yrs Employed (Mean)	15	7	3	16	18	6	16	16	14	17	8
<10 (%)	30	81	30	21	25	88	18	39	33	35	69
10 - <20 (%)	35	19	60	50	22	0	51	11	47	22	20
≥20 (%)	35	0	10	29	53	12	31	50	20	43	11
Education Level (%):											
≤High School	73	60	N/A	24	69	65	N/A	69	N/A	12	2
Some College	25	40	N/A	75	30	35	N/A	31	N/A	87	98
Current Smoker (%)	34	46	53	22	29	41	41	28	39	16	21
Pack Yrs. (Mean)	21	21	15	24	26	22	17	25	14	24	26
Ex-Smoker (%)	28	17	24	34	38	12	33	35	28	35	36
Pack Yrs. (Mean)	20	16	16	15	18	12	12	19	12	17	17
Never Smoker (%)	38	37	23	44	33	47	26	37	33	49	43

TABLE 4. RESPIRATORY SYMPTOM* PREVALENCE (%) AMONG PARTICIPANTS BY SITE AND EXPOSURE GROUP

SITE: Exposure Group	N	Chronic Cough	Chronic Phlegm	Persistent Wheeze	Wheeze + Breathless	Dyspnea	Pulmonary Disease DX
MONROE COUNTY:							
-Toner Exp	324	6.8	10.2	17.0	6.5	6.5	8.0
-Other Exp	844	7.7	10.2	16.1	8.3	2.4	10.1
-Never Exp	475	6.1	9.7	15.0	7.4	3.4	9.9
-Salaried	515	8.0	7.6	12.8	9.1	3.7	10.7
OKLAHOMA CITY:							
-Toner Exp	174	11.5	13.8	19.5	9.2	4.0	16.1
-Other Exp	17	0	5.9	25.0	0	5.9	17.6
-Salaried	62	6.5	1.6	14.5	8.1	1.6	6.5
VENRAY:							
-Toner Exp	82	8.5	17.1	15.9	14.6	4.9	17.1
-Other Exp	346	6.1	7.2	14.7	9.2	4.3	6.1
-Never Exp	456	5.5	6.4	7.5	5.9	3.9	5.7
LEESBURG:	1260	7.6	9.1	13.7	7.9	2.6	9.9
Yrs Employed							
<10	260	8.1	12.7	16.6	10.4	3.5	11.2
10 - <20	631	6.3	8.4	13.3	7.8	2.2	9.2
20 +	369	9.5	7.9	12.2	6.2	2.7	10.3

*SYMPTOM:
- Chronic Cough = "Yes" to questions 82, 84 or 85, AND to 86
- Chronic Phlegm = "Yes" to questions 88, 90 or 91, AND to 92
- Persistent Wheeze = "Yes" to question 97 OR 98
- Wheeze + Breathless = "Yes" to question 100 AND 102 or 103
- Dyspnea = "Yes" to any of questions 106 - 109
- Pulmonary Disease DX (Diagnosis) = "Yes" to any of 124 (chronic bronchitis), 128 (emphysema/COPD), 132 (asthma), or 136 (CARA - Venray questionnaire)

TABLE 5. PREVALENCE (%) OF SPECIFIC SYMPTOMS/CONDITIONS AMONG PARTICIPANTS BY SITE AND EXPOSURE GROUP

SITE: Exposure Group	Work-Related Irritation of: Skin	Eyes	Operation on: Skin	Eyes	Hives	Eye Injury	Migraine, Tension Headache	Sinus Problems	Allergies
MONROE COUNTY:									
-Toner	11.4	9.6	2.2	4.6	6.2	6.5	10.2	29.2	19.4
-Other Exp	7.7	7.8	1.3	3.1	9.4	7.2	10.2	31.5	19.6
-Never Exp	6.1	2.7	1.5	4.0	7.4	3.6	12.0	30.4	17.7
-Salaried	4.1	4.1	4.7	5.4	7.0	5.4	13.0	30.0	26.2
OKLAHOMA CITY:									
-Toner Exp	5.8	7.5	2.3	2.9	6.4	10.9	12.6	43.4	15.5
-Other Exp	5.9	5.9	0	0	0	5.9	5.9	41.2	11.8
-Salaried	1.6	4.8	6.5	6.5	8.1	4.8	14.8	40.3	25.8
VENRAY:									
-Toner Exp	11.0	7.3	0	7.3	1.2	11.0	9.8	6.1	20.7
-Other Exp	9.6	10.1	2.0	5.2	0.9	11.6	13.9	4.0	16.8
-Never Exp	6.6	4.4	1.1	4.2	1.8	7.7	12.9	4.4	12.3
LEESBURG:	7.3	8.7	2.9	3.8	7.0	7.4	10.6	35.3	18.6
Yrs Employed									
<10	6.2	8.5	0.8	3.8	6.6	7.3	13.8	32.8	20.4
10 - <20	7.4	7.1	2.5	3.6	6.5	8.2	9.4	36.6	19.8
20 +	7.9	11.7	4.9	4.1	8.2	6.0	10.6	35.0	15.2

TABLE 6. ODDS RATIOS[1] FOR SPECIFIC SYMPTOM/CONDITION PREVALENCE IN TONER EXPOSED COMPARED TO NEVER EXPOSED PARTICIPANTS IN MONROE COUNTY (MCO), OKLAHOMA CITY (OKC) AND VENRAY (VEN)

		Ever Toner vs Never Exposed			Current Toner vs Never Exposed		
	Parameter	OKC[2]	MCO	VEN[3]	OKC[2]	MCO	VEN[3]
Chronic Cough	SmkCur	3.54*	3.56*	5.22*	3.80*	2.85*	b
	SmkEx	1.22	1.18	0.29	1.33	0.98	b
	ExpTon	1.65	0.85	1.28	1.95	0.84	b
Chronic Phlegm	SmkCur	8.15*	6.25*	2.54*	8.29*	6.96*	2.67*
	SmkEx	2.37	1.88	0.70	2.80*	2.22	0.67
	ExpTon	1.30	0.94	2.78*	2.04*	1.15	2.22[c]
Persistent Wheeze	SmkCur	2.84*	3.39*	7.70*	3.05*	3.39*	7.41*
	SmkEx	0.79	1.16	2.09	0.74	0.99	1.84
	ExpTon	1.08	1.01	1.78	1.17	0.94	1.83
Wheeze + Breathless	SmkCur	1.67	1.52	2.01	1.51	1.64	1.92
	SmkEx	0.74	1.42	1.31	0.72	1.08	1.20
	ExpTon	1.17	0.83	2.32*	1.11	0.88	2.61*
Dyspnea	SmkCur	1.41	1.59	1.39	1.74	1.43	1.83
	SmkEx	2.69	2.14	0.58	4.26*	2.25	0.48
	ExpTon	1.29	2.15*	1.21	1.09	2.12	0.83
Pulmonary Disease DX	SmkCur	1.07	1.10	1.32	0.83	1.14	1.18
	SmkEx	0.76	1.29	1.72	0.51	0.95	1.35
	ExpTon	1.66	0.67	3.14*	1.70	0.52	2.56*

NOTE: TABLE 6 continues on next page.

TABLE 6. (Contd) ODDS RATIOS[1] FOR SPECIFIC SYMPTOM/CONDITION PREVALENCE IN TONER EXPOSED COMPARED TO NEVER EXPOSED PARTICIPANTS IN MONROE COUNTY (MCO), OKLAHOMA CITY (OKC) AND VENRAY (VEN)

		Ever Toner vs Never Exposed			Current Toner vs Never Exposed		
	Parameter	OKC[2]	MCO	VEN[3]	OKC[2]	MCO	VEN[3]
Skin Irritation, Work-related	SmkCur	1.13	1.17	a	1.01	1.00	a
	SmkEx	0.81	1.17	a	0.78	0.94	a
	ExpTon	0.91	1.68[d]	a	0.58	1.47	a
Eye Irritation, Work-related	SmkCur	0.94	0.61	a	0.87	0.80	a
	SmkEx	1.03	1.11	a	1.04	1.12	a
	ExpTon	2.97*	3.18*	a	4.83*	3.54*	a
Allergies	SmkCur	a	a	1.25	a	a	1.28
	SmkEx	a	a	1.19	a	a	1.31
	ExpTon	a	a	1.76	a	a	2.25*

[1]Logistic regression model 1 included variables for smoking history and toner exposure.
[2]Compared to MCO Never Exposed.
[3]Analyses include males only.

*Statistically significant at $p<0.05$.

[a]Fisher's exact test not significant; modeling not done.
[b]Solution could not be reached.
[c]Statistically significant in model II (included additional variables: age, education and pack-years); OR = 2.75.
[d]Statistically significant in model IV (variables = gender, age, race, education, and current toner exposure); OR = 2.00.

TABLE 7. PULMONARY FUNCTION TEST RESULTS AMONG PARTICIPANTS BY SITE AND EXPOSURE GROUP

SITE: Exposure Group	# Valid Tests[2]	% PREDICTED[1]: FEV_1 (Mean)	FEV_1 LT 80 (%)	FVC (Mean)	FVC LT 80 (%)	$FEF_{25-75\%}$ (Mean)
MONROE COUNTY:						
-Toner Exp	281	96.7	13.9	102.7	2.8	84.6
-Other Exp	757	98.2	8.1	104.9	3.3	83.1
-Never Exp	401	98.7	7.5	105.3	2.5	83.9
-Salaried	442	100.3	7.7	106.4	0.2	86.2
OKLAHOMA CITY:						
-Toner Exp	165	101.7	4.8	108.6	0.6	86.6
-Other Exp	17	101.2	5.9	107.4	0	89.4
-Salaried	56	104.0	3.6	110.2	1.8	92.5
VENRAY:						
-Toner Exp	76	103.1	9.2	107.4	3.9	89.8
-Other Exp	301	104.7	3.0	111.4	0	84.9
-Never Exp	398	103.7	4.5	110.4	0.8	85.0
LEESBURG:	958	100.4	5.6	108.1	1.5	83.5
Yrs Employed						
<10	197	98.3	7.6	104.3	2.5	86.1
10 - <20	481	101.7	4.2	108.7	1.0	86.1
20 +	280	99.8	6.8	109.8	1.4	77.0

[1]% Predicted values for USA populations based on Knudson 1983 equations; Venray based on European Standardized Equations.
[2]Valid Test = Meets ATS criteria for acceptability and reproducibility; excludes tests of employees <25 yrs of age.

TABLE 8. ODDS RATIOS[1] AND PARAMETER ESTIMATES (EST)[2] FOR PULMONARY FUNCTION IN TONER EXPOSED COMPARED TO NEVER EXPOSED PARTICIPANTS IN MONROE COUNTY (MCO), OKLAHOMA CITY (OKC) AND VENRAY (VEN)

		Ever Toner vs Never Exposed			Current Toner vs Never Exposed		
	Parameter	OKC[3]	MCO	VEN[4]	OKC[3]	MCO	VEN[4]
% Predicted FEV_1 (EST)	SmkCur	- 3.27*	- 4.23*	- 4.75*	- 2.94	- 3.61*	- 4.93*
	SmkEx	- 1.48	- 0.88	1.61	- 0.97	- 0.63	1.48
	ExpTon	3.25*	- 1.51	0.01	2.68	- 2.13	1.06
% Predicted FEV_1 LT 80 (Odds Ratio)	SmkCur	0.48	2.14*	1.48	0.54	1.99	1.81
	SmkEx	0.58	1.51	0.61	0.53	1.91	0.74
	ExpTon	1.61	1.78*	1.85	1.79	2.39*	2.29
% Predicted FVC (EST)	SmkCur	1.20	- 0.26	0.10	0.89	0.64	- 0.09
	SmkEx	1.84	2.40	4.47*	2.30	2.36	4.27*
	ExpTon	3.62*	- 2.22*	- 2.81[a]	2.28	- 3.52*	- 1.32
% Predicted FVC LT 80 (Odds Ratio)	SmkCur	0.32	2.80	0.43	[b]	2.51	0.72
	SmkEx	3.06	0.21	0.35	[b]	0.26	0.56
	ExpTon	5.89	0.80	5.22*	[b]	0.48	4.64
% Predicted $FEF_{25-75\%}$ (EST)	SmkCur	- 12.11*	- 12.91*	- 14.22*	- 11.31*	- 13.15*	- 14.13*
	SmkEx	- 9.77*	- 10.05*	- 5.60*	- 9.54*	- 9.01*	- 5.36
	ExpTon	2.73	1.27	6.23	5.38	3.61	6.17

[1]Logistic regression model 1 included variables for smoking history and toner exposure.
[2]Linear regression model 1 variables as in 1.
[3]Compared to MCO Never Exposed.
[4]Analyses include males only.

*Statistically significant at $p < 0.05$

[a]Exposure parameter statistically significant (- 6.279) in Model II (included additional variables: education, pack-years and current toner exposure).
[b]Solution could not be reached.

TABLE 9. ODDS RATIOS (OR) FOR PULMONARY FUNCTION IN TONER EXPOSED COMPARED TO NEVER EXPOSED BY SMOKING STATUS (CURRENT AND NEVER SMOKER) IN MONROE COUNTY

	CURRENT SMOKERS (n = 184)		NEVER SMOKERS (n = 248)	
	Number with outcome	OR for ever-toner exposed compared to never exposed (95% Confidence Interval)	Number with outcome	OR for ever-toner exposed compared to never exposed (95% Confidence Interval)
OUTCOME				
% Predicted FVC <80	10	0.86 (0.23, 3.15)	5	0.89 (0.15, 5.43)
% Predicted FEV_1 <80	25	2.6* (1.10, 6.34)	17	2.0 (0.74, 5.47)

*Statistically significant at $p<0.05$

TABLE 10. PREVALENCE (%)* OF OPERATIONS AMONG PARTICIPANTS IN MONROE COUNTY (MCO), OKLAHOMA CITY (OKC), LEESBURG (LSBG), AND VENRAY

*Rates shown for Toner Exposed and for All employees; LSBG rates for those employed 20 + years and All employees.

CONDITION	MCO Toner/All Emp.		OKC Toner/All Emp.		LSBG 20 Yr/All Emp.		VENRAY Toner/All Emp.	
Operation:								
-Brain	0	0.2	0	0	0.8	0 3	1.2	0.2
-Ear	1.2	2.1	3.4	2.8	2.4	2.3	4.9	6
-Lung	0	0.2	0	0	0	0.2	0	0.2
-Heart	1.2	0.9	1.2	1.2	1.6	0.7	0	0
-Blood Vessels	2.5	2.6	0.6	1.2	1.6	1.1	3.7	2.4
-Skeletal	13.9	16.1	17.2	15	22.5	19.4	24.4	22.1
-Digestive	8	11.3	9.8	9.5	11.1	10.7	11	9.3
-Hernia	8.6	11.5	6.3	7.9	11.7	9.6	11	7.1
-Pilonidal Cyst	2.2	3.1	2.9	2.8	4.3	2.9	N/A	N/A
-Rectum	4.9	6.3	4.6	4.4	8.7	4.5	3.7	2.8
-Urinary Tract	2.2	2.5	1.2	2.4	3.3	2.2	0	1.8
-Reproductive	20.7	25.6	27.6	24.9	29	23.4	N/A	N/A

TABLE 11. PREVALENCE (%)* OF OTHER HEALTH CONDITIONS/SYMPTOMS AMONG PARTICIPANTS IN MONROE COUNTY (MCO), OKLAHOMA CITY (OKC), LEESBURG (LSBG), AND VENRAY

*Rates shown for Toner Exposed and for All employees; LSBG rates for those employed 20 + years and All employees.

CONDITION: (Question #)	MCO Toner/All Emp.		OKC Toner/All Emp.		LSBG 20 Yr/All Emp.		VENRAY Toner/All Emp.	
Skin:								
-Non-Work-Rel. Dermatitis (#176a)	10.5	10.1	10.9	10.3	12	12.3	15.9	12.2
Eye:								
-Glaucoma (#179)	1.9	1.3	0	0	1.4	0.9	1.2	1.5
-Cataracts (#180)	1.5	1.2	0.6	1.2	1.4	1.0	0	0.5
-Double Vision (#181)	2.5	2	0.6	0.8	1.6	1.9	1.2	1.8
Hearing:								
-Hearing Loss (#187)	18.2	17.4	13.8	14.2	37.1	26.1	12.2	10.1
Neurological:								
-Loss of Balance & Dizziness (#190 + 191)	2.5	2.1	2.3	2	2.5	2.1	2.4	1.7

CONDITION: (Question #)	MCO Toner/All Emp.		OKC Toner/All Emp.		LSBG 20 Yr/All Emp.		VENRAY Toner/All Emp.	
-Weakness + Numbness of extremities (#192 + 193)	3.7	2.9	4	3.2	1.9	2	2.4	2.6
-Nerve Disease of arms or legs (#194)	1.2	0.9	0	0	1.1	1.1	2.4	2.8
-Seizures (#195)	1.5	1.1	0.6	0.4	1.1	0.8	2.4	1
-Concentration, memory, irritable (#198 - 200)	3.1	2.8	1.7	2	3	2.9	0	1.4
-Stress (#201)	6.8	9.5	7.5	8.7	13	11.4	7.3	8.4
Musculoskeletal:								
-Disc (#203)	12.4	11.6	7.5	6.7	15.8	12	13.4	10.2
-Other Back (#204)	25.2	24.7	19.1	18.3	37.6	31.3	25.6	27.8
-Knee (#205)	14.6	18.2	13.3	15.5	42.8	36.3	26.8	21.2
-Carpal Tunnel (MD Confirmed) (#206 + 207)	4.9	5.5	1.2	1.2	3.3	3	0	0.5

CONDITION: (Question #)	MCO Toner/All Emp.		OKC Toner/All Emp.		LSBG 20 Yr/All Emp.		VENRAY Toner/All Emp.	
-Arthritis (MD Confirmed) (#208 + 209)	10.2	11.3	5.8	5.6	10.9	7.9	1.2	0.5
-Bursitis/tendinitis (#210)	18.3	18.2	14	12.4	16.8	13	3.7	5.9
Circulatory:								
-Hypertension (#212)	15.5	16.2	11.5	11.5	17.4	12.9	17.1	17.9
-Stroke (#216)	0.3	0.4	0	0	0.3	0.3	0	0.1
-Heart Attack (#217)	1.9	1.7	0.6	0.4	1.1	0.6	0	0.6
-Anemia (#218)	4.6	5.9	9.2	7.5	4.1	3.3	4.9	3.7
Males	2	1.8	1.6	1.7	4.1	2.2	4.9	2.2
Females	14.3	21.3	26.9	21.3	-	38.9	-	27.8
Digestive:								
-Ulcer (Confirmed) (#220)	7.4	6.6	8.7	8.3	10.6	7.1	7.3	4.9
-Hiatal Hernia (#221)	6.2	7.9	2.3	2	8.7	4.4	0	1.6
-Colitis, etc. (#223)	1.2	1.5	1.7	1.6	2.7	1.7	0	0.9

CONDITION: (Question #)	MCO Toner/All Emp.		OKC Toner/All Emp.		LSBG 20 Yr/All Emp.		VENRAY Toner/All Emp.	
-Hepatitis (#224)	2.5	2.5	4	4	3	2.5	6.1	6
-Gall Bladder (#225)	2.2	2.7	4.6	3.6	1.4	1.1	0	0.6
Urinary Tract:								
-Kidney Stone (#228)	7.7	6.3	2.3	3.2	9.8	6.7	2.4	3.8
-Kidney Dis./Inf. (#229)	4	2.8	2.3	2.8	3.3	2.7	2.4	1.4
Reproductive:								
-Infertility (#235)	2.5	3.8	4.7	3.6	4.6	5.9		
-Miscarriage (#236)	13	12.8	14	12.8	16	13.6		
-Stillbirth (#237)	0.9	1.2	0	0.8	2.2	1.3		
-Premature (#238)	5	4.7	2.3	2	4.1	3.3		
-Death at birth (#239)	2.2	1.9	0.6	0.8	1.4	1.1		
-Birth defect (#240)	3.7	3.5	3.5	2.8	4.1	3.7		

CONDITION: (Question#)	MCO Toner/All Emp.		OKC Toner/All Emp.		LSBG 20 Yr/All Emp.		VENRAY Toner/All Emp.	
Other Medical:								
-Thyroid (#243)	1.5	2.5	4.6	4.3	2.7	2.4	1.2	0.7
-Diabetes (#244)	3.4	2.9	0	0	1.6	1.3	0	0.7
-Cancer (#247)	2.2	2.7	2.3	2.4	6	2.9	0	0.5
Excluding Skin Cancer	*1.5*	*1.7*	*2.3*	*1.6*	*1.6*	*1.2*	*0*	*0.3*

APPENDIX 1. STATISTICAL POWER AND PRECISION ASSESSMENT

A major objective of the study was to examine differences in the outcome variables percent predicted FVC and FEV_1, percent with abnormal FVC and FEV_1, and percent with various respiratory symptoms, comparing toner-exposed and non-toner-exposed groups. All of these outcomes were considered in the design of the study. At that time, it was hypothesized that the participation rates at the Monroe County site would be similar to those observed in a previous health monitoring program. These rates would have resulted in sample sizes for the toner-exposed and the never-toner-exposed groups of 465 and 698, respectively. With these sample sizes, this study would have had significant power to discern differences of 2% to 4% in percent predicted FVC and FEV_1 between the toner-exposed and never-toner-exposed workers, as shown in Table A.

TABLE A. POWER OF DESIGNED STUDY (MONROE COUNTY)

Subset of Workers	Difference (%) in % predicted FVC or FEV_1	Power (%) with sample sizes, assuming 465 in toner-exposed group and 698 in the never-toner-exposed group	Power (%) with observed sample sizes, 1992 - 93 PHP Program
All	2	85	72
Current Smokers	3	80	58
Never Smokers	4	91	86

The actual participation rate among workers was less than anticipated, with resulting samples sizes for the toner-exposed and the never-toner-exposed group of 324 and 475 respectively. This decrease of approximately 30% in the sample size reduced the power and the precision of the estimates. As shown in Table A, except for the comparison among current smokers, the reduction in power was only 5 to 7%.

From the analysis of the Monroe County 1992 - 93 PHP data, estimates and 95% confidence intervals for the differences in FVC and FEV_1 for these subgroups were obtained. These results are given in Table B. The negative values indicate that the percent predicted value was lower for the toner-exposed group. As shown in Table B, a statistically significant difference (estimate = -2.2%) was detected in percent predicted FVC comparing All toner-exposed to never-toner-exposed. Power to detect this difference was relatively high.

TABLE B. ESTIMATES OF DIFFERENCES IN PULMONARY FUNCTION BETWEEN THE TONER-EXPOSED AND NEVER-TONER-EXPOSED GROUPS

Subset of workers	Difference (%) (95% confidence intervals)			
	FVC		FEV_1	
All	- 2.20[1]	(- 4.31, - 0.13)	- 1.50[1]	(- 3.66, 0.65)
Current Smokers	- 3.93	(- 8.19, 0.32)	- 3.72	(- 8.14, 0.70)
Never Smokers	- 2.23	(- 5.53, 1.06)	- 1.15	(- 4.51, 2.20)

[1]Obtained from a model with adjustment for smoking status.

FIGURE 1

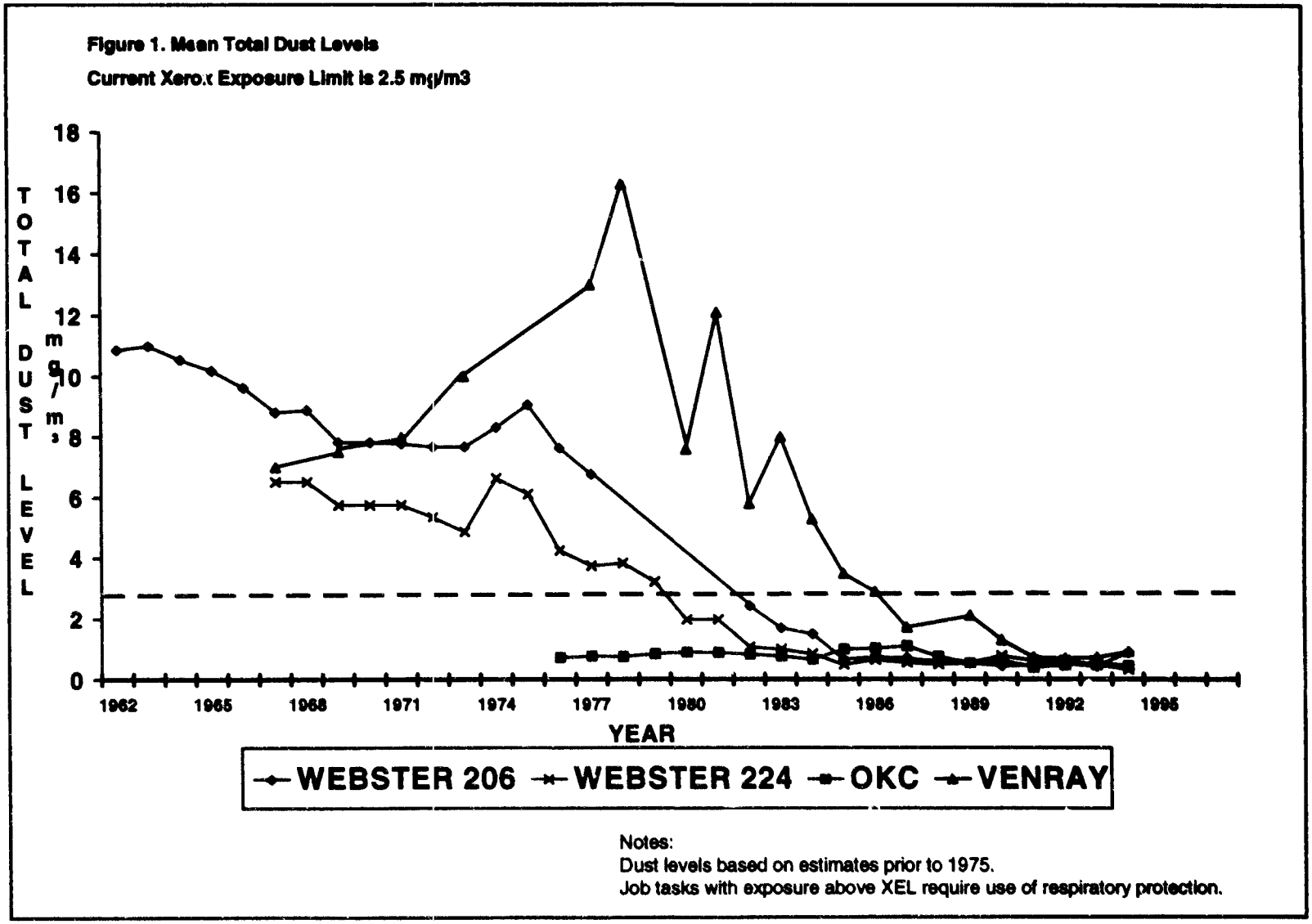
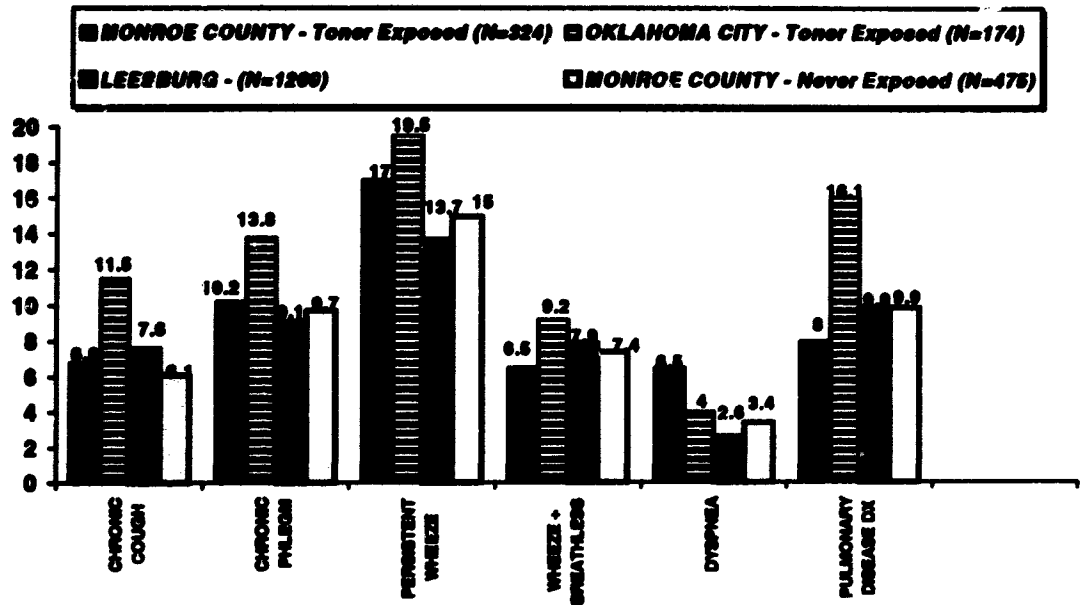


Figure 1. Mean Total Dust Levels
Current Xerox Exposure Limit is 2.5 mg/m3
TOTAL DUST LEVEL mg/m3
18
16
14
12
10
8
6
4
2
0
1962
1965
1968
1971
1974
1977
1980
1983
1986
1989
1992
1995
YEAR
WEBSTER 206
WEBSTER 224
OKC
VENRAY
Notes:
Dust levels based on estimates prior to 1975.
Job tasks with exposure above XEL require use of respiratory protection.

FIGURE 2

RESPIRATORY SYMTOM PREVALENCE (%) AMONG TONER EXPOSED AND NEVER EXPOSED

USA SITES % within each exposure group



VENRAY % within each exposure group

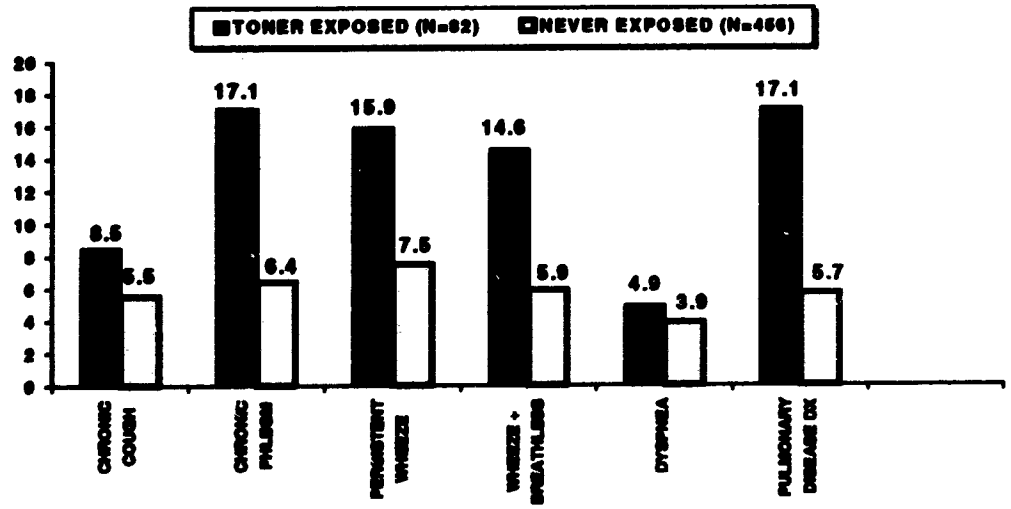
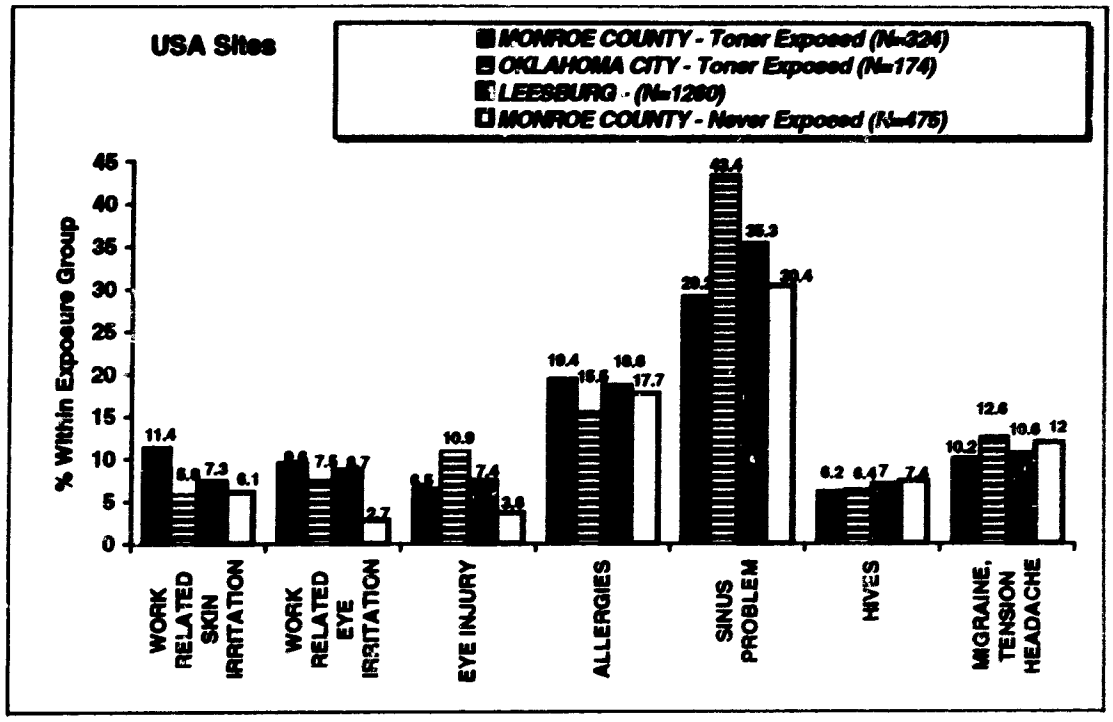


FIGURE 3. PREVALENCE (%) OF SPECIFIC SYMPTOMS/CONDITIONS AMONG TONER EXPOSED AND NEVER EXPOSED



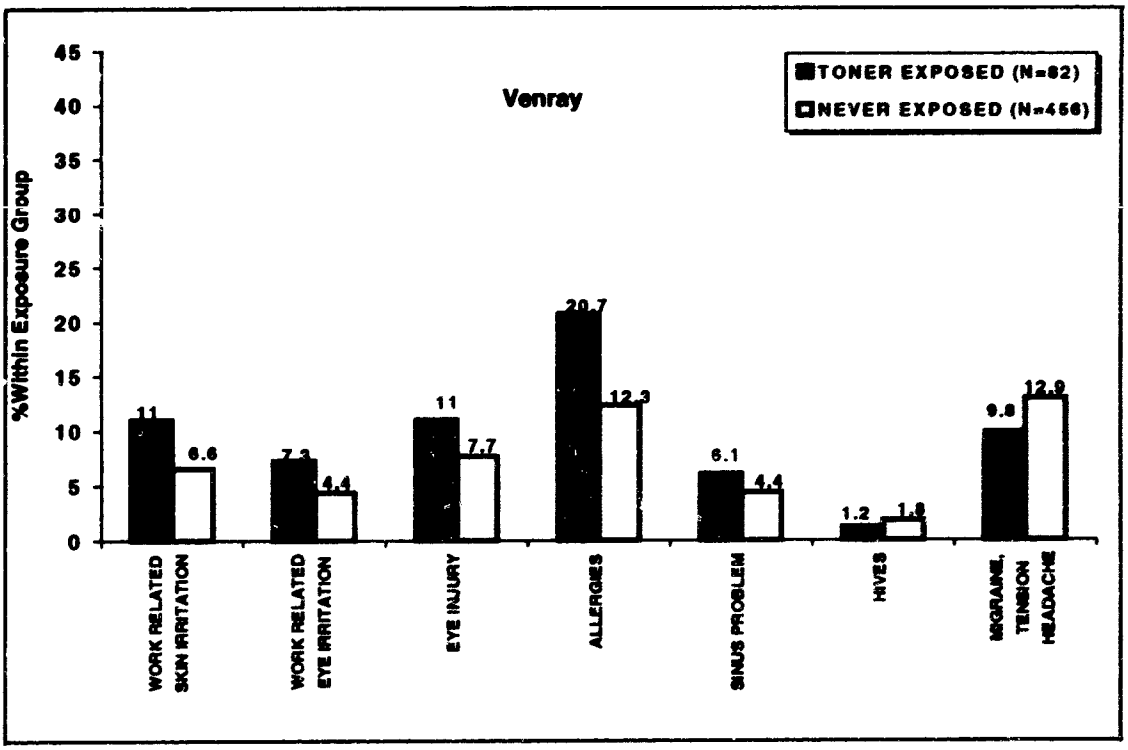


Figure 4. % Predicted Forced Expiratory Volume in 1 Second (FEV_1) in Toner Exposed and Never Exposed

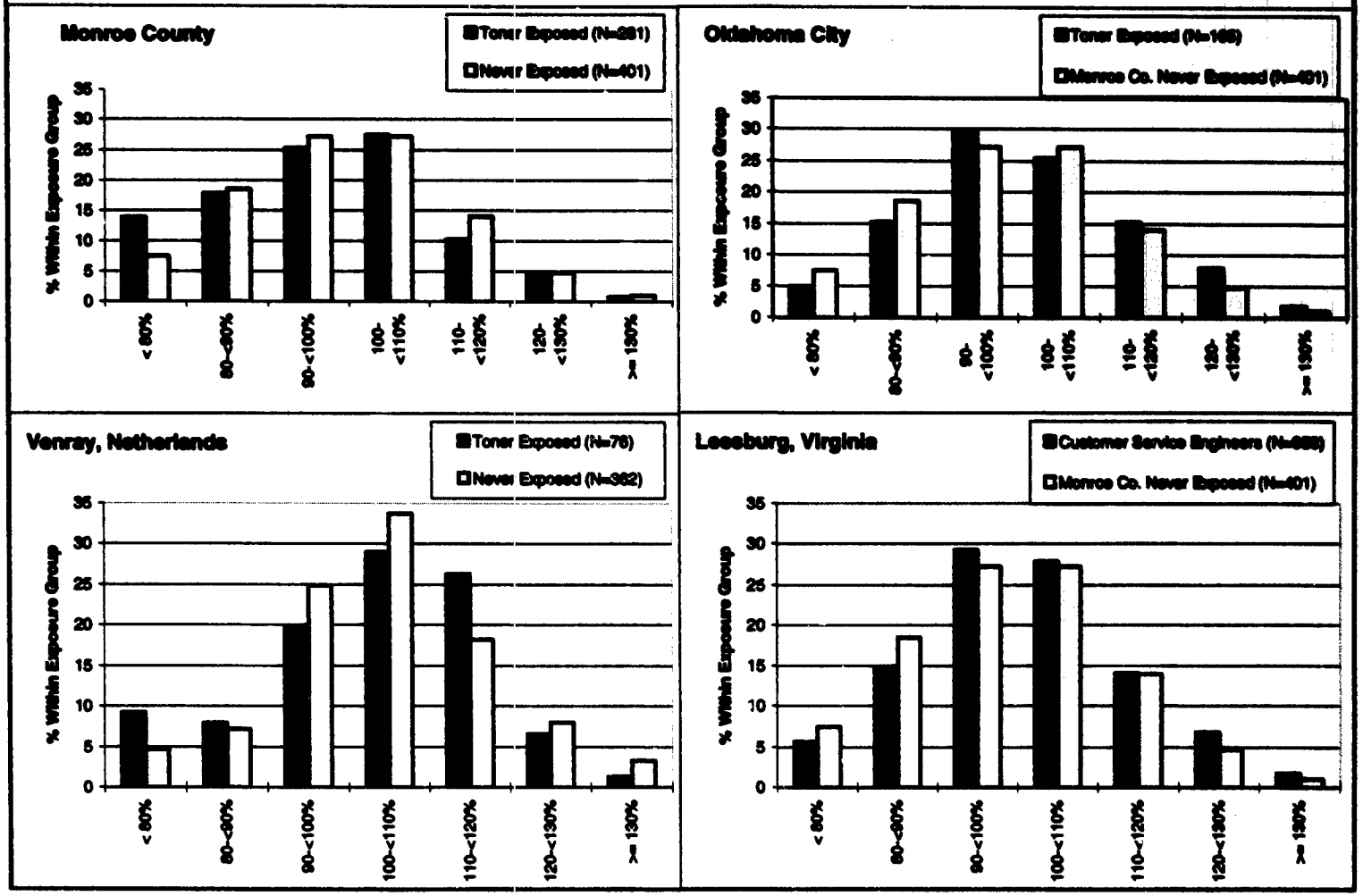


Figure 5. % Predicted Forced Vital Capacity (FVC) in Toner Exposed and Never Exposed