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October 17, 2006

8EHQ-81-394

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Attention: 8(e) Coordinator
Office of Pollution and Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Ave., NW
Washington, D.C. 20460

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Dear 8(e) Coordinator:

8EHQ-0381-0394
Ammonium Perfluorooctanoate (APFO)

This letter is to inform you of the results of a recently completed epidemiology study entitled "Ammonium Perfluorooctanoate: Phase II. Retrospective Cohort Mortality Analyses Related to a Serum Biomarker of Exposure in a Polymer Production Plant".

A copy of the final report is enclosed.

The plant site where this study was conducted comprises several businesses with a diverse range of polymer manufacturing processes, most of which do not involve the use of APFO. Approximately one-half of the employees at the site have been assigned to APFO areas at some time in their careers. As part of a large project on occupational exposure to PFOA, this study's objective is to determine whether workplace exposure to PFOA is related to increased mortality risk for any cause (Phase II).[1]

The overall project comprised two studies: Phase I, a cross-sectional surveillance that analyzed several types of clinical data (blood chemistries such as lipids, enzymes, and blood counts, among others) and a biomarker of exposure (serum PFOA) for potential relationships (to be issued in a separate report); and Phase II, a retrospective cohort study that examined site-wide standardized mortality analyses, and also utilized job history information as well as serum PFOA data to classify each member of the historical cohort by level of potential occupational exposure for a more detailed analysis of ischemic heart disease. Based on the results of the cross-sectional study, we concluded that workers in all areas across the entire plant site show some measurable level of serum PFOA (range: 0.005 ppm to 9.55 ppm).

The cohort for Phase II was defined as all individuals who have ever worked at the Washington Works plant at any time between January 1, 1948 (plant start-up) and December 31, 2002. The cohort (n = 6,027) was ascertained primarily through the DuPont Epidemiology Registries; additional members were identified from plant-based work history records.

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[1] APFO and its salts are soluble in water and readily dissociates to the perfluorooctanoate anion (PFOA). The biomarker measured in serum is the dissociated anion (PFOA).

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STUDY TITLE

Ammonium Perfluorooctanoate:
Phase II. Retrospective Cohort Mortality Analyses
Related to a Serum Biomarker of Exposure in a Polymer Production Plant

AUTHOR: Robin C. Leonard, Ph.D.

STUDY COMPLETED ON: September 15, 2006

PERFORMING LABORATORY: DuPont Epidemiology Program
DuPont Haskell Laboratory for Health and Environmental Sciences
1090 Elkton Road, Newark, DE 19714

LABORATORY PROJECT ID: DuPont-14809 (Phase II)

WORK REQUEST NUMBER: 15259

SERVICE CODE NUMBER: 1242

SPONSOR: E.I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

MR# 299531

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Good Epidemiology Practice Compliance Statement

This study was conducted according to guidance provided by the American College of Epidemiology Ethics and Standards Practice Committee which can be accessed at http://www.acepidemiology2.org/policystmts/EthicsGuide.asp.

Applicant / Sponsor: E.I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

Principal Investigator: Robin C Leonard, Ph.D. 12 October 2006
Robin C. Leonard, Ph.D. Date
Principal Research Epidemiologist

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DuPont Approval: We, the undersigned, declare that this report provides an accurate evaluation of data obtained from this study.

Approved by: A. Michael Kaplan 12 Oct. 2006

A. Michael Kaplan, Ph.D.
Director, Regulatory Affairs and Occupational Health
DuPont Haskell Laboratory for Health and
Environmental Sciences

Date

Approved by: Robert W. Rickard 12 October 2006

Robert W. Rickard, Ph.D.
Science Director
DuPont Haskell Laboratory for Health and
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Date

Approved by:

S Sax 12-Oct-06

Sol Sax, M.D.
Chief Medical Officer
E.I. du Pont de Nemours, Inc.

Date

Issued by Principal Investigator: Robin C. Leonard, Ph.D. 12 October 2006

Robin C. Leonard, Ph.D.
DuPont Haskell Laboratory for Health and
Environmental Sciences

Date

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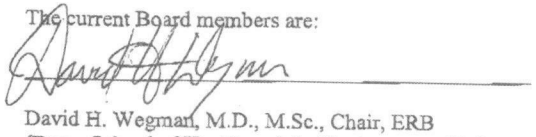
Epidemiology Review Board

The DuPont Epidemiology Program retains an external advisory Board, the Epidemiology Review Board (ERB), which is comprised of academic experts in the areas of occupational epidemiology, biostatistics, biomedical ethics, and occupational medicine. The objectives of the ERB are to enhance the quality, integrity, and acceptability of epidemiologic research activities sponsored by the DuPont Company. The ERB members have reviewed this study, and reached consensus that the research is relevant, ethical, technically sound, and that the conclusions arise appropriately from the data and analyses.

The current Board members are:



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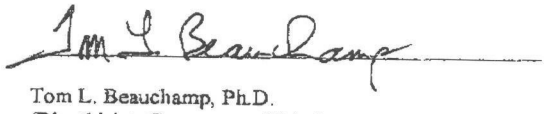
David H. Wegman, M.D., M.Sc., Chair, ERB
(Dean, School of Health and the Environment, Univ. of Mass. Lowell)



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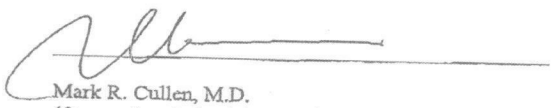

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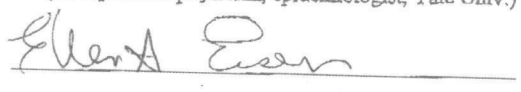

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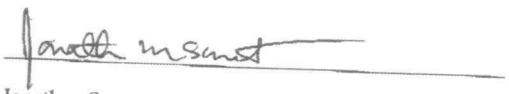

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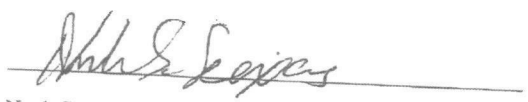
Jonathan Samet, M.D., M.S.
(Chair, Dept. of Epidemiology, Johns Hopkins Bloomberg School of Public Health)



9/28/06
Date

Noah S. Seixas, Ph.D., C.I.H.
(Industrial hygienist, epidemiologist, Univ. of Washington)

Each ERB member was asked to sign off on this report using their own separate signature page, and then to fax their signature to the DuPont Epidemiology Department. Once received by the DuPont Epidemiology department, each fax was then scanned into the computer system as jpeg files. The jpeg files were then cropped to display only the signature. Each cropped image was then inserted into this page, using Microsoft Word. The original faxes will be retained in the DuPont archives.

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Abbreviations and Symbols

AIC	Akaike Information Criterion, a partial likelihood test statistic
APFO	Ammonium perfluorooctanoate
BMI	Body mass index
CI	Confidence interval
CPHM	Cox proportional hazards model
CSHS	Cross-sectional health survey
FLAIR	Fluoropolymers Laboratory Analysis Information Retrieval
GI	Gastrointestinal
HDL	High-density lipoprotein
HWE	Healthy worker effect
HWSE	Healthy worker survivor effect
IHD	Ischemic heart disease
LDL	Low-density lipoprotein
MRR	Mortality rate ratio
NDI	National Death Index (USA)
OCMAP	Occupational Mortality Analysis Program® (University of Pittsburgh)
PFOA	Perfluorooctanoic acid
PPE	Personal protective equipment
PPM	Parts per million
PPM-Years	Parts per million per year, accumulated
SMR	Standardized mortality ratio
VLDL	Very low-density lipoprotein

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Executive Summary

Ammonium perfluorooctaonate (APFO) is the ammonium salt of the fully fluorinated, 8-carbon carboxylic acid. APFO is used to aid in the emulsion polymerization of fluoropolymers. APFO and its salts are soluble in water and readily dissociate to the perfluorooctanoate anion (PFOA). APFO is a surfactant that enables the fluoropolymer components to remain emulsified during polymerization and is not incorporated into the polymer itself. It is the ammonium salt (APFO) to which workers may be exposed; the biomarker measured in serum is the dissociated anion (PFOA).

As a result of the presence and biopersistence of PFOA in the blood of humans, the potential health effects of the chemical have been examined, primarily in occupational cohorts. The plant site where this study was conducted comprises several businesses with a diverse range of polymer manufacturing processes, most of which do not involve the use of APFO. Approximately one-half of the employees at the site have been assigned to APFO areas at some time in their careers. As part of a large project on occupational exposure to PFOA, this study's objective is to determine whether workplace exposure to PFOA is related to increased mortality risk for any cause (Phase II).

The overall project comprised two studies: Phase I, a cross-sectional surveillance that analyzed several types of clinical data (blood chemistries such as lipids, enzymes, and blood counts, among others) and a biomarker of exposure (serum PFOA) for potential relationships (to be issued in a separate report); and Phase II, a retrospective cohort study that examined site-wide standardized mortality analyses, and also utilized job history information as well as serum PFOA data to classify each member of the historical cohort by level of potential occupational exposure for a more detailed analysis of ischemic heart disease. Based on the results of the cross-sectional study, we concluded that workers in all areas across the entire plant site show some measurable level of serum PFOA (range: 0.005 ppm to 9.55 ppm).

The cohort for Phase II was defined as all individuals who have ever worked at the Washington Works plant at any time between January 1, 1948 (plant start-up) and December 31, 2002. The cohort (n = 6,027) was ascertained primarily through the DuPont Epidemiology Registries; additional members were identified from plant-based work history records.

Standardized mortality ratios were calculated for the study cohort for all causes of death, death from all cancers combined, and disease-specific causes of death by comparing the cohort to rates for three reference populations: the general population of the U.S.A., the West Virginia general population, and the population of DuPont workers residing in West Virginia and seven neighboring states in the region (DuPont Region 1). In addition, Cox proportional hazards models provided an internal comparison based on exposure categories of serum PFOA for mortality due to ischemic heart disease.

Mortality rates at this site are generally well within expected values and support the presence of a healthy worker effect. Analyses specific to PFOA categories were conducted for ischemic heart disease mortality. The analyses based on average intensity of exposure showed no relationship to PFOA exposure levels. The analyses based on cumulative exposure indicated an increasing trend for the mortality rate ratio with increasing exposure category if those categories were based

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on the distribution of case exposures, but not if those categories were based on the distribution of exposures in the entire cohort. In no case were the mortality rate ratio estimates statistically significant.

Prostate cancer and cerebrovascular disease, both reported as increased in previous 3M Company occupational epidemiology reports [1,2], were reduced in this cohort against all reference populations, cerebrovascular disease significantly so for the U.S.A. and West Virginia populations. The few cases of each of these causes of death did not allow meaningful internal comparisons.

Comparisons using DuPont Region 1 reference rates, but not U.S.A. or West Virginia rates, do indicate statistically non-significant elevations in SMRs for kidney cancer mortality (SMR=185; 95% CI=95—323, $p>0.05$), and a statistically significant increase in diabetes mortality (SMR=197; 95% CI=123—298, $p<0.05$) in males and females combined at this plant site. While few kidney cancer cases had been employed in APFO areas, the data from this study are inadequate for examining in appropriate detail rare outcomes such as kidney cancer. Similarly, the difficulties in examining mortality for diabetes prevent drawing conclusions based on these data.

The results reported here show no convincing evidence of increased mortality risk associated with APFO exposure for workers at this plant. These results do show statistically non-significant elevations in relative risk for kidney cancer and a statistically significant increase in diabetes mortality for workers at this site. However, given the size and length of follow-up of the study population, the evidence to thoroughly examine mortality events like kidney cancer or even diabetes, may not be adequate. Proportional hazards analyses for ischemic heart disease mortality showed an increase in the model based on equal distribution of cases across cumulative exposure categories in one lagged analysis (the 10-year lag period). Other exposure lags showed no effect, and results for a second set of models using a different set of exposure cutpoints were attenuated toward the null. None of the hazard estimates themselves were statistically significant. Thus the positive finding in the proportional hazard analysis, as well as the increased diabetes mortality, might be due to chance. Because of the complexity of the exposure assessment and limited power for some analyses, additional investigations are needed.

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Ammonium Perfluorooctanoate: Phase II. Retrospective Cohort Mortality Analyses Related to a Serum Biomarker of Exposure in a Polymer Production Plant

Introduction

Ammonium perfluorooctanoate (APFO) is the ammonium salt of a fully fluorinated carboxylic acid, perfluorooctanoic acid (PFOA). APFO is used to aid in the emulsion polymerization of fluoropolymers. The salts of PFOA are soluble in water and readily dissociate to the carboxylate anion (PFOA). APFO is a process additive, i.e., it is the surfactant that enables the fluoropolymer components to remain emulsified in order for polymerization to occur. Neither APFO nor PFOA is incorporated into the fluoropolymer.

As a result of industrial use of APFO and biopersistence of PFOA in the blood of humans, the potential health effects of APFO have been examined in multiple studies, primarily in occupational cohorts [1-7]. A study of community exposure to PFOA was conducted to determine the relationships between serum concentrations and exposure sources, and also to examine the relationships between PFOA and hematologic and biochemical clinical markers. This community study indicated that water, not air, was the likely source of exposure; no associations were seen with adverse health effects [8-9]. Some general population samples have been used to examine biomonitoring data that indicated that age, gender, and possible duration of exposure had little to do with the background levels in the population. [10-12].

A retrospective cohort mortality study was conducted at a 3M plant in Cottage Grove, Minnesota, that produced APFO [1]. The cohort consisted of 3,537 workers employed for at least six months between January 1947 and December 1983. Follow-up was nearly complete (99.5%) for the study participants, and 398 deaths were recorded. Since APFO production was limited to the Chemical Division, the two exposure categories were "exposed" (worked at least one month in the Chemical Division) and "not exposed" (worked one month or less in the Chemical Division).

Standardized mortality ratios (SMRs) were calculated comparing the Cottage Grove cohort with mortality rates for the populations of the U.S.A. and the state of Minnesota, using stratification for duration of employment and 3 exposure latency periods. When exposure status was taken into account, most SMRs were significantly lower than the expected rate, a not surprising finding, considering the potential for healthy worker bias. The SMR for prostate cancer was elevated in the Chemical Division (area of APFO production), but this increase was not statistically significant as it was based on only four cases. Internal comparisons were performed using proportional hazards modeling for various categories of causes of death, including prostate cancer. The only mortality rate ratio that was statistically significantly greater than 1.0 was for the association between prostate cancer and duration of work in the Chemical Division. However, given that there were only four cases in the Chemical Division and an additional two cases in the rest of the cohort, it is difficult to emphasize this finding.

This study was updated through 1997; the updated cohort consisted of 3,992 workers who had worked for at least one year at the Cottage Grove Plant. [2] The exposure categories were changed to comprise three groups: "definite" (based on tasks performed in the Chemical Division); "probable" (tasks involving transient, lower exposures); and "non-exposed" (primarily non-Chemical Division jobs). A few SMRs were elevated: cancer of the prostate (N=1;

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SMR=1.30, 95% CI: 0.03—7.20); pancreatic cancer (N=1; SMR=1.34, 95% CI: 0.03—7.42); and cerebrovascular disease (N=5; SMR=2.58, 95% CI: 0.84—6.03); but none were statistically significant, and all elevated SMRs were based on very few cases.

The DuPont Epidemiology Program conducted a cross-sectional health survey (Phase I) of 1,025 employees at the Washington Works, West Virginia polymer production facility. That investigation used epidemiologic and statistical analyses of several types of clinical data and a biomarker of exposure (serum PFOA) to determine the presence of any association between occupational exposure to APFO and measurable changes in clinical laboratory measurements or physical examination endpoints. The results of this study indicated a positive association between serum level of PFOA in workers at the polymer production plant and serum cholesterol, triglycerides, and LDL cholesterol. No association was seen with HDL cholesterol [3]. These results were similar to those published by Olsen et al. [4] from a cross-sectional study on 3M workers at two plants. After adjustment for potential confounders including body mass index (BMI), current alcohol use, smoking, and age, a statistically significant association between increased serum levels of PFOA and increased levels of both cholesterol and triglycerides were observed in multivariable linear regression analyses. Longitudinal analyses for the 3M workers also showed that PFOA was positively associated with serum cholesterol (log-linear regression coefficient = 1.03; 95% CI: 1.01—1.05) and serum triglycerides (log-linear regression coefficient = 1.10; 95% CI: 1.05—1.16). However, as in our own study, the percent of variation explained by the model, as well as by serum PFOA, was small, and there was no association of serum PFOA with HDL cholesterol. The 3M investigators had concluded that since their results were opposite to those expected based on animal studies, their findings were probably spurious.

DuPont conducted a cross-sectional medical surveillance for altered liver function on the workers at the Washington Work plant site in 1979. These results indicated no changes in levels of liver enzymes associated with work area assignment [5]. Gilliland and Mandel examined clinical chemistries in 3M workers and reported no abnormalities or associations with total organic fluorine levels [6]. They did suggest that serum total organic fluorine levels might modulate hepatic responses to obesity and alcohol, but this suggestion was not supported by results of subsequent surveillance examinations among those workers [7].

The current study examines all-causes of death combined and cause-specific mortality rates for the DuPont employees at the Washington Works, West Virginia, polymer manufacturing facility. This facility produces several types of polymers, most of which are made by processes not involving APFO. Approximately one-third of the employees at the plant works in APFO-using areas. SMRs were calculated by using three different reference populations: the general U.S.A. population, the state population of West Virginia, and an eight-state regional DuPont employee population (DuPont Region 1). Because increased lipids levels are a risk factor for cardiovascular diseases, we also used Cox proportional hazards models to estimate mortality rate ratios (MRR) for an internal comparison of mortality due to ischemic heart disease associated with categories of exposure to APFO. The exposure assessment for PFOA was based on a combination of work history information for each subject and serum PFOA levels obtained from the Phase I cross-sectional survey of the active workers in 2004.

Methods

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Cohort Ascertainment

The cohort was defined as all individuals who have ever worked at the Washington Works plant at any time between January 1, 1948 (plant start-up) and December 31, 2002. The cohort was ascertained primarily through the DuPont Epidemiology Registries; additional members were identified from plant-based work history records.

DuPont Mortality Registry

The DuPont Company has maintained a Mortality Registry for all active and pensioned U.S.A. employees since 1957. This Registry provides the expected numbers of deaths used in the DuPont Epidemiology Surveillance Program SMR calculations to compare each plant site in the U.S.A. to the rest of the U.S.A. DuPont population. Deaths are reported to the Registry by the corporate Benefits division through death certificates that accompany life insurance claims filed by beneficiaries of deceased employees and pensioners. Until recently, employment duration of at least 15 years was required for pensioning. However, additional changes in vesting strategies and insurance policies created fiduciary responsibility on the part of the Company that requires notification of death of additional former employees. Deaths are ascribed to the observed numbers for the plant site at which the employee worked at the time of death, or the site at which the pensioner worked at the time of retirement. For those who left the Company between 1950 and 1979, 91.7% were either pensioned or covered by some other vested benefit. Of the employees leaving the company between 1980 and 2005, only 60% were pensioned or covered by other vested benefits. However, deceased non-pensioned employees terminating after 1979 have been added to the Registry through the use of the National Death Index database, NDI *Plus*. In addition, the social security numbers for each cohort member were submitted to the Social Security Administration for confirmation of vital status.

The Employee Registry, which provides the demographic information on all individuals ever employed by DuPont in the United States, is updated from a monthly upload from Corporate Human Resources. The Epidemiology Employee Registry currently includes approximately 265,000 individuals, 6,027 who ever worked at Washington Works, approximately 2000 of whom are presently located at that site.

Exposure Categorization

While the half-life of PFOA in humans is estimated to be about 4 years [13], the kinetics of PFOA in humans are not well characterized. APFO can be absorbed via inhalation, as well as orally and dermally. Dermal absorption is very slow, and is an issue only for occupational exposure [14,15]. Serum PFOA levels were considered the best measure of exposure, because serum levels integrate all routes of exposure and provide an estimate of the amount of the compound delivered internally to the organ tissues. Information regarding the relationship between an individual's job and the measured serum PFOA level was based on the Phase I cross-sectional health survey conducted in 2004 and incorporated into the exposure assessment for the retrospective cohort mortality study. There were four major steps in determining exposure categories in Phase I.

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1) Establish relative exposure categories for current job titles using serum PFOA.
    a. Link individually measured serum PFOA levels measured with the job title held by the individual at the time of sampling.
    b. Examine the median, range, and distribution of serum levels for each job to determine the typical exposure for that job title.
    c. Based on the "typical" exposures, assign each job title to one of three relative exposure categories (Job Exposure Category: low, medium, high).
2) Apply Job Exposure Categories to historical job titles.
    a. Link unique job titles from work history files with job titles and assign the historic job titles to the corresponding Job Exposure Category.
    b. Apply appropriate Job Exposure Category to each record in the cohort work history.
3) Calculate individual exposure metrics
    a. Multiply the time each individual spent in each Job Exposure Category by the intensity factor associated with that category and sum across all categories to calculate individual Cumulative Exposure.
    b. Calculate Average Intensity by dividing cumulative exposure by duration of hire.
4) Validate exposure classification by plotting exposure variables (average exposure intensity, cumulative exposure, and concurrent job intensity factor) versus the measured serum PFOA levels collected as part of a plant-site voluntary biomonitoring program

Establish Job Exposure Categories

Exposure and employment data were collected for 1,025 Washington Works employees as part of the Phase I cross-sectional health survey conducted in 2004. These data were combined to establish exposure categories for job titles. In the cross-sectional study, work divisions at the plant site were designated as "APFO-use" or "no APFO use" based on the potential for exposure to APFO, with the understanding that some individuals within APFO-use divisions may not have had exposure to APFO and some individuals in no APFO-use divisions may have had undocumented exposure to APFO.

Median, minimum, and maximum serum PFOA levels were calculated for each no APFO-use division, using only individuals who had never worked in an APFO-use division, to establish the criteria for the low-intensity job exposure category. Next, the median, minimum, and maximum serum PFOA levels were calculated for each job title in the APFO-use divisions. The divisions designated as "APFO-use" Divisions included: TEFLON® Maintenance, TEFLON Polymers Production, TEFLON Copolymers Production, Research, and Technical. The distribution of serum PFOA levels within each job title was examined. See Appendix D.

APFO-use jobs were then grouped into three job-exposure categories based on job-specific PFOA serum level information:

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- Job Exposure Category 1 consisted of all no APFO-use division jobs, and APFO-use jobs within the same serum level range as those employees who had never had a job assignment in any APFO-use division--median<0.25 ppm.
- Job Exposure Category 2 consisted of APFO-use jobs with a median serum level >0.25 ppm and ≤0.75 ppm.
- Job Exposure Category 3 comprised all APFO-use jobs with a median serum level >0.75 ppm.

Some latitude was allowed in the use of median serum levels as the only criterion in the assignment of a given job title to a job exposure category. In instances where a job title was categorized differently than similar job titles as a result of a median serum value from a very small sample, the job title was grouped with the similar job titles. (See Exhibit 1.)

Exhibit 1. Group changes based on similar job titles

		Serum PFOA				Job Exposure Category		
Division	Job	Median	Min	Max	n	From	To	Reason
APFO-USE@ COPOLYMERS PROD.	AREA SPECIALIST	0.255	0.255	0.255	1	2	1	Moved to be in same category as other "Specialists" (n=11) with similar exposure (Range: 0.025 -0.272)
APFO-USE@ POLYMERS PROD.	SR ENGINEER	0.765	0.412	1.59	4	3	2	Moved to be with other "Sr Engineers" in Job Exposure Category 2 (n= 8; Range: 0.097 – 0.576)
TECHNICAL	TECH SPEC	0.783	0.783	0.783	1	3	2	Moved to be with other "Specialists" in Job Exposure Category 2 (n= 7; Range: 0.134 – 1.28)
APFO-USE@ COPOLYMERS PROD.	TECH SPEC	1.46	1.46	1.46	1	3	2	

The resulting numbers of cross-sectional study participants with jobs in Job Exposure Categories 1, 2, and 3 were 784, 107, and 134, respectively. The mean serum levels within the respective groups were 0.21, 0.43, and 1.69 ppm. Those mean serum levels served as the intensity factors for the three Job Exposure Categories.

Because PFOA is believed to have a half-life of about 4 years in humans [13], the length of time spent in the assignments used to define the Job Exposure Categories was examined to ensure that the job titles would not be misclassified as a result of individuals with either very short or very long stays in the job. Each participant's serum PFOA level was plotted against the time in the concurrent job by Job Exposure Category. The resulting correlation indicated that time in job was not strongly associated with serum PFOA level and should not substantially contribute to misclassification of job titles.

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Application of Job Exposure Categories to Historical Job Titles

Complete job histories for all Washington Works employees were obtained via electronic files from the Human Resources department at the plant site. In addition, historical work divisions were designated as "APFO-use" or "no APFO-use" based on the potential for occupational exposure to APFO. All historical job titles in the "no APFO-use" work divisions were assigned to Job Exposure Category 1. Approximately 1600 unique "APFO-use" job titles were identified in the work history files. Most of those unique job titles resulted from variations in spelling or abbreviations, or division name changes for common job titles. Historic job titles were matched with similar titles identified in the cross-sectional survey and assigned to the corresponding Job Exposure Category.

Calculation of Individual Exposure Metrics

Cumulative exposure was calculated for each individual in the full cohort by multiplying time in the various job exposure categories by the intensity factor associated with job exposure categories 1 through 3, either 0.21, 0.43, or 1.69 ppm, respectively.

Average intensity was also calculated for each cohort member by dividing the individual's cumulative exposure by their duration of hire, as shown in Exhibit 2 below.

Exhibit 2. Example of calculation of average intensity of exposure*.

	Time in Category	Intensity Factor	Exposure
JobExpCat1	2.50	0.21	0.52
JobExpCat2	12.00	0.43	5.16
JobExpCat3	7.25	1.69	12.25
Duration of Work	21.75		
Cumulative Exposure			17.94
			17.94 / 21.75
Average Intensity			0.825

*Values are at end of follow-up

Validate Exposure Classification

To validate the assignment of Job Exposure Categories to historical job titles, relationships were examined between calculated exposure values and measured PFOA serum levels in the Phase III Longitudinal Study dataset [16] (see Figures 4, 5, and 6). The Longitudinal Study dataset was comprised of sampling data for individuals with more than one sample from the Fluoropolymers Laboratory Analysis Information Retrieval (FLAIR) biomonitoring database together with the Phase I study. The FLAIR biomonitoring database archived serum PFOA data collected on a voluntary basis to ensure the effectiveness of workplace controls. Samples had been collected between 1979 and 2002.

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Since the assignment of Job Exposure Categories to historical job titles was based on blood PFOA measurements that were taken in Phase I, those values were removed for the validation analysis. There were also 40 observations from the FLAIR database (corresponding to 23 employees) where the PFOA blood sample was taken after the employee had stopped working at the plant. These 40 observations were also removed from the validation analysis. Our validation was performed on dataset 6 as described in Exhibit 3.

Exhibit 3 Etiology of Validation Data Set

Data set		Date of Collection	Number of Participants	Number of Observations
1	FLAIR database	1979-2002	891	1947
2	Cross-Sectional Study	2004	1025	1025
3	All FLAIR data and Cross-sectional data of FLAIR participants	1979-2004	891	2148
4	FLAIR and Cross-sectional participants with more than 1 measurement each	1979-2004	461	1718
5	FLAIR and Cross-sectional participants with more than 1 measurement each minus the Cross-sectional samples	1979-2002	461	1517
6	FLAIR and Cross-sectional participants with more than 1 measurement each minus the Cross-sectional samples and retiree samples	1979-2002	451	1477

Cumulative exposure, average intensity, and concurrent job intensity factor were calculated for each individual up to the time of the sampling (from hire date to sample date). The relationships between each serum PFOA value and the corresponding average intensity, cumulative exposure, and concurrent job intensity factor were analyzed. There were 21 missing values for job intensity factor and 6 missing observations for average intensity.

First, the observations were treated as being independent (although many employees had more than one observation) and examined in a general linear model. Then the associations between serum PFOA and the exposures of interest (average intensity, cumulative exposure, and concurrent job intensity factor) were examined in mixed models.

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Exhibit 4. Results of mixed model used to validate cumulative exposure to PFOA: serum PFOA as a function of estimates of PFOA exposure based on job.

	Correlation Coefficient	P value
Average Intensity	0.40	<0.0001
Cumulative Exposure	0.36	<0.0001
Intensity Factor	0.39	<0.0001

Prior to fitting the mixed models, sample variograms were created for the outcome variable (blood PFOA) to evaluate the serial correlation, the measurement error and the random effect for each mixed model. The spatial power covariance structure was found to have the best fit for the data and was therefore used. This structure allows the correlations between errors to be modeled in such a way that two points that are close in time are more correlated than two points that are further apart in time. This covariance structure is appropriate for unequally spaced measurements, which was the case in our dataset since employees were having their blood PFOA checked voluntarily and at different time intervals.

Each model included the exposure of interest (average intensity, cumulative exposure, or we calculated the numbers of years since January 1, 1979 that would correspond to each calendar date (example: (blood sample date-January 1, 1979)/365.25). An interaction term between the exposure variable and the date variable was also added to the model.

All exposure variables were positively and significantly associated with the outcome (serum PFOA), suggesting that historical job titles were properly categorized (see Exhibit 5). Time was negatively associated with serum PFOA, supporting the observation that PFOA is reduced over time. The model that gave the best fit was the mixed model that included the exposure variable and the time variable, without the interaction term. The concurrent job intensity factor model had the best fit for the data as suggested by the lowest fit statistic test. Therefore intensity factor explains serum PFOA better than cumulative exposure and average intensity. This suggests that concurrent exposure has greater influence on serum PFOA levels than past exposure and, therefore, the use of concurrent measured serum levels to characterize job titles into relative exposure categories is a valid approach for this compound despite the concerns around half-life.

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Exhibit 5. Validation of exposure using repeated measurements (mixed model) to predict serum PFOA

A. Predictor variable: average intensity

	Coefficient	p
Average intensity	0.899	<0.0001
Time *	-0.036	0.0006

Fit statistic: AIC = 5445.7**

B. Predictor variable: cumulative exposure

	Coefficient	p
Cumulative exposure	0.0002	<0.0001
Time *	-0.034	0.0014

Fit statistic: AIC = 5477.6 **

C. Predictor variable: intensity factor

	Coefficient	p
Intensity factor	0.796	<0.0001
Time *	-0.036	0.0006

Fit statistic: AIC = 5407.8 **

* Time is calculated as number of years since 1979
** For AIC (Akaike Information Criterion), the smaller value indicates better fit.

Mortality Analyses and Development of Occupational Reference Files

All SMRs were calculated using OCMAP (Occupational Mortality Analysis Program) developed by the University of Pittsburgh [17]. This software compares observed numbers of deaths in the study population to expected numbers of deaths based on rates for chosen reference populations for specific gender, 5-year time, and 5-year age categories by cause of death. State and U.S.A. reference rate files were acquired directly from the University of Pittsburgh.

Estimating relative risks by SMRs is a standard epidemiological approach to adjust for confounding by age and other characteristics that differ between populations. Typically, the general U.S.A. population is used as the reference group; however, it is not an appropriate comparison group for a worker cohort. Because healthier people are selectively hired to work, these populations may not be comparable in terms of health status. This may introduce a downward bias in estimates of the SMR due to confounding by the healthy worker effect [18-20]. While the effect is generally stronger for chronic diseases, the downward bias in comparative estimates has also been demonstrated for cancer [21].

One approach for reducing healthy worker bias is to choose a reference population composed of workers unexposed to the particular hazardous agent of interest. Restricting the comparison group to the same geographical region as the exposed cohort also improves comparability by

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reducing likelihood of unmeasured confounding by commonly shared regional characteristics such as diet and lifestyle. Preliminary results from our work on another large occupational cohort indicated that the most appropriate comparison for occupational cohorts is the working population of the same company drawn from the same region as the study plant site (manuscript in preparation). Potentially biased estimates of reduced SMRs usually seen when comparisons are made to general non-occupational populations are not observed using this comparison, presumably because the healthy worker effect is reduced. Additionally, comparing mortality rates for workers from the same general region adjusts for local socio-cultural factors, although not all local effects are likely to be removed.

A second component of healthy worker bias arises from the healthy worker survivor effect (HWSE). This bias is introduced when less healthy workers leave the workforce earlier than healthy workers, thereby having no opportunity to accrue cumulative exposures as large as more healthy workers. One approach that has been proposed to reduce this healthy worker survivor effect, is to assign zero weight to exposures in the 5 to 10 years proximate to the date of death (or diagnosis) in order to discount the effect of exposures during periods of time closer to the event of interest [22-23].

For the DuPont employee comparisons, we created a DuPont regional reference file (DuPont Region 1) that included all DuPont employees in West Virginia and seven neighboring states: Ohio, Virginia, Kentucky, Indiana, Pennsylvania, Tennessee, and North Carolina (excluding those employees at the Washington Works site). For the DuPont worker mortality rates, race was not an adjustment variable. No follow-up methods or efforts additional to those used in Registry ascertainment were applied to the cohort files.

The first level of cohort analysis was the calculation of SMRs for the entire Washington Works cohort, with follow-up from 1948 to 2002, the last year for which the Registry has been updated through NDI *Plus*. SMRs were calculated based on comparisons to the U.S.A. general population, the state of West Virginia, and the DuPont Region 1 reference file.

Cox Proportional Hazards Modeling

SMRs are useful for comparing mortality between an exposed to an unexposed reference group. However, in order to take full advantage of the exposure assessment for PFOA and examine exposure-response relationships we turned to Cox models for one outcome—ischemic heart disease. Cox proportional hazards models (CPHM), with age as the time metameter, were used to estimate adjusted mortality rate ratios (MRRs) for ordinal PFOA exposure categories. These categories were based on the cumulative exposure calculated for each member of the historical cohort based on the categorization of jobs. The cumulative exposure thus calculated was then used to derive the average exposure intensity for each cohort member, based on the job history data. Ischemic heart disease mortality was chosen based on the fact that increased lipids are a risk factor for ischemic heart disease, and there were sufficient cases to enable division into exposure groups. For ischemic heart disease, we estimated mortality rate ratios using lagged exposure (5, 10, 15, and 20 years) to reduce any bias introduced by the healthy worker survivor effect.

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CPHM is a statistical model used to investigate the relationship between survival time (or time to event) and one or more independent variables [24]. An assumption that must be met for these analyses to be meaningful is that the hazard rates are proportional to one another at all ages. This means that at any given age (t), the hazard rate for those exposed to a risk factor [$h_1(t)$] is a constant multiple of the underlying hazard [$h_0(t)$] for that age. A significant advantage to the approach is that the baseline hazard function does not have to be explicitly described, since the different risks are relative. The model can be stated as follows:

$$h_1(t) = h_0(t) \times B$$

Estimating the constant multiplication factor for changes in risk (B) is conveniently done using an exponential function, $B = e^b$. Reformulating equation 1 yields

$$h_1(t) = h_0(t) \times e^b.$$

Therefore, if $h_0(t)$ represents the hazard in the unexposed group at any given time, the hazard ratio (HR) comparing the exposed and unexposed is

$HR = [h_1(t)] / [h_0(t)] = e^b$, or taking logarithms, $\log(HR) = b$.

All CPHM was conducted using SAS Proc PHREG, version 9.01.

Description of Methods Specific to Ischemic Heart Disease

There were only three cases of IHD among women and only one non-white male case. Therefore, women and non-whites were excluded from all proportional hazards analysis.

Person-time for the risk set of each index case was comprised of people who had started working by the age of the case that defined the risk set (case age at death), and were still alive at that age. In addition to exposure to PFOA, the regression models also included calendar year of death in order to control for secular trends over the follow-up period.

There were 235 cases of ischemic heart disease available for analysis. Since cases were hired on average 20 years earlier than the non-cases, year of hire was also included to adjust for confounding. Because half of the cases were hired before 1954, we created a binary variable for year of hire (before or after 1954) that was included in the model. The correlation between calendar year of death and the binary variable, hired pre- or post-1954, was – 0.44 ($p<0.0001$).

We chose to use average intensity and cumulative exposure as the exposure metrics for CPHM analysis. Because heart disease mortality is known to be strongly affected by the healthy worker survivor effect, we chose to lag both exposure metrics 5, 10, 15, and 20 years. These lags eliminated the more recent exposures to reduce bias engendered by healthier workers staying in the workplace longer periods of time thus accumulating more exposure.

Categories of exposure for average intensity:
In each Cox model, workers whose jobs were categorized as having the lowest exposure to PFOA (lowest average intensity) and who also never worked in any APFO-using division were considered the reference group, thus enabling an internal analysis. Both the APFO areas of the plant site and the non-APFO areas comprise a wide diversity of jobs (mechanics, engineers, supervisors, administrative, etc.) This diversity of job types in all non-APFO areas of the plant

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should make this group of workers comparable to those workers who ever worked with APFO in all characteristics except for exposure to APFO.

Five categories of average intensity of exposure to APFO were specified to ensure that an adequate number of cases would be in each category, thus increasing the stability of the MRR estimates. The exposure categories are ordinal, with 0 comprising the reference group, 1 being the lowest exposure, and 4 being the highest exposure category, for those analyses that comprised four categories. These exposure category definitions are presented in Exhibit 6.

Exhibit 6. Average intensity of exposure categories for proportional hazards analyses for ischemic heart disease mortality, stratified by exposure lag period.

No lag of exposure
N = 4,460

o Reference: x = 0.21 ppm and Never APFO-use	167 cases
o Category 1: x = 0.21 ppm and Ever APFO-use	28 cases
o Category 2: 0.21<x<= 0.250 ppm	12 cases
o Category 3: 0.250<x<=0.371 ppm	14 cases
o Category 4: > 0.371 ppm	14 cases

Exposure lagging 5 years
N = 4,440

o Reference: x = 0.21 ppm and Never APFO-use	162 cases
o Category 1: x = 0.21 ppm and Ever APFO-use	30 cases
o Category 2: 0.211 <= x <= 0.254 ppm	12 cases
o Category 3: 0.261 <= x <= 0.551 ppm	13 cases
o Category 4: 0.592 <= x <= 1.524 ppm	12 cases

Exposure lagging 10 years
N = 3,989

o Reference: x = 0.21 ppm and Never APFO-use	152 cases
o Category 1: x = 0.21 ppm and Ever APFO-use	30 cases
o Category 2: 0.211 <= x <= 0.256 ppm	11 cases
o Category 3: 0.261 <= x <= 0.555 ppm	12 cases
o Category 4: 0.565 <= x <= 1.524 ppm	12 cases

Exposure lagging 15 years
N = 3,986

o Reference: x = 0.21 ppm and Never APFO-use	142 cases
o Category 1: x = 0.21 ppm and Ever APFO-use	30 cases
o Category 2: 0.21 < x <= 0.269 ppm	11 cases
o Category 3: 0.269< x <= 0.591 ppm	12 cases
o Category 4: x > 0.591 ppm	12 cases

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Exposure lagging 20 years
N = 3,440

- Reference: x = 0.21 ppm and Never APFO-use — 130 cases
- Category 1: x = 0.21 ppm and Ever APFO-use — 28 cases
- Category 2: 0.21< x <= 0.330 ppm — 16 cases
- Category 3: x > 0.330 ppm — 15 cases

Categories of exposure for cumulative exposure
Cumulative exposure was estimated as the total attained exposure for each case event at the time of death. Analytic strata were created for each case event by matching all eligible non-case subjects (workers who had not died by the date of the case event) and assigning cumulative exposure based on total attained exposure for each worker at the same age as the case event. Given that there is debate on the implications of the statistical aspects of the categorization of cumulative exposure, two different approaches were used to determine four cumulative exposure categories. The two approaches thus provided a form of sensitivity analysis. In the first analysis (exhibit 7A), quartiles of the cumulative exposure were determined by the distribution of exposures for case subjects. In a second analysis designed to test the model sensitivity to cumulative exposure categorization, quartiles were determined by the distribution of exposures for all workers in the cohort (exhibit 7B). For each lagged analysis, the exposure values for the four categories are shown for both strategies, and the number of cases of IHD mortality are listed. Cox models analyzing the proportional hazards for cumulative exposure categories with the lowest exposure group serving as the referent also included variables adjusting for calendar year of the case event and pre-1954 hire period.

Exhibit 7A. Cumulative exposure categories for proportional hazards analyses for ischemic heart disease mortality, stratified by exposure lag period; quartiles determined by cumulative exposure distribution of cases among white males.

No lag of exposure
N = 4,460

- Reference: x <= 3.81 ppm years — 58 cases
- Category 1: 3.81<x< = 5.45 ppm years — 59 cases
- Category 2: 5.45<x<= 6.78 ppm years — 59 cases
- Category 3: x>6.78 ppm years — 59 cases

Exposure lagging 5 years
N = 4,440

- Reference: x <= 3.42 ppm years — 57 cases
- Category 1: 3.42<x< = 5.28 ppm years — 57 cases
- Category 2: 5.28<x<= 6.51 ppm years — 57 cases
- Category 3: x>6.51 ppm years — 58 cases

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Exposure lagging 10 years
N = 3,989

- Reference: x <= 3.12 ppm years — 54 cases
- Category 1: 3.12<x< = 4.90 ppm years — 54 cases
- Category 2: 4.90<x<= 6.40 ppm years — 54 cases
- Category 3: x>6.40 ppm years — 55 cases

Exposure lagging 15 years
N = 3,986

- Reference: x <= 2.43 ppm years — 51 cases
- Category 1: 2.43<x< = 4.19 ppm years — 52 cases
- Category 2: 4.19<x<= 5.66 ppm years — 52 cases
- Category 3: x>5.66 ppm years — 52 cases

Exposure lagging 20 years
N = 3,440

- Reference: x <= 1.66 ppm years — 47 cases
- Category 1: 1.66<x< = 3.48 ppm years — 47 cases
- Category 2: 3.48<x<= 5.07 ppm years — 47 cases
- Category 3: x>5.07 ppm years — 48 cases

Exhibit 7B. Cumulative exposure categories for proportional hazards analyses for ischemic heart disease mortality, stratified by exposure lag period; quartiles determined by cumulative exposure distribution of entire cohort.

No lag of exposure
N = 4,460

- Reference: x <= 0.99 ppm years — 10 cases
- Category 1: 0.99<x< = 4.29 ppm years — 61 cases
- Category 2: 4.29<x<= 6.98 ppm years — 114 cases
- Category 3: x>6.98 ppm years — 50 cases

Exposure lagging 5 years
N = 4,440

- Reference: x <= 1.97 ppm years — 26 cases
- Category 1: 1.97<x< = 4.42 ppm years — 61 cases
- Category 2: 4.42<x<= 6.24 ppm years — 76 cases
- Category 3: x>6.24 ppm years — 66 cases

Exposure lagging 10 years
N = 3,989

- Reference: x <= 2.28 ppm years — 37 cases
- Category 1: 2.28<x< = 3.85 ppm years — 46 cases
- Category 2: 3.85<x<= 5.23 ppm years — 37 cases
- Category 3: x>5.23 ppm years — 97 cases

Exposure lagging 15 years

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N = 3,986

- Reference: x <= 1.86 ppm years — 38 cases
- Category 1: 1.86<x< = 3.16 ppm years — 34 cases
- Category 2: 3.16<x<= 4.27 ppm years — 33 cases
- Category 3: x>4.27 ppm years — 102 cases

Exposure lagging 20 years

N = 3,440

- Reference: x <= 1.19 ppm years — 27 cases
- Category 1: 1.19<x< = 2.38 ppm years — 34 cases
- Category 2: 2.38<x<= 3.24 ppm years — 28 cases
- Category 3: x>3.24 ppm years — 100 cases

Results

Cohort Description

The Washington Works cohort consists of individuals who worked at the plant at any time between 1948 and 2002. First, 5,476 individuals were originally identified from the Epidemiology Employee Registry. Of these persons, 22 individuals were excluded for the following reasons; 1 had no verifiable birth date, and 21 had transferred to the Washington Works location after December 31, 2002, the end of the mortality surveillance period. This resulted in 5,454 individuals who were included from the Epidemiology Employee Registry with an additional 573 individuals included based on work history records obtained from the plant site Human Resources Department. The resulting cohort for all analyses included 6,027 individuals. Table 1 shows the descriptive statistics for the historical Washington Works cohort.

Total person-years were 127,513.2 for males, and 18,224.5 for females. Person-years ascribed to the three cumulative exposure categories were 74,603.6 for Group 1 (lowest potential exposure to APFO); 52,461.8 for Group 2; and 18,672.3 for Group 3 (highest potential exposure to APFO).

Mortality Analyses on Entire Cohort

While the DuPont Regional population appears to be the most appropriate reference group for mortality rate comparisons, we also report SMRs based on both the U.S.A. and West Virginia rates. The U.S.A. comparisons provide some context for other studies in the published literature, and the comparisons to the West Virginia state population are presented in response to a request from study participants. As would be expected, almost all SMRs comparing Washington Works mortality rates for defined causes to the U.S.A. and West Virginia population mortality rates were below 100, the standard metric of the SMR indicating no observed differences in the mortality rates between the compared populations. Further, many SMR estimates were statistically significantly below this estimate of no effect indicating that Washington Works employees had lower mortality rates for many causes of death compared to the general population. Due to concerns about statistical precision, only those causes of death for which there were at least five deaths observed were considered relevant for consideration of increased or decreased risk.

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Table 2 shows selected SMRs for Washington Works males and females when compared to the three reference populations. These causes of death were selected based on results from animal studies and other occupational studies, and are detailed below. Complete SMR analysis results are presented in Appendices A-C. There were only 33 deaths among females workers; limiting the statistical power to detect significant differences in disease-specific mortality rates among female workers and restricting interpretations of SMRs to all causes of death combined and all cancers combined.

All Causes of Death

For males, the SMR for all causes of death was 94 (95% CI: 87—100) based on the Region 1 DuPont population. The SMRs for all causes based on comparisons to West Virginia and total U.S.A. were 58 (95% CI: 54—62) and 66 (95% CI: 62—71), respectively.

For females, the SMR for all causes of death was 147 (95% CI: 101—207) based on the Region 1 DuPont population. The SMRs for all causes based on comparisons to West Virginia and total U.S.A. were 73 (95% CI: 51—103) and 81 (95% CI: 56—113), respectively.

All Malignant Neoplasms

For males, the SMR for all malignant neoplasms was 100 (95% CI: 88—114) based on the Region 1 DuPont population. The SMRs for all malignant neoplasms based on comparisons to West Virginia and total U.S.A. were 68 (95% CI: 60—78) (WV) and 74 (95% CI: 64—84) (U.S.A.)

For females, the SMRs for all malignant neoplasms were 149 (95% CI: 77—260); 79 (95% CI: 41—139), and 87 (95% CI: 45—151) when comparing against the Region 1 DuPont Population, West Virginia, and total U.S.A., respectively.

Cancer of Biliary Passages and Liver

Based on seven deaths, the SMRs in males for cancer of biliary passages and liver were 133 (95% CI: 53—274), 104 (95% CI: 42—215), and 90 (95% CI: 36—185) when comparing against the Region 1 DuPont Population, West Virginia, and total U.S.A., respectively.

There was only one death due to cancer of biliary passages and liver among females.

Cancer of Pancreas

For males, the SMRs for cancer of the pancreas were 100 (95% CI: 50—180), 83 (95% CI: 41—148), and 71 (95% CI: 36—128) when comparing against the Region 1 DuPont Population, West Virginia, and total U.S.A., respectively.

There were no reported cases of cancer of the pancreas in females.

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Urinary Tract Cancers

There were 12 deaths from kidney cancer in males; the SMRs were 185 (95% CI: 95—323), 155 (95% CI: 80—272), and 156 (95% CI: 80—272) when comparing against the Region 1 DuPont Population, West Virginia, and total U.S.A., respectively.

No deaths from kidney cancer were seen in females.

There were 7 deaths from cancer of the bladder and other urinary organs in males; the SMRs were 131 (95% CI: 53—269), 105 (95% CI: 42—216), and 101 (95% CI: 41—209) when comparing against the Region 1 DuPont Population, West Virginia, and total U.S.A., respectively.

One death from bladder cancer was seen in females.

Because there were few deaths from kidney cancer, there was not sufficient statistical power to fit Cox proportional hazard models for assessing the association of this outcome with exposure categories. Examination of job histories showed that only half the cases had ever worked in the APFO-use divisions.

Cancer of Bronchus, Trachea, Lung

For males, the SMR for cancer of the bronchus, trachea, and lung was 81 (95% CI: 63—104) based on the Region 1 DuPont population The SMRs for cancer of the bronchus, trachea, and lung based on comparisons to West Virginia and total U.S.A. were 49 (95% CI: 38—163) (WV) and 61 (95% CI: 47—77) (U.S.A.)

Cancer of Prostate

The SMR for cancer of the prostate was 65 (95% CI: 34—114), and 58 (95% CI: 30—100)), based on the Region 1 DuPont population and West Virginia, respectively. The SMR for cancer of the prostate based on comparisons to the total U.S.A. was 52 (95% CI: 27—91).

Cerebrovascular Disease

For males, the SMR for cerebrovascular disease was 86 (95% CI: 60—120) based on the Region 1 DuPont population. The SMRs for cerebrovascular disease based on comparisons to West Virginia and total U.S.A. were 60 (95% CI: 42—84) (WV) and 61 ((95% CI: 42—85) (U.S.A.).

For females, only one death was due to cerebrovascular disease.

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All Heart Disease

For males, the SMR for all heart disease was 110 (95% CI: 98—123) based on the Region 1 DuPont population. The SMRs for all heart disease based on comparisons to West Virginia and total U.S.A. were 66 (95% CI: 59—74) (WV) and 80 ((95% CI: 71—89) (U.S.A.).

For females, the SMRs for all heart disease were 143 (95% CI: 46—333), 51 (95% CI: 17—119), and 64 (95% CI: 21—150) when comparing against the Region 1 DuPont Population, West Virginia, and total U.S.A., respectively.

Ischemic Heart Disease

In males, the SMRs for ischemic heart disease were 109 (95% CI: 96—124), and 69 (95% CI: 61—78), based on the Region 1 DuPont population and West Virginia, respectively. The SMR for ischemic heart disease based on comparisons to total U.S.A. was 81 (95% CI: 71—93).

There were only three deaths due to ischemic heart disease in females.

Diabetes Mellitus

Mortality from diabetes mellitus among males was significantly elevated based on comparison to the DuPont Region 1 population (SMR= 183; 95% CI=112—283), but was below 100.0 in comparisons to both the West Virginia (SMR= 67; 95% CI=41—104) and U.S.A. population (SMR= 81; 95% CI=50—125).

There were only two deaths attributed to diabetes among females.

Cox Proportional Hazards Modeling

Ischemic Heart Disease

Table 3 presents the descriptive statistics for the white males used in the proportional hazards models for IHD, stratified by case/non-case status, and Table 4 shows descriptive statistics for this subset, stratified by never-APFO-use/ever-APFO-use.

The first CHPM for ischemic heart disease was fit to data for 4,460 white males using the average intensity as the exposure of interest, with zero lag for exposure. Two models are presented in Table 5: each includes PFOA exposure variables, and one adjusts for calendar year of the event and the other adjusts for hire date (pre or post-1954) in the model (1954 was the median date of hire).

Table 5 also shows the mortality rate ratios by exposure category for the no-lag models using case calendar-year or the binary variable for hired before 1954 as a potential confounder. When we looked separately at calendar year of death and date of hire, these two variables were both statistically significant. For calendar year of death, the MRR is less than one, which means that the background death rate for ischemic heart disease is going down over the study period. This is also true for the national mortality rates from ischemic heart disease in the U.S.A. (Figure 7). As for the date of hire, those hired prior to 1954 had higher risk of death from IHD than those hired

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after 1954. However, when both of these variables (date of hire and calendar year of death) were accounted for in the model, only calendar year of death remained significant which means that the effect of the date of hire was confounded by the calendar year of death.

Table 6 presents a summary of the CPHM analyses on IHD conducted for all white males in the cohort without lagging average intensity exposures, and those with lags of different time intervals (5, 10, 15, 20 years) to adjust for potential effects of HWSE with the inclusion of both potential time confounders (case calendar-year and hired before 1954).

These results show no significantly increased MRRs for IHD mortality between exposure categories for all analyses, with and without lags. Additionally, no trends of increasing MRRs are seen across exposure categories with the exception of category 4, the highest exposure group. The increase in MRR with increasing lag provides evidence that analysis using lagged exposures compensates for the healthy worker survivor effect for this cause of death. Details of these analyses are presented in Table 6.

Table 7 displays the results from both analyses of cumulative exposure categories for Cox proportional hazard models of the association between cumulative exposure and IHD mortality. In the first part of the table (section A), results are reported for categories determined by quartiles of cumulative exposure among case subjects only. This method ensures that each exposure category contains one-fourth of the cases (see exhibit 7A) for the corresponding lag model. Though no estimates of the hazard ratio are statistically significant in any model, the results from the 10-year lagged exposure model suggest an increasing trend in the mortality rate ratio for the highest two exposure categories.

Due to the lack of consensus on a universally "best" approach to cumulative exposure categorization, we performed a second set of analyses using quartiles determined by the entire WW cohort as a form of sensitivity analysis. Table 7B lists the results of these models corresponding to cutpoints described in exhibit 7B. Although all estimates were still not statistically significant, mortality rate ratio estimates for this analysis attenuated towards the null value of 1.0 for all lagged exposure models including those for the 10-year lag.

Discussion

In this retrospective cohort mortality study, we assessed whether workers at a polymer production plant exhibited increased mortality from any specific cause of death, as well as the more general categories of all causes and all malignant diseases. SMRs were generated using three different reference populations—a regional population from the same company, which reduced the bias from both the healthy worker effect and regional socio-cultural attributes; the state population in which the plant was located; and the general U.S.A. population. Although the site of the study is a manufacturing plant that produces a wide variety of products from many different chemicals, the only occupational exposure examined was APFO. The areas where this chemical is used employs about one-third of the site's workers.

Exposure to APFO has been shown to cause benign neoplasms in rodent toxicology studies. Liver, Leydig-cell, and pancreatic acinar-cell tumors were observed in rats, but all of those findings are hypothesized to be mediated via PPARα. Humans have low PPARα receptor expression, and are not as responsive to PPARα agonists [25]. This study had low power to

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detect excess risk for these rare tumors, and the increased SMR of 135 for cancer of the biliary passages and liver, based on seven cases in males, was not statistically significant.

Prostate cancer and cerebrovascular disease, both reported as increased in previous 3M Company occupational epidemiology reports [1,2], were reduced in this cohort against all reference populations, cerebrovascular disease significantly so for the U.S.A and West Virginia populations. The few cases of each of these causes of death did not allow meaningful internal comparisons.

Despite limited statistical power to evaluate mortality rates for specific cancers, some elevated relative risks did emerge that bear further scrutiny by worker surveillance and exposure monitoring. Although animal toxicology data and published occupational studies on workers exposed to PFOA do not provide any *a priori* reason to suggest a potential effect on risk for kidney cancer, comparisons against DuPont Region 1 returned increased, but non-significant SMRs. However, examination of work histories showed that few cases had spent appreciable time in the APFO areas.

We did identify an increased mortality risk for diabetes mellitus in this cohort of workers—driven largely by 20 cases in males and two in females—when comparisons were made to the regional worker population from the same company (SMR= 183; 95% CI=112—283). However, comparisons to West Virginia (SMR= 67; 95% CI=41—104) and to the general U.S.A. population (SMR= 81; 95% CI=50—125) did not indicate an increased risk of mortality due to diabetes. Although Cox proportional hazard modeling could be done, the small number of cases would severely limit the value of the estimates.

There is a substantial literature supporting the under-reporting of diabetes, especially of late-onset or type II diabetes, on death certificates. Differences between countries' mortality reporting for diabetes has been shown to depend, among other factors, on physician differences in reporting this disease in Part I of the death certificate or as the underlying cause [26]. In the U.S.A., a study of the frequency of reporting diabetes on death certificates of 540 known diabetics showed that diabetes was recorded on just 39 percent of the death certificates and as the underlying cause of death for only 10 percent of decedents with diabetes. In addition, diabetes was significantly less likely to be reported on the death certificates of decedents dying of cancer [27]. Our SMR analyses are based on the underlying cause of death, and it is reasonable to assume that the prevalence of diabetes in this cohort has been under-ascertained. We know of no reason why the same under-ascertainment should not apply to the reference populations as well; thus, any bias in ascertainment would be non-differential. Cardiovascular death rates are higher in diabetics than in non-diabetics [28-29]. Although cardiovascular disease and late-onset diabetes share several risk factors (diets high in refined carbohydrates, sedentary lifestyle, age, and body mass index, for example), a study conducted in Iceland identified an independent effect of diabetes on coronary heart disease after adjustment for blood pressure, serum lipids, uric acid, smoking, and height and weight [30]. As discussed below, no increase in cardiovascular disease was noted for this cohort. Given the number of endpoints examined in the SMR analyses, it is not surprising to find an isolated increase in one of the causes of death. The lack of agreement with other studies of PFOA workers, and the lack of any animal toxicology findings to support this association suggest that the finding is due to chance. However, we will follow up on these results in future surveillance.

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Our initial proportional hazards models of ischemic heart disease, an outcome potentially influenced by increased serum lipids, utilized cumulative exposure. This metric seemed to be the most biologically appropriate. The results of these models, conducted without lagging of exposure, showed significantly reduced rate ratios, which were assumed to be due to confounding by the healthy worker survivor effect (age was controlled for by using it as the time metric in the Cox model). We then turned to average intensity of exposure. With these analyses, we introduced the five-year lag of exposure, which appeared to mitigate the effects of the healthy worker survivor effect, prompting the re-analysis of cumulative exposure with lags. In order to stabilize the estimates of the mortality rate ratio, the exposure cutpoints were determined first by dividing the cases into quartiles, as is commonly done in occupational studies.

The multi-dimensionality of occupational exposure metrics contributes to discussion about which metrics are the more robust, least biased, and most biologically meaningful [31]. In light of this debate, we have presented analyses using both average intensity and cumulative exposure, with lagging and without. In addition, we conducted analyses on cumulative exposure with the cutpoints driven both by case and total cohort distributions of exposure, which provides a sensitivity analysis for the impact of cut-point selection on the observed exposure-response relationships.

For ischemic heart disease mortality, no increases in mortality rate ratios were seen in the results of any analyses conducted using average exposure intensity. Many of the MRRs were below 1.0. It is well known, however, that for a chronic disease such as IHD, mortality underestimates morbidity and is therefore not an ideal endpoint for epidemiologic analysis. Furthermore, the rate ratio for IHD may also be biased by the HWSE, even in internal analyses. The use of lagged exposures by 5 year periods to adjust for the healthy worker survivor effect did not have much effect, as estimates of the mortality rate ratio were still less than 1.0. There was, however, an increased trend in MRRs as the lag time increased from 0 to 20 years by 5-year intervals for Exposure Category 4 (highest exposure category). While these findings remain statistically non-significant, the increase in the MRR as the lag increased for the highest exposure group demonstrated that this approach did indeed compensate for the healthy worker survivor effect among those who worked long enough to achieve exposures in the highest category.

For proportional hazards models of cumulative exposure, no significant increase in the MRR was observed with the exception of the 10-year lag model based on the set of exposure categories with an equal distribution of cases assigned to each exposure group. An elevated relative risk of 1.6 was found in the highest exposure category, and there was an increasing trend in MRR with increasing exposure. While neither MRR estimate for the upper two exposure categories in the 10-year lag model was statistically significant, the apparent trend cannot be ignored.

In order to investigate the sensitivity of the model to the categorization of cumulative exposure, we redefined cumulative exposure categories based on quartiles of the entire WW cohort. Effect estimates from this model were attenuated towards a null value. The highest relative risk was again seen in the 10-year lagged model where the MRR was 1.3 for the highest exposure category, but there was no apparent trend. The overall absence of positive effect estimates using either the 5-, 15-, or 20-year exposure lags suggest that the positive exposure-response trend for cumulative exposure lagged by 10 years requires further investigation before firm conclusions can be reached.

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When we looked separately at calendar year of death and date of hire (before or after 1954 for IHD), both time variables were statistically significant. For calendar year of death, the MRR was less than one, which indicates that the background death rate for ischemic heart disease was going down over the study period. This is also true for the national mortality rates from ischemic heart disease in the U.S.A. As for the date of hire, those hired prior to 1954 had higher risk of death from IHD than those hired after 1954. However, when both of these variables (date of hire and calendar year of death) were accounted for in the model, only calendar year of death remained significant, evidence that the effect of the date of hire was confounded by the calendar year of death. This finding underlines the importance of exploring in detail all potential time-varying confounders in this type of analysis.

Strengths of this study include the availability of biomonitoring data to support retrospective exposure classification and a large cohort with over fifty years of follow-up. In addition, there were sufficient mortality data to enable several types of analysis using both external and internal comparisons, including Cox proportional hazards analysis for ischemic heart disease.

Limitations of this study include the potential loss to follow-up of decedents prior to 1979, a period where exposures may have been less well-controlled, causing potential bias towards the null due to the healthy worker survivor effect. Although this loss could have been as high as 10 percent, due to the ascertainment procedures for the DuPont Mortality Registry, it was likely much smaller due to the establishment of vital status of all cohort members through the Social Security Administration. Moreover, the lagged exposure approach applied to the ischemic heart disease analysis was designed to reduce such bias. A major limitation is likely to be the lack of accounting for confounding by other occupational and non-occupational risk factors. Most importantly, information was not available for members of the cohort about the major risk factors for cardiovascular disease (smoking, diet, and other life-style factors). Additionally, no information was available for cohort members who were being treated with medications such as statins or anti-hypertensive medications.

Conclusions

The results reported here show no convincing evidence of increased mortality risk associated with APFO exposure for workers at this plant. These results do show statistically non-significant elevations in relative risk for kidney cancer and a statistically significant increase in diabetes mortality for workers at this site. However, given the size and length of follow-up of the study population, the evidence to thoroughly examine mortality events like kidney cancer or even diabetes, may not be adequate. Proportional hazards analyses for ischemic heart disease mortality showed an increase in the model based on equal distribution of cases across cumulative exposure categories in one lagged analysis (the 10-year lag period). Other exposure lags showed no effect, and results for a second set of models using a different set of exposure cutpoints were attenuated toward the null. None of the hazard estimates themselves were statistically significant. Thus the positive finding in the proportional hazard analysis, as well as the increased diabetes mortality, might be due to chance. Because of the complexity of the exposure assessment and limited power for some analyses, additional investigations are needed.

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TABLES

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Table 1
Washington Works mortality study cohort

Washington Works Mortality Study Cohort	(as of 12/31/2002)							
	Males				Females			
	n	Mean	Min	Max	n	Mean	Min	Max
Cohort	4872				1155			
Age at Hire		29	11	70		27	17	56
Year of Hire		1974	1948	2002		1986	1948	2002
Age at Termination		50	19	74		32	18	71
Year of Termination		1989	1955	2004		1993	1967	2004
Duration of Hire (Yrs)		19	0	49		10	0	44
Yrs of Follow Up		26	0	55		16	0	55
Age at End of Follow Up		55	20	96		43	21	85
% White	95.40%				92.29%			
#Active	1650				429			
Duration of Hire (Yrs)		17	0	41		14	0	40
Age at End of Follow Up		46	23	68		44	22	67
#Dead	773				33			
#Cancer Deaths	222				12			
AgeAtDeath		66	22	96		58	22	85
%White	99.09%				96.97%			

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Table 2
SMRs for selected causes of death in Washington Works males, females compared to DuPont Region 1 (West Virginia (less Washington Works), Ohio, Virginia, Kentucky, Indiana, Pennsylvania, Tennessee, and North Carolina), U.S.A. national population, West Virginia state population

	MALES N=4872 Total Mortality: 773 Person Years: 127,513.2				FEMALES N=1155 Total Mortality: 33 Person Years: 18,224.5			
Cause of Death	**N**	**DuPont Region 1 SMR**	**U.S.A. National SMR**	**West Virginia State SMR**	**N**	**DuPont Region 1 SMR**	**U.S.A. National SMR**	**West Virginia State SMR**
All Causes of Death	(773)	93.6	66.2**	58.1**	(33)	147.2*	80.7	73.4
All Malignant Neoplasms	(222)	100.4	73.7**	68.3**	(12)	149.0	86.6	79.4
Cancer of Biliary Passages & Liver	(7)	133.1	89.7	104.2	(1)	384.8#	394.5#	551.8#
Cancer of Pancreas	(11)	100.5	74.0	82.9	0	0	0	0
Cancer of Bronchus, Trachea, Lung	(64)	81.3	60.6**	49.0**	(2)	132.9^	69.5^	56.6^
Cancer of Prostate (Males only)	(12)	65.3	51.8**	57.5	N/A	0	0	0
Cancer of Breast	(0)	0	0	0	(2)	77.4^	61.1^	63.5^
Cancer of Kidney	(12)	184.7	155.7	155.2	0	N/A	N/A	N/A
Diabetes	(20)	183.1*	81.2	67.0	(2)	796.1^	160.8^	121.7^
Cerebrovascular Disease	(34)	86.1	60.9**	60.1**	(1)	90.5#	48.7#	49.7#
All Heart Disease	(309)	109.9	80.0**	66.3**	(5)	142.7	64.4	51.1
Ischemic Heart Disease	(236)	109.3	81.4**	69.0	(3)	135.0	64.0	49.7

(*) SIGNIFICANT AT 5% LEVEL; (**) SIGNIFICANT AT 1% LEVEL; (#) BASED ON 1 CASE; (^) BASED ON 2 CASES
N/A Not Applicable

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Table 3
White male workers included in the risk-sets of the proportional hazard analysis for IHD stratified by case/non-case status

Variable	CASES N(%) or Mean (SD) [Minimum-Maximum]	NON-CASES N(%) or Mean (SD) [Minimum-Maximum]
Total Number	**235** (5.27 %)	**4225** (94.73 %)
Males	**235** (100 %)	**4225** (100 %)
White Race (v/s non white)	**235** (100 %)	**4225** (100 %)
Age at hire	**33.72** (9.82) [18.21-65.85]	**29.06** (8.77) [11.23-70.17]
Year of birth	**1921** (11.20) [1892-1958]	**1945** (15.97) [1890-1973]
Year of hire	**1955** (8.92) [1948-1995]	**1974** (15.71) [1948-2002]
Year of death	**1987** (11.30) [1958-2002]	**NA**
Ever-APFO-use	**68** (28.94 %)	**2185** (51.72%)

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Table 4
White male workers included in the risk-sets of the proportional hazard analysis stratified by never-APFO-use/ever-APFO-use status

Variable	NEVER-APFO-USE N(%) or Mean (SD) [Minimum-Maximum]	EVER-APFO-USE N(%) or Mean (SD) [Minimum-Maximum]
Total Number	**2207** (49.48 %)	**2253** (50.52 %)
Males	**2207** (100 %)	**2253** (100%)
White Race (v/s non white)	**2207** (100 %)	**2253** (100%)
Age at hire	**30.89** (9.42) [14.40-70.17]	**27.74** (8.04) [11.23-64.15]
Year of birth	**1941** (18.37) [1890-1972]	**1947** (14.10) [1903-1973]
Year of hire	**1972** (17.10) [1948-2002]	**1974** (14.72) [1948-2002]
Average intensity (at end of follow-up)	**0.21** (0) [0.21-0.21]	**0.42** (0.35) [0.21-1.69]
Cumulative exposure (at end of follow-up)	**4.06** (2.51) [0.00-9.02]	**9.10** (10.00) [0.01-71.85]
Time since hire (at end of follow-up)	**18.83** (12.20) [0.00-42.27]	**21.00** (12.63) [0.05-48.54]
Cases	**167** (7.57 %)	**68** (3.02 %)

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Table 5
Mortality rate ratios for IHD by exposure category for no-lag analyses using case calendar-year and year of hire (pre-1954) as potential confounders

	Hired pre-1954 NO LAG N = 4,460	**Case-calendar year NO LAG N = 4,460**
	MRR (95 % CI)	MRR (95 % CI)
Reference	1	1
Category 1	**0.858** (0.569-1.293)	**0.996** (0.657-1.509)
Category 2	**0.575** (0.319-1.035)	**0.715** (0.394-1.298)
Category 3	**0.767** (0.444-1.327)	**0.944** (0.542-1.645)
Category 4	**0.558** (0.323-0.966)	**0.646** (0.372-1.123)
Case Calendar-Year	---	**0.965** (0.952-0.978)
Hired before 1954	**1.422** (1.075-1.881)	---

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Table 6
Mortality rate ratios for IHD by average intensity exposure category, including increasing 5-year lags of exposure, using case calendar-year and year of hire (pre-1954) as potential confounders

	NO LAG N = 4,460	5-YEAR LAG N = 4,440	10-YEAR LAG N = 3,989	15-YEAR LAG N = 3,986	20-YEAR LAG N = 3,440
	MRR (95 % CI)	MRR (95 % CI)	MRR (95 % CI)	MRR (95 % CI)	MRR (95 % CI)
Reference*	1	1	1	1	1
Category 1	**0.996** (0.657-1.510)	**1.035** (0.689-1.557)	**1.048** (0.693-1.582)	**0.976** (0.643-1.482)	**0.884** (0.574-1.362)
Category 2	**0.715** (0.394-1.298)	**0.657** (0.361-1.195)	**0.688** (0.369-1.284)	**0.763** (0.409-1.427)	**0.976** (0.573-1.663)
Category 3	**0.944** (0.541-1.646)	**0.738** (0.416-1.310)	**0.802** (0.442-1.457)	**0.943** (0.519-1.715)	**0.828** (0.481-1.424)
Category 4	**0.646** (0.372-1.123)	**0.842** (0.466-1.521)	**0.890** (0.491-1.611)	**0.975** (0.538-1.769)	---
Case Calendar-Year	**0.965** (0.951-0.979)	**0.965** (0.950-0.980)	**0.963** (0.947-0.979)	**0.963** (0.946-0.981)	**0.964** (0.944-0.985)
Hired before 1954	**1.001** (0.738-1.360)	**1.042** (0.764-1.421)	**1.089** (0.791-1.501)	**1.087** (0.780-1.513)	**1.053** (0.744-1.492)

* Exposure distributions for each category by lag period are listed in exhibit 6.

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Table 7
Mortality rate ratios for IHD by cumulative exposure category, including increasing 5-year lags of exposure, using case calendar-year and year of hire (pre-1954) as potential confounders; A) exposure categories based on case distribution, B) exposure categories based on cohort distribution.

A)	NO LAG N = 4,460	5-YEAR LAG N = 4,440	10-YEAR LAG N = 3,989	15-YEAR LAG N = 3,986	20-YEAR LAG N = 3,440
	MRR (95 % CI)	MRR (95 % CI)	MRR (95 % CI)	MRR (95 % CI)	MRR (95 % CI)
Reference*	1	1	1	1	1
Category 1	**1.046** (0.711-1.539)	**0.864** (0.579-1.291)	**0.996** (0.647-1.531)	**0.935** (0.598-1.461)	**0.647** (0.407-1.029)
Category 2	**1.156** (0.745-1.793)	**1.204** (0.757-1.914)	**1.377** (0.829-2.287)	**1.102** (0.644-1.887)	**0.692** (0.388-1.233)
Category 3	**1.110** (0.698-1.767)	**1.077** (0.657-1.764)	**1.610** (0.942-2.753)	**1.089** (0.597-1.984)	**0.764** (0.393-1.489)
Case Calendar-Year	**0.959** (0.942-0.977)	**0.958** (0.940-0.976)	**0.948** (0.928-0.968)	**0.958** (0.935-0.982)	**0.969** (0.943-0.997)
Hired before 1954	**0.946** (0.672-1.333)	**0.952** (0.671-1.352)	**0.903** (0.633-1.289)	**1.032** (0.710-1.501)	**1.096** (0.733-1.639)
B)					
Reference†	1	1	1	1	1
Category 1	**1.018** (0.515-2.010)	**0.980** (0.607-1.582)	**1.062** (0.662-1.680)	**0.914** (0.557-1.502)	**0.967** (0.568-1.647)
Category 2	**1.132** (0.573-2.235)	**1.014** (0.603-1.705)	**0.825** (0.483-1.409)	**0.860** (0.494-1.497)	**0.931** (0.505-1.717)
Category 3	**1.027** (0.496-2.127)	**1.019** (0.571-1.817)	**1.256** (0.721-2.191)	**1.069** (0.598-1.910)	**0.882** (0.461-1.688)
Case Calendar-Year	**0.961** (0.945-0.978)	**0.961** (0.943-0.980)	**0.954** (0.934-0.975)	**0.958** (0.936-0.981)	**0.967** (0.940-0.994)
Hired before 1954	**0.969** (0.692-1.357)	**1.008** (0.711-1.429)	**0.974** (0.679-1.398)	**1.027** (0.710-1.484)	**1.095** (0.742-1.614)

* Exposure distributions for each category by lag period are listed in exhibit 7A.

† Exposure distributions for each category by lag period are listed in exhibit 7B.

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FIGURES

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Figure 1.
Time in Job vs Serum PFOA–Cross-Sectional Study–Job Exposure Category 1

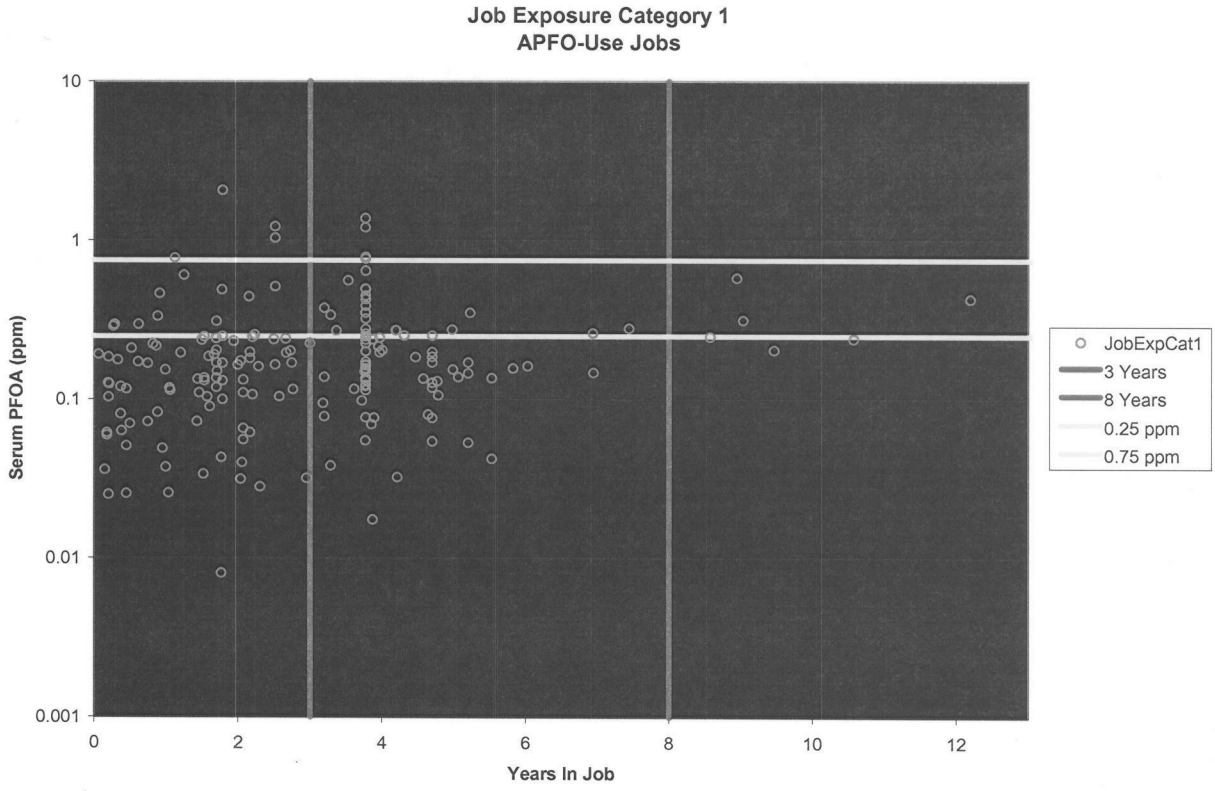

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Figure 2.
Time in Job vs Serum PFOA–Cross-Sectional Study–Job Exposure Category 2

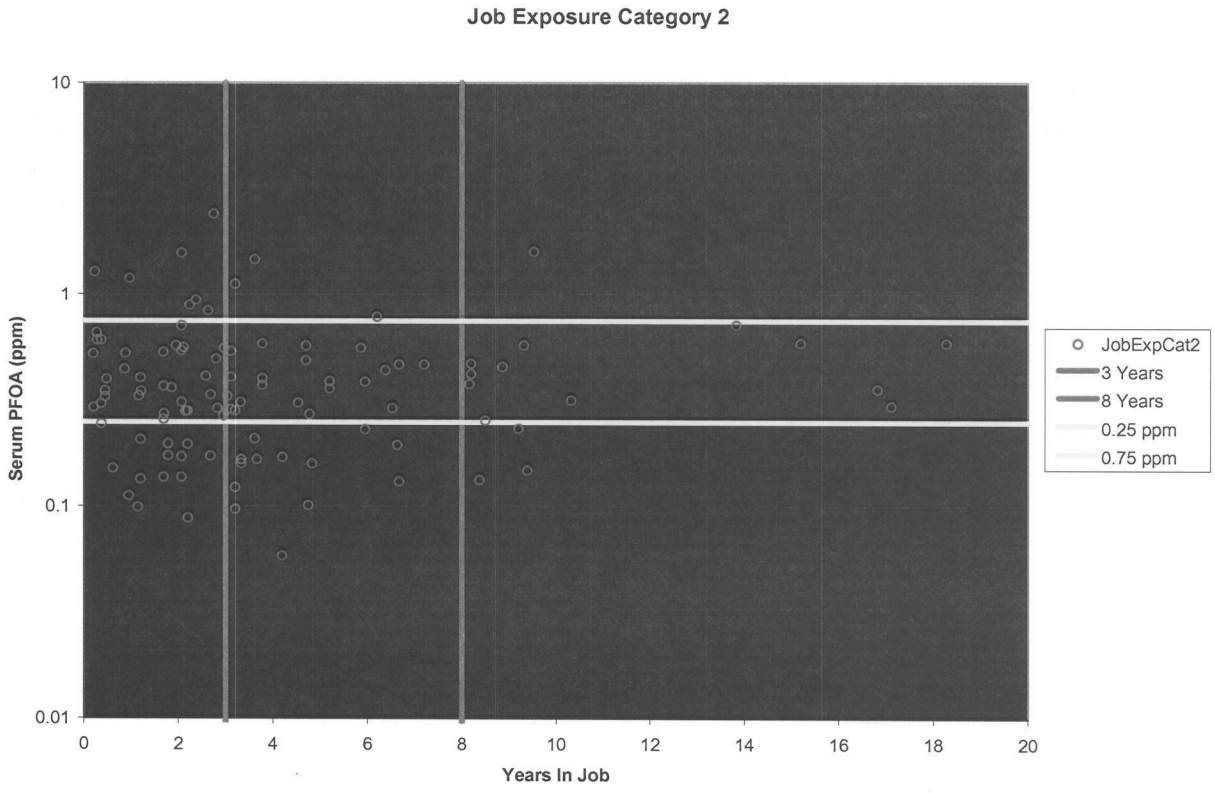

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Figure 3.
Time in Job vs Serum PFOA–Cross-Sectional Study–Job Exposure Category 3

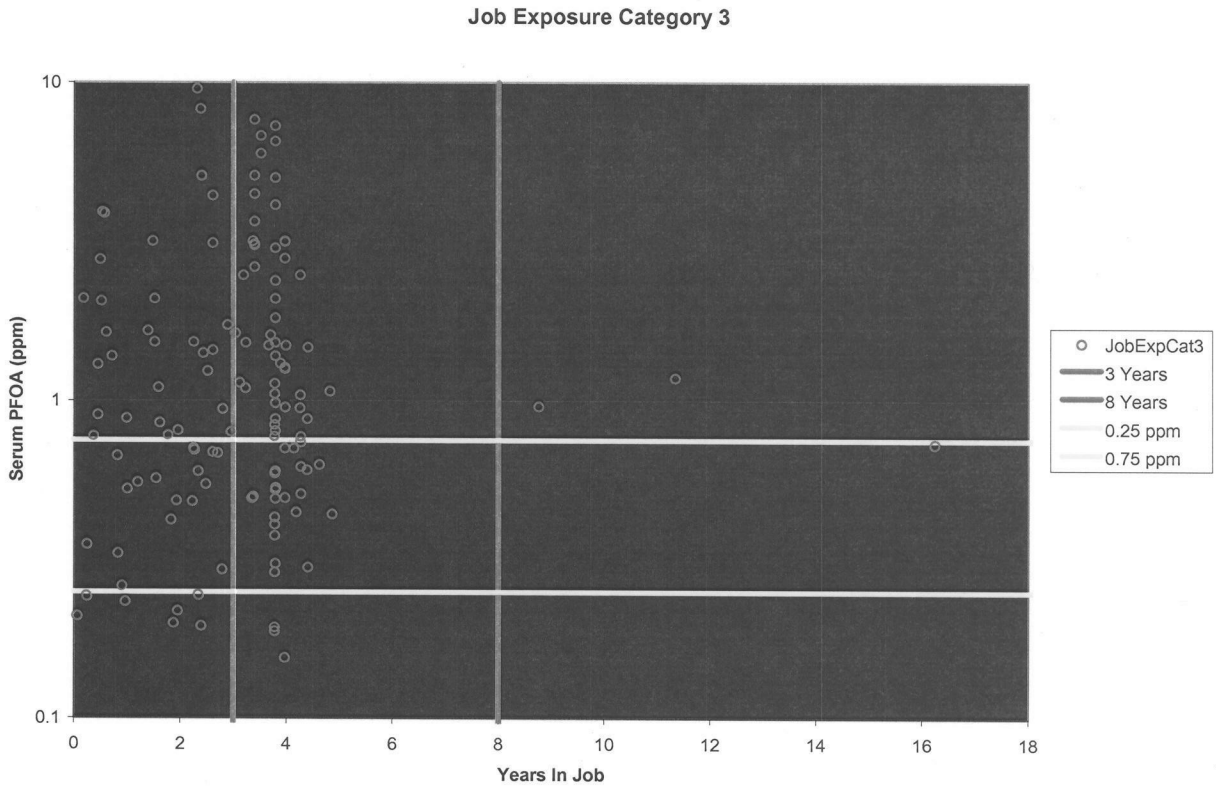

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Figure 4.
Serum PFOA vs Cumulative Exposure - FLAIR Data

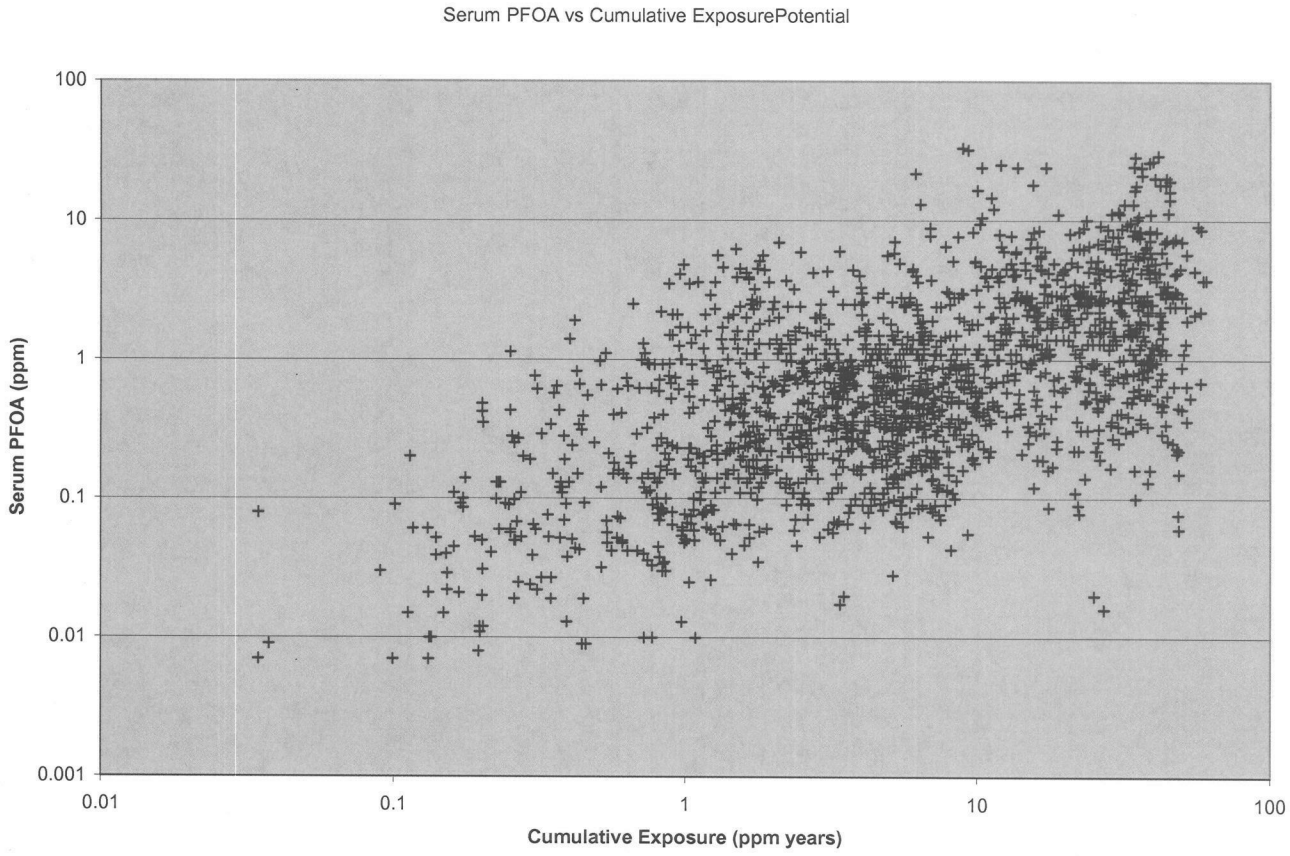

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Figure 5.
Serum PFOA vs Average Intensity of Exposure - FLAIR Data

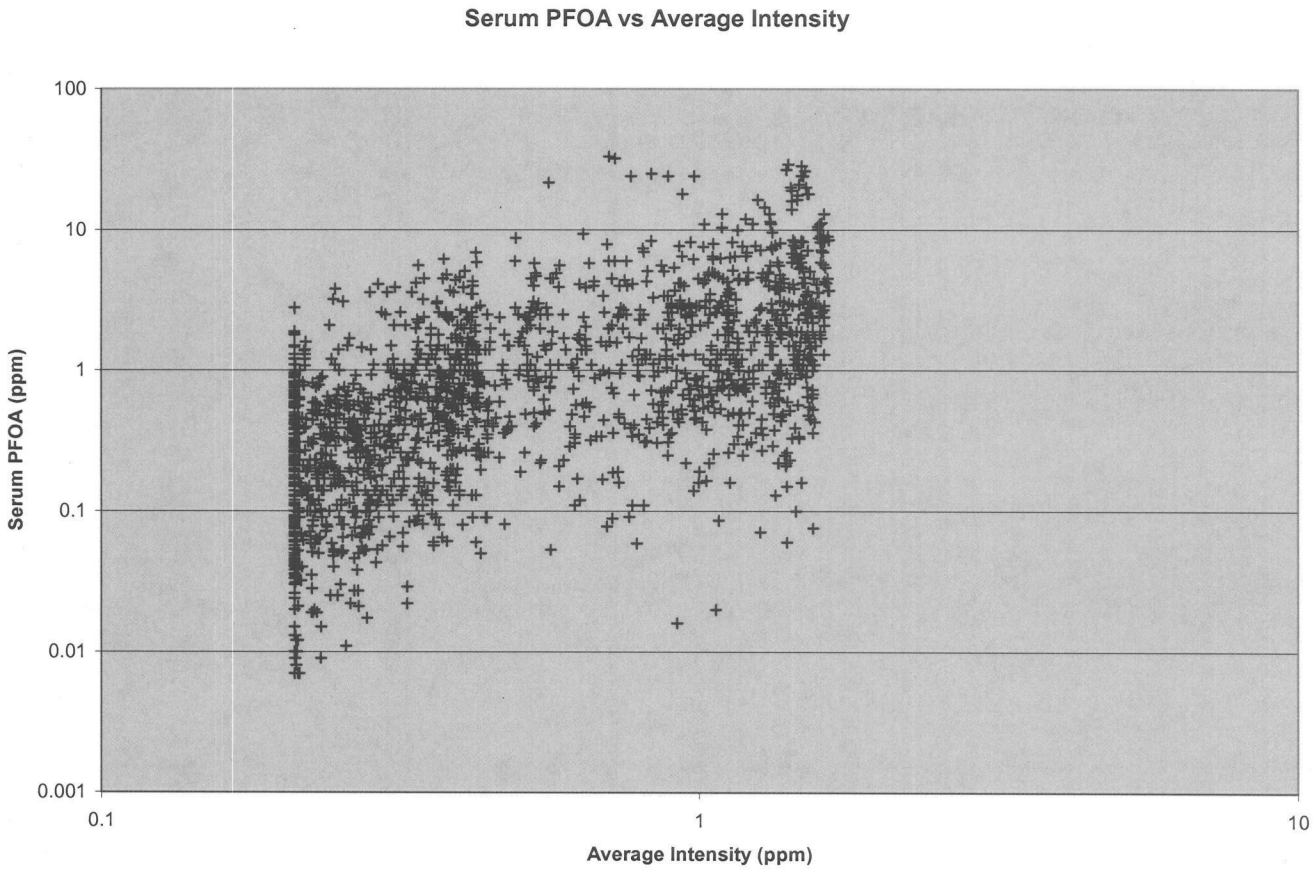

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Figure 6.
Serum PFOA vs Concurrent Job Intensity Factor - FLAIR Data

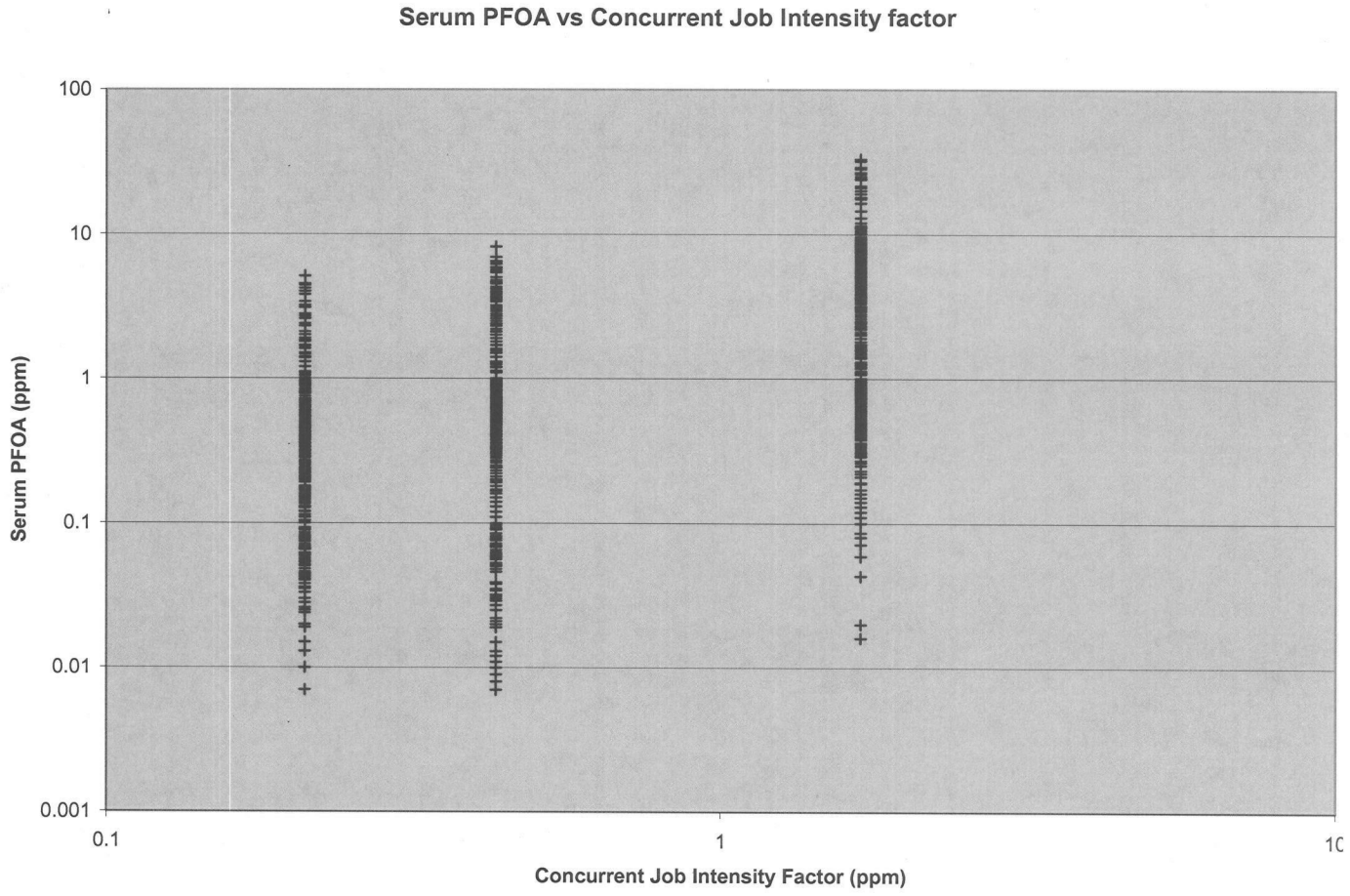

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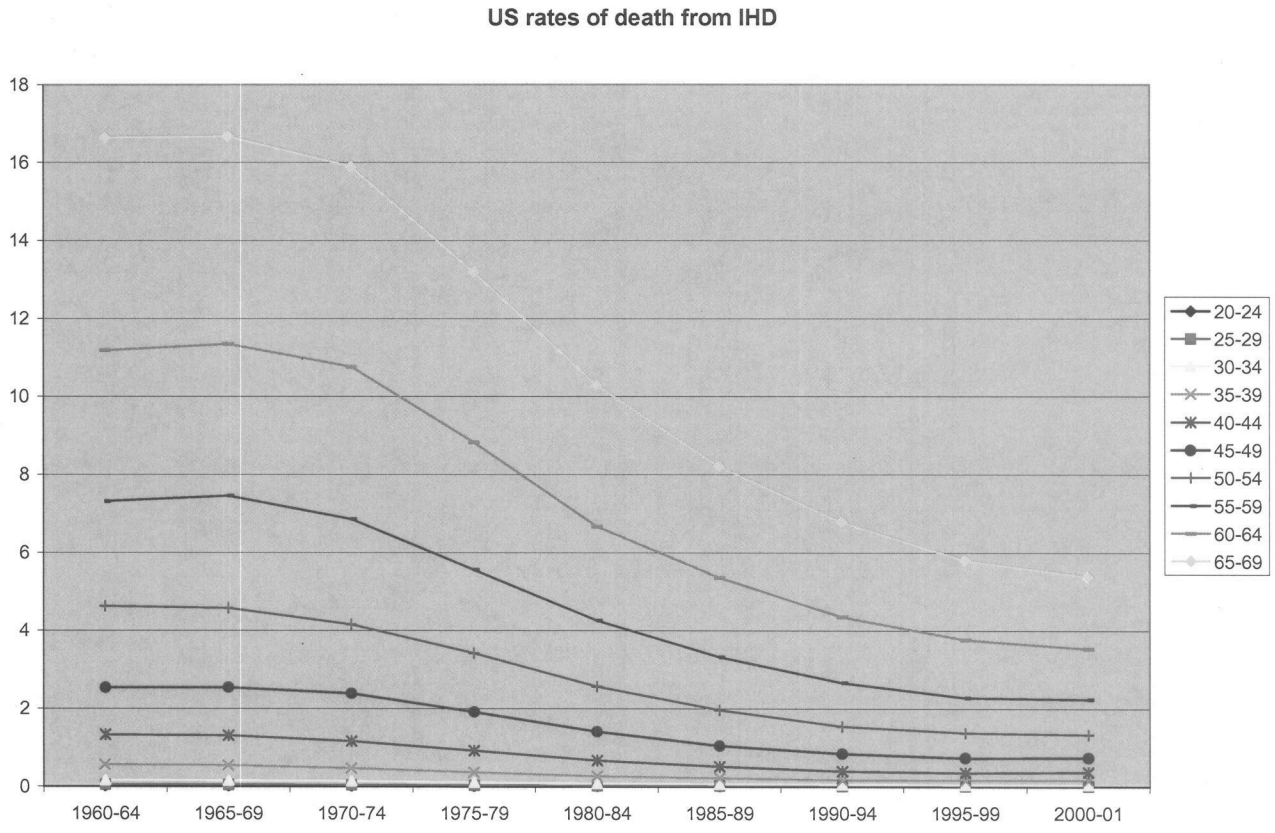
Figure 7.
Decreasing IHD mortality rates in the U.S.A.



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APPENDICES

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Appendix A
Washington Works vs Region 1
All-Cause Mortality Surveillance Report: Males

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
All Causes of Death	773	826.1	93.6		87.1	100.4	85.1	102.6
Tuberculosis	0	0.4	N/A		0.0	866.9	0.0	1245.0
All Malignant Neoplasms	222	221.2	100.4		87.6	114.5	83.8	119.1
Cancer of Buccal Cavity & Pharynx	4	3.2	123.5		33.6	316.1	20.7	388.7
Cancer of Digestive Organs & Peritoneum	49	52.6	93.2		69.0	123.2	62.5	133.3
Cancer of Esophagus	4	4.8	83.5		22.8	213.8	14.0	262.9
Cancer of Stomach	2	5.7	35.0		4.2	126.3	1.8	162.1
Cancer of Large Intestine	17	20.9	81.5		47.5	130.4	39.5	147.5
Cancer of Rectum	5	3.7	135.3		43.9	315.6	29.2	382.8
Cancer of Biliary Passages & Liver	7	5.3	133.1		53.5	274.2	38.7	325.7
Cancer of Pancreas	11	10.9	100.5		50.2	179.8	39.5	208.1
Cancer of All Other Digestive Organs	3	1.3	232.8		48.0	680.4	26.2	852.0
Cancer of Respiratory System	70	82.3	85.1		66.3	107.5	61.2	115.0
Cancer of Larynx	3	1.5	195.6		40.4	571.7	22.0	715.8
Cancer of Bronchus, Trachea, Lung	64	78.7	81.3		62.6	103.8	57.5	111.3
Cancer of All Other Respiratory	3	2.0	151.0		31.2	441.2	17.0	552.5
Cancer of Breast	0	0.3	N/A		0.0	1425.3	0.0	2046.9
Cancer of Prostate (males only)	12	18.4	65.3		33.8	114.1	26.9	131.5
Cancer of Testes and Other male genital Organs	1	0.6	169.7		4.2	945.7	0.8	1261.1
Cancer of Kidney	12	6.5	184.7		95.4	322.6	76.1	371.6
Cancer of Bladder and Other Urinary Organs	7	5.4	130.7		52.6	269.4	38.0	320.0
Malignant Melanoma of Skin	2	4.4	45.5		5.5	164.4	2.3	211.0
Cancer of Eye	0	0.4	N/A		0.0	886.7	0.0	1273.5
Cancer of Central Nervous System	9	6.9	130.1		59.5	246.9	45.3	289.0
Cancer of Thyroid & Other Endocrine Glands	3	0.5	633.2	*	130.7	1850.4	71.3	2316.9
Cancer of Bone	2	0.3	648.3		78.4	2342.1	33.4	3006.3
Cancer of All Lymphatic, Haematopoietic Tissue	29	24.0	120.7		80.8	173.4	70.8	191.4
Non-Hodgkins Lymphoma	9	8.2	109.9		50.3	208.6	38.2	244.2
Hodgkins Disease	2	1.1	179.8		21.8	649.5	9.3	833.7
Leukemia & Aleukemia	12	10.3	116.1		60.0	202.8	47.8	233.6
Cancer of All Other Lymphopoietic Tissue	6	4.4	136.7		50.2	297.6	35.0	356.9
All Other Malignant Neoplasms	22	15.5	141.9		88.9	214.8	76.0	240.0

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Appendix A
Washington Works vs Region 1
All-Cause Mortality Surveillance Report: Males (Continued)

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
Benign Neoplasms	1	2.4	42.0		1.0	233.8	0.2	311.7
Diabetes Mellitus	20	10.9	183.1	*	111.8	282.8	94.8	317.4
Cerebrovascular Disease	34	39.5	86.1		59.6	120.3	52.8	132.0
All Heart Disease	309	281.0	109.9		98.0	122.9	94.5	127.1
Rheumatic Heart Disease	5	1.7	302.5		98.2	706.0	65.2	856.2
Ischemic Heart Disease	236	215.9	109.3		95.8	124.2	91.8	129.0
Chronic Endocard. Dis.; Other Myocard. Insuff.	11	10.3	106.4		53.1	190.3	41.8	220.2
Hypertension with Heart Disease	1	6.2	16.2	*	0.4	90.1	0.1	120.1
All Other Heart Disease	56	46.9	119.4		90.2	155.0	82.3	166.9
Hypertension w/o Heart Disease	5	2.3	214.4		69.6	500.4	46.2	606.8
Non-malignant Respiratory Disease	46	50.5	91.1		66.7	121.6	60.2	131.8
Influenza & Pneumonia	14	15.4	90.7		49.6	152.1	40.4	173.8
Bronchitis, Emphysema, Asthma	11	11.2	98.6		49.2	176.5	38.7	204.2
Bronchitis	5	3.7	133.8		43.4	312.1	28.8	378.5
Emphysema	6	6.7	88.9		32.6	193.6	22.8	232.1
Asthma	0	0.7	N/A		0.0	551.5	0.0	792.0
Other Non-malignant Respiratory Disease	21	23.9	88.0		54.4	134.4	46.4	150.6
Ulcer of Stomach & Duodenum	0	1.5	N/A		0.0	242.9	0.0	348.8
Cirrhosis of Liver	8	9.2	86.9		37.5	171.2	27.9	201.8
Nephritis & Nephrosis	8	6.0	132.5		57.2	261.1	42.6	307.8
All External Causes of Death	41	65.2	62.9	**	45.1	85.3	40.5	92.9
Accidents	31	40.4	76.7		52.1	108.9	45.9	119.9
Motor Vehicle Accidents	20	22.8	87.6		53.5	135.3	45.3	151.9
All Other Accidents	11	17.6	62.6		31.3	112.0	24.6	129.7
Suicides	8	19.1	41.8	**	18.1	82.4	13.4	97.2
Homicides & Other External Causes	2	5.7	35.3		4.3	127.4	1.8	163.5
All Other Causes of Death	78	72.1	108.1		85.5	134.9	79.2	143.8
CERTAIN INFECTIOUS AND PARASITIC DISEASES	1	1.0	100.1		2.5	557.9	0.5	743.9
Unknown Causes (In All Causes Category Only)	0							
(*) SIGNIFICANT AT 5% LEVEL; (**) SIGNIFICANT AT 1% LEVEL								

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Appendix A
Washington Works vs Region 1
All-Cause Mortality Surveillance Report: Females

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
All Causes of Death	33	22.4	147.2	*	101.3	206.7	89.5	226.9
Tuberculosis	0	0.0	N/A		0.0	491866.7	0.0	706400.0
All Malignant Neoplasms	12	8.1	149.0		77.0	260.3	61.4	299.8
Cancer of Buccal Cavity & Pharynx	0	0.2	N/A		0.0	2064.0	0.0	2964.2
Cancer of Digestive Organs & Peritoneum	2	1.5	130.2		15.8	470.4	6.7	603.8
Cancer of Esophagus	0	0.0	N/A		0.0	14899.0	0.0	21397.4
Cancer of Stomach	1	0.0	2586.7		64.7	14412.8	12.9	19218.8
Cancer of Large Intestine	0	0.8	N/A		0.0	440.6	0.0	632.7
Cancer of Rectum	0	0.1	N/A		0.0	4151.5	0.0	5962.2
Cancer of Biliary Passages & Liver	1	0.3	384.8		9.6	2144.2	1.9	2859.2
Cancer of Pancreas	0	0.3	N/A		0.0	1467.2	0.0	2107.1
Cancer of All Other Digestive Organs	0	0.0	N/A		0.0	10537.0	0.0	15132.8
Cancer of Respiratory System	2	1.5	132.2		16.0	477.5	6.8	613.0
Cancer of Larynx	0	0.0	N/A		0.0	43969.0	0.0	63146.6
Cancer of Bronchus, Trachea, Lung	2	1.5	132.9		16.1	480.2	6.8	616.4
Cancer of All Other Respiratory	0	0.0	N/A		N/A			
Cancer of Breast	2	2.6	77.4		9.4	279.8	4.0	359.1
All Uterine Cancers (Females only)	0	0.0	N/A		0.0	17174.1	0.0	24664.8
Cancer of Cervix Uteri (Females only)	0	0.0	N/A		0.0	20449.0	0.0	29368.1
Cancer of Other Female Genital Organs	0	0.7	N/A		0.0	516.9	0.0	742.3
Cancer of Kidney	0	0.1	N/A		0.0	2793.4	0.0	4011.8
Cancer of Bladder and Other Urinary Organs	0	0.0	N/A		0.0	20841.8	0.0	29932.2
Malignant Melanoma of Skin	1	0.0	2138.6		53.5	11916.2	10.7	15889.6
Cancer of Eye	0	0.0	N/A		0.0	40988.9	0.0	58866.7
Cancer of Central Nervous System	0	0.2	N/A		0.0	1903.6	0.0	2733.9
Cancer of Thyroid & Other Endocrine Glands	0	0.0	N/A		0.0	105702.0	0.0	151805.2
Cancer of Bone	0	0.0	N/A		N/A			
Cancer of All Lymphatic, Haematopoietic Tissue	3	0.8	395.0		81.5	1154.4	44.5	1445.4
Non-Hodgkins Lymphoma	0	0.1	N/A		0.0	2890.2	0.0	4150.7
Hodgkins Disease	0	0.2	N/A		0.0	2072.1	0.0	2975.9
Leukemia & Aleukemia	1	0.3	292.7		7.3	1630.9	1.5	2174.7
Cancer of All Other Lymphopoietic Tissue	2	0.1	1783.8	*	215.8	6444.0	91.9	8271.5
All Other Malignant Neoplasms	2	0.3	611.0		73.9	2207.3	31.5	2833.3

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Appendix A
Washington Works vs Region 1
All-Cause Mortality Surveillance Report: Females (continued)

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
Benign Neoplasms	0	0.0	N/A		0.0	18528.4	0.0	26609.7
Diabetes Mellitus	2	0.3	796.1		96.3	2876.1	41.0	3691.7
Cerebrovascular Disease	1	1.1	90.5		2.3	504.4	0.5	672.6
All Heart Disease	5	3.5	142.7		46.3	333.0	30.8	403.8
Rheumatic Heart Disease	0	0.1	N/A		0.0	4456.4	0.0	6400.1
Ischemic Heart Disease	3	2.2	135.0		27.8	394.4	15.2	493.8
Chronic Endocard. Dis.; Other Myocard. Insuff.	0	0.1	N/A		0.0	3005.8	0.0	4316.8
Hypertension with Heart Disease	0	0.2	N/A		0.0	1724.2	0.0	2476.3
All Other Heart Disease	2	0.9	232.2		28.1	838.7	12.0	1076.5
Hypertension w/o Heart Disease	0	0.1	N/A		0.0	3461.6	0.0	4971.4
Non-malignant Respiratory Disease	3	1.0	294.6		60.8	860.8	33.2	1077.8
Influenza & Pneumonia	0	0.3	N/A		0.0	1292.5	0.0	1856.3
Bronchitis, Emphysema, Asthma	2	0.3	679.9		82.3	2456.1	35.0	3152.6
Bronchitis	1	0.1	756.4		18.9	4214.8	3.8	5620.3
Emphysema	1	0.1	1411.6		35.3	7865.6	7.1	10488.4
Asthma	0	0.1	N/A		0.0	4048.1	0.0	5813.7
Other Non-malignant Respiratory Disease	1	0.4	227.9		5.7	1269.6	1.1	1692.9
Ulcer of Stomach & Duodenum	0	0.0	N/A		0.0	8221.5	0.0	11807.4
Cirrhosis of Liver	1	0.1	804.8		20.1	4484.5	4.0	5979.9
Nephritis & Nephrosis	0	0.1	N/A		0.0	2671.3	0.0	3836.4
All External Causes of Death	4	3.1	130.8		35.7	335.0	22.0	412.0
Accidents	4	1.6	247.3		67.4	633.3	41.6	778.7
Motor Vehicle Accidents	3	1.4	215.7		44.5	630.4	24.3	789.3
All Other Accidents	1	0.2	441.4		11.0	2459.5	2.2	3279.6
Suicides	0	0.6	N/A		0.0	660.3	0.0	948.3
Homicides & Other External Causes	0	0.9	N/A		0.0	418.6	0.0	601.2
All Other Causes of Death	5	2.2	223.2		72.4	520.7	48.1	631.5
CERTAIN INFECTIOUS AND PARASITIC DISEASES	0	0.1	N/A		0.0	6277.0	0.0	9014.8
Unknown Causes (In All Causes Category Only)	0							
(*) SIGNIFICANT AT 5% LEVEL; (**) SIGNIFICANT AT 1% LEVEL								

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Appendix A
Washington Works vs Region 1
All-Cause Mortality Surveillance Report: Totals (Males and Females)

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
All Causes of Death	806	848.5	95.0		88.5	101.8	86.6	104.0
Tuberculosis	0	0.4	N/A		0.0	865.4	0.0	1242.8
All Malignant Neoplasms	234	229.2	102.1		89.4	116.0	85.7	120.6
Cancer of Buccal Cavity & Pharynx	4	3.4	117.0		31.9	299.6	19.7	368.4
Cancer of Digestive Organs & Peritoneum	51	54.1	94.3		70.2	123.9	63.7	133.9
Cancer of Esophagus	4	4.8	83.1		22.6	212.7	14.0	261.5
Cancer of Stomach	3	5.8	52.1		10.7	152.2	5.9	190.6
Cancer of Large Intestine	17	21.7	78.3		45.6	125.4	38.0	141.9
Cancer of Rectum	5	3.8	132.1		42.9	308.2	28.5	373.8
Cancer of Biliary Passages & Liver	8	5.5	144.9		62.6	285.6	46.6	336.6
Cancer of Pancreas	11	11.2	98.2		49.0	175.8	38.6	203.4
Cancer of All Other Digestive Organs	3	1.3	226.7		46.8	662.4	25.5	829.4
Cancer of Respiratory System	72	83.8	85.9		67.2	108.2	62.1	115.6
Cancer of Larynx	3	1.5	194.6		40.1	568.6	21.9	711.9
Cancer of Bronchus, Trachea, Lung	66	80.3	82.2		63.6	104.6	58.5	112.1
Cancer of All Other Respiratory	3	2.0	151.0		31.2	441.2	17.0	552.5
Cancer of Breast	2	2.8	70.4		8.5	254.3	3.6	326.4
All Uterine Cancers (females only)	0	0.0	N/A		0.0	17174.1	0.0	24664.8
Cancer of Cervix Uteri (females only)	0	0.0	N/A		0.0	20449.0	0.0	29368.1
Cancer of Other Female genital Organs	0	0.7	N/A		0.0	516.9	0.0	742.3
Cancer of Prostate (males only)	12	18.4	65.3		33.8	114.1	26.9	131.5
Cancer of Testes and Other male genital Organs	1	0.6	169.7		4.2	945.7	0.8	1261.1
Cancer of Kidney	12	6.6	181.0		93.5	316.2	74.6	364.2
Cancer of Bladder and Other Urinary Organs	7	5.4	130.3		52.4	268.5	37.9	318.9
Malignant Melanoma of Skin	3	4.4	67.5		13.9	197.4	7.6	247.2
Cancer of Eye	0	0.4	N/A		0.0	867.9	0.0	1246.5
Cancer of Central Nervous System	9	7.1	126.5		57.8	240.2	44.0	281.1
Cancer of Thyroid & Other Endocrine Glands	3	0.5	628.6	*	129.7	1836.9	70.8	2300.0
Cancer of Bone	2	0.3	648.3		78.4	2342.1	33.4	3006.3
Cancer of All Lymphatic, Haematopoietic Tissue	32	24.8	129.1		88.3	182.3	77.9	200.4
Non-Hodgkins Lymphoma	9	8.3	108.2		49.5	205.4	37.7	240.5
Hodgkins Disease	2	1.3	155.0		18.8	559.9	8.0	718.7
Leukemia & Aleukemia	13	10.7	121.8		64.8	208.2	52.3	238.8
Cancer of All Other Lymphopoietic Tissue	8	4.5	177.8		76.8	350.3	57.1	412.8
All Other Malignant Neoplasms	24	15.8	151.6		97.1	225.5	83.7	251.0

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Appendix A
Washington Works vs Region 1
All-Cause Mortality Surveillance Report: Totals (Males and Females) (continued)

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
Benign Neoplasms	1	2.4	41.6		1.0	231.8	0.2	309.2
Diabetes Mellitus	22	11.2	196.9	**	123.4	298.1	105.5	333.1
Cerebrovascular Disease	35	40.6	86.2		60.1	119.9	53.3	131.4
All Heart Disease	314	284.5	110.4		98.5	123.3	94.9	127.5
Rheumatic Heart Disease	5	1.7	288.1		93.5	672.3	62.1	815.3
Ischemic Heart Disease	239	218.2	109.5		96.1	124.4	92.1	129.2
Chronic Endocard. Dis.; Other Myocard. Insuff.	11	10.5	105.1		52.5	188.1	41.3	217.7
Hypertension with Heart Disease	1	6.4	15.6	*	0.4	87.1	0.1	116.1
All Other Heart Disease	58	47.8	121.4		92.2	156.9	84.3	168.8
Hypertension w/o Heart Disease	5	2.4	205.1		66.6	478.5	44.2	580.3
Non-malignant Respiratory Disease	49	51.5	95.2		70.4	125.8	63.8	136.1
Influenza & Pneumonia	14	15.7	89.0		48.7	149.4	39.6	170.6
Bronchitis, Emphysema, Asthma	13	11.4	113.6		60.5	194.2	48.7	222.7
Bronchitis	6	3.9	155.0		56.9	337.4	39.7	404.6
Emphysema	7	6.8	102.7		41.3	211.5	29.9	251.3
Asthma	0	0.8	N/A		0.0	485.4	0.0	697.1
Other Non-malignant Respiratory Disease	22	24.3	90.5		56.7	137.0	48.5	153.1
Ulcer of Stomach & Duodenum	0	1.6	N/A		0.0	235.9	0.0	338.8
Cirrhosis of Liver	9	9.3	96.5		44.1	183.1	33.6	214.3
Nephritis & Nephrosis	8	6.2	129.6		55.9	255.3	41.6	300.9
All External Causes of Death	45	68.2	65.9	**	48.1	88.2	43.4	95.7
Accidents	35	42.0	83.3		58.0	115.9	51.5	126.9
Motor Vehicle Accidents	23	24.2	95.0		60.2	142.5	51.7	158.9
All Other Accidents	12	17.8	67.4		34.9	117.8	27.8	135.7
Suicides	8	19.7	40.7	**	17.6	80.1	13.1	94.4
Homicides & Other External Causes	2	6.6	30.5		3.7	110.3	1.6	141.5
All Other Causes of Death	83	74.4	111.6		88.9	138.3	82.6	147.2
CERTAIN INFECTIOUS AND PARASITIC DISEASES	1	1.1	94.6		2.4	526.9	0.5	702.6
Unknown Causes (In All Causes Category Only)	0							
(*) SIGNIFICANT AT 5% LEVEL; (**) SIGNIFICANT AT 1% LEVEL								

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Appendix B
Washington Works vs USA
All-Cause Mortality Surveillance Report: Males

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
All Causes of Death	773	1167.0	66.2	**	61.6	71.1	60.3	72.6
Tuberculosis	0	2.0	N/A		0.0	183.7	0.0	263.9
All Malignant Neoplasms	222	301.2	73.7	**	64.3	84.1	61.6	87.5
Cancer of Buccal Cavity & Pharynx	4	7.6	52.9		14.4	135.5	8.9	166.6
Cancer of Digestive Organs & Peritoneum	49	74.1	66.2	**	49.0	87.5	44.4	94.6
Cancer of Esophagus	4	9.6	41.5		11.3	106.4	7.0	130.8
Cancer of Stomach	2	9.8	20.5	**	2.5	74.0	1.1	95.0
Cancer of Large Intestine	17	24.5	69.4		40.4	111.1	33.7	125.7
Cancer of Rectum	5	5.3	94.7		30.7	220.9	20.4	267.9
Cancer of Biliary Passages & Liver	7	7.8	89.7		36.1	184.9	26.1	219.6
Cancer of Pancreas	11	14.9	74.0		36.9	132.3	29.1	153.2
Cancer of All Other Digestive Organs	3	2.2	135.9		28.0	397.2	15.3	497.3
Cancer of Respiratory System	70	110.6	63.3	**	49.3	80.0	45.5	85.5
Cancer of Larynx	3	3.9	76.7		15.8	224.0	8.6	280.5
Cancer of Bronchus, Trachea, Lung	64	105.6	60.6	**	46.7	77.4	42.9	83.0
Cancer of All Other Respiratory	3	1.0	293.1		60.5	856.5	33.0	1072.4
Cancer of Breast	0	0.4	N/A		0.0	952.7	0.0	1368.3
Cancer of Prostate (males only)	12	23.2	51.8	*	26.8	90.5	21.3	104.2
Cancer of Testes and other male Genital Organs	1	1.2	86.9		2.2	484.0	0.4	645.4
Cancer of Kidney	12	7.7	155.7		80.4	271.9	64.1	313.2
Cancer of Bladder and Other Urinary Organs	7	6.9	101.4		40.8	208.9	29.5	248.1
Malignant Melanoma of Skin	2	5.1	39.0		4.7	140.7	2.0	180.7
Cancer of Eye	0	0.2	N/A		0.0	2299.0	0.0	3301.8
Cancer of Central Nervous System	9	8.6	105.0		48.0	199.4	36.5	233.3
Cancer of Thyroid & Other Endocrine Glands	3	0.9	332.2		68.5	970.7	37.4	1215.3
Cancer of Bone	2	0.8	251.6		30.4	909.0	13.0	1166.8
Cancer of All Lymphatic, Haematopoietic Tissue	29	29.6	98.0		65.6	140.7	57.4	155.3
Hodgkins Disease	2	1.9	103.3		12.5	373.0	5.3	478.8
Non-Hodgkins Lymphoma	9	11.3	80.0		36.6	151.9	27.8	177.8
Leukemia & Aleukemia	12	11.1	107.8		55.7	188.3	44.4	216.9
Cancer of All Other Lymphopoietic Tissue	6	5.3	113.8		41.8	247.8	29.2	297.1
All Other Malignant Neoplasms	22	24.5	89.9		56.3	136.1	48.2	152.1

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Appendix B
Washington Works vs USA
All-Cause Mortality Surveillance Report: Males (continued)

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
Benign Neoplasms	1	2.9	35.1		0.9	195.3	0.2	260.5
Diabetes Mellitus	20	24.6	81.2		49.6	125.3	42.0	140.7
Cerebrovascular Disease	34	55.8	60.9	**	42.2	85.1	37.3	93.3
All Heart Disease	309	386.5	80.0	**	71.3	89.4	68.7	92.5
Rheumatic Heart Disease	5	4.0	125.7		40.8	293.4	27.1	355.8
Ischemic Heart Disease	236	289.8	81.4	**	71.4	92.5	68.4	96.1
Chronic Endocard. Dis.; Other Myocard. Insuff.	11	13.1	83.7		41.8	149.7	32.9	173.2
Hypertension with Heart Disease	1	11.8	8.5	**	0.2	47.3	0.0	63.1
All Other Heart Disease	56	67.8	82.6		62.4	107.3	57.0	115.6
Hypertension w/o Heart Disease	5	4.6	108.3		35.2	252.8	23.4	306.6
Non-malignant Respiratory Disease	46	85.4	53.9	**	39.4	71.9	35.6	77.9
Influenza & Pneumonia	14	25.8	54.3	*	29.7	91.1	24.2	104.1
Bronchitis, Emphysema, Asthma	11	23.3	47.2	**	23.6	84.5	18.5	97.7
Bronchitis	5	11.2	44.7		14.5	104.4	9.6	126.6
Emphysema	6	10.3	58.5		21.5	127.3	15.0	152.7
Asthma	0	1.9	N/A		0.0	197.5	0.0	283.7
Other Non-malignant Respiratory Disease	21	36.3	57.9	**	35.8	88.5	30.5	99.0
Ulcer of Stomach & Duodenum	0	3.5	N/A		0.0	105.7	0.0	151.7
Cirrhosis of Liver	8	29.0	27.6	**	11.9	54.4	8.9	64.1
Nephritis & Nephrosis	8	10.7	74.7		32.3	147.2	24.0	173.5
All External Causes of Death	41	124.4	33.0	**	23.7	44.7	21.2	48.7
Accidents	31	73.9	42.0	**	28.5	59.6	25.1	65.6
Motor Vehicle Accidents	20	36.2	55.2	**	33.7	85.2	28.6	95.7
All Other Accidents	11	37.7	29.2	**	14.6	52.3	11.5	60.5
Suicides	8	28.5	28.0	**	12.1	55.2	9.0	65.1
Homicides & Other External Causes	2	22.0	9.1	**	1.1	32.9	0.5	42.2
All Other Causes of Death	78	127.4	61.2	**	48.4	76.4	44.9	81.5
Certain Infectious and Parasitic Diseases	1	14.3	7.0	**	0.2	38.9	0.0	51.9
Unknown Causes (In All Causes Category Only)	0							
(*) SIGNIFICANT AT 5% LEVEL; (**) SIGNIFICANT AT 1% LEVEL								

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Appendix B
Washington Works vs USA
All-Cause Mortality Surveillance Report: Females

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
All Causes of Death	33	40.9	80.7		55.5	113.3	49.1	124.4
Tuberculosis	0	0.0	N/A		0.0	8275.0	0.0	11884.3
All Malignant Neoplasms	12	13.8	86.6		44.8	151.4	35.7	174.3
Cancer of Buccal Cavity & Pharynx	0	0.1	N/A		0.0	2486.0	0.0	3570.3
Cancer of Digestive Organs & Peritoneum	2	2.4	84.0		10.2	303.4	4.3	389.5
Cancer of Esophagus	0	0.1	N/A		0.0	3070.1	0.0	4409.1
Cancer of Stomach	1	0.3	397.1		9.9	2212.9	2.0	2950.8
Cancer of Large Intestine	0	0.9	N/A		0.0	388.6	0.0	558.0
Cancer of Rectum	0	0.2	N/A		0.0	2150.8	0.0	3088.9
Cancer of Biliary Passages & Liver	1	0.3	394.5		9.9	2197.9	2.0	2930.9
Cancer of Pancreas	0	0.5	N/A		0.0	698.4	0.0	1003.0
Cancer of All Other Digestive Organs	0	0.1	N/A		0.0	3466.8	0.0	4978.9
Cancer of Respiratory System	2	3.0	67.7		8.2	244.5	3.5	313.9
Cancer of Larynx	0	0.0	N/A		0.0	8045.8	0.0	11555.1
Cancer of Bronchus, Trachea, Lung	2	2.9	69.5		8.4	251.0	3.6	322.2
Cancer of All Other Respiratory	0	0.0	N/A		0.0	11919.2	0.0	17117.9
Cancer of Breast	2	3.3	61.1		7.4	220.6	3.1	283.1
All Uterine Cancers (Females only)	0	0.9	N/A		0.0	419.5	0.0	602.5
Cancer of Cervix Uteri (Females only)	0	0.6	N/A		0.0	636.4	0.0	914.0
Cancer of Other Female Genital Organs	0	0.9	N/A		0.0	416.4	0.0	598.0
Cancer of Kidney	0	0.2	N/A		0.0	1793.7	0.0	2576.0
Cancer of Bladder and Other Urinary Organs	0	0.1	N/A		0.0	3722.5	0.0	5346.1
Malignant Melanoma of Skin	1	0.2	422.2		10.6	2352.3	2.1	3136.7
Cancer of Eye	0	0.0	N/A		0.0	52400.6	0.0	75255.7
Cancer of Central Nervous System	0	0.4	N/A		0.0	834.8	0.0	1199.0
Cancer of Thyroid & Other Endocrine Glands	0	0.1	N/A		0.0	6334.1	0.0	9096.8
Cancer of Bone	0	0.0	N/A		0.0	8833.8	0.0	12686.8
Cancer of All Lymphatic, Haematopoietic Tissue	3	1.2	245.5		50.6	717.4	27.7	898.2
Hodgkins Disease	0	0.1	N/A		0.0	3891.4	0.0	5588.6
Non-Hodgkins Lymphoma	0	0.5	N/A		0.0	811.3	0.0	1165.2
Leukemia & Aleukemia	1	0.5	207.0		5.2	1153.4	1.0	1538.0
Cancer of All Other Lymphopoietic Tissue	2	0.2	1057.3	*	127.9	3819.5	54.5	4902.7
All Other Malignant Neoplasms	2	1.0	197.7		23.9	714.1	10.2	916.6

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Appendix B
Washington Works vs USA
All-Cause Mortality Surveillance Report: Females (continued)

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
Benign Neoplasms	0	0.1	N/A		0.0	2467.4	0.0	3543.6
Diabetes Mellitus	2	1.2	160.8		19.5	580.7	8.3	745.4
Cerebrovascular Disease	1	2.1	48.7		1.2	271.6	0.2	362.2
All Heart Disease	5	7.8	64.4		20.9	150.2	13.9	182.2
Rheumatic Heart Disease	0	0.2	N/A		0.0	1694.6	0.0	2433.7
Ischemic Heart Disease	3	4.7	64.0		13.2	187.1	7.2	234.3
Chronic Endocard. Dis.; Other Myocard. Insuff.	0	0.4	N/A		0.0	1017.5	0.0	1461.3
Hypertension with Heart Disease	0	0.4	N/A		0.0	852.1	0.0	1223.7
All Other Heart Disease	2	2.1	96.7		11.7	349.4	5.0	448.5
Hypertension w/o Heart Disease	0	0.2	N/A		0.0	2038.1	0.0	2927.1
Non-malignant Respiratory Disease	3	2.5	119.6		24.7	349.5	13.5	437.6
Influenza & Pneumonia	0	0.7	N/A		0.0	535.7	0.0	769.4
Bronchitis, Emphysema, Asthma	2	0.9	228.8		27.7	826.4	11.8	1060.8
Bronchitis	1	0.4	236.2		5.9	1315.9	1.2	1754.7
Emphysema	1	0.2	447.2		11.2	2491.9	2.2	3322.9
Asthma	0	0.2	N/A		0.0	1623.5	0.0	2331.6
Other Non-malignant Respiratory Disease	1	0.9	105.7		2.6	589.2	0.5	785.6
Ulcer of Stomach & Duodenum	0	0.1	N/A		0.0	4846.9	0.0	6961.0
Cirrhosis of Liver	1	0.9	105.5		2.6	588.0	0.5	784.1
Nephritis & Nephrosis	0	0.4	N/A		0.0	915.7	0.0	1315.1
All External Causes of Death	4	5.3	75.5		20.6	193.2	12.7	237.6
Accidents	4	3.1	129.6		35.3	331.7	21.8	407.9
Motor Vehicle Accidents	3	1.9	156.4		32.3	457.0	17.6	572.2
All Other Accidents	1	1.2	85.6		2.1	476.7	0.4	635.7
Suicides	0	1.1	N/A		0.0	328.2	0.0	471.3
Homicides & Other External Causes	0	1.1	N/A		0.0	338.6	0.0	486.3
All Other Causes of Death	5	5.8	86.1		27.9	200.8	18.6	243.6
Certain Infectious and Parasitic Diseases	0	0.7	N/A		0.0	543.5	0.0	780.6
Unknown Causes (In All Causes Category Only)	0							
(*) SIGNIFICANT AT 5% LEVEL; (**) SIGNIFICANT AT 1% LEVEL								

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Appendix B
Washington Works vs USA
All-Cause Mortality Surveillance Report: Totals (Males and Females)

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
All Causes of Death	806	1207.9	66.7	**	62.2	71.5	60.8	73.0
Tuberculosis	0	2.1	N/A		0.0	179.7	0.0	258.1
All Malignant Neoplasms	234	315.0	74.3	**	65.1	84.4	62.4	87.8
Cancer of Buccal Cavity & Pharynx	4	7.7	51.9		14.1	132.9	8.7	163.4
Cancer of Digestive Organs & Peritoneum	51	76.4	66.7	**	49.7	87.7	45.1	94.8
Cancer of Esophagus	4	9.7	41.0		11.2	105.1	6.9	129.2
Cancer of Stomach	3	10.0	30.0	*	6.2	87.6	3.4	109.6
Cancer of Large Intestine	17	25.4	66.8		38.9	107.0	32.4	121.0
Cancer of Rectum	5	5.5	91.7		29.8	213.9	19.8	259.5
Cancer of Biliary Passages & Liver	8	8.1	99.3		42.9	195.7	31.9	230.6
Cancer of Pancreas	11	15.4	71.4		35.7	127.8	28.1	147.9
Cancer of All Other Digestive Organs	3	2.3	129.7		26.8	378.9	14.6	474.5
Cancer of Respiratory System	72	113.5	63.4	**	49.6	79.9	45.8	85.3
Cancer of Larynx	3	4.0	75.8		15.6	221.4	8.5	277.2
Cancer of Bronchus, Trachea, Lung	66	108.5	60.8	**	47.0	77.4	43.3	82.9
Cancer of All Other Respiratory	3	1.1	284.5		58.7	831.4	32.1	1041.0
Cancer of Breast	2	3.7	54.6		6.6	197.2	2.8	253.2
All Uterine Cancers (Females only)	0	0.9	N/A		0.0	419.5	0.0	602.5
Cancer of Cervix Uteri (Females only)	0	0.6	N/A		0.0	636.4	0.0	914.0
Cancer of Other Female Genital Organs	0	0.9	N/A		0.0	416.4	0.0	598.0
Cancer of Prostate (Males only)	12	23.2	51.8	*	26.8	90.5	21.3	104.2
Cancer of Testes and Other Male Genital Organs	1	1.2	86.9		2.2	484.0	0.4	645.4
Cancer of Kidney	12	7.9	151.6		78.4	264.9	62.5	305.1
Cancer of Bladder and Other Urinary Organs	7	7.0	99.9		40.2	205.9	29.1	244.6
Malignant Melanoma of Skin	3	5.4	55.9		11.5	163.2	6.3	204.4
Cancer of Eye	0	0.2	N/A		0.0	2202.4	0.0	3163.0
Cancer of Central Nervous System	9	9.0	99.9		45.7	189.6	34.8	221.9
Cancer of Thyroid & Other Endocrine Glands	3	1.0	312.0		64.4	911.9	35.2	1141.7
Cancer of Bone	2	0.8	239.1		28.9	863.6	12.3	1108.5
Cancer of All Lymphatic, Haematopoietic Tissue	32	30.8	103.8		71.0	146.6	62.6	161.1
Hodgkins Disease	2	2.0	98.4		11.9	355.6	5.1	456.5
Non-Hodgkins Lymphoma	9	11.7	76.9		35.2	146.0	26.8	170.8
Leukemia & Aleukemia	13	11.6	111.9		59.6	191.4	48.0	219.5
Cancer of All Other Lymphopoietic Tissue	8	5.5	146.5		63.3	288.7	47.1	340.3
All Other Malignant Neoplasms	24	25.5	94.2		60.3	140.1	52.0	155.9

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Appendix B
Washington Works vs USA
All-Cause Mortality Surveillance Report: Totals (Males and Females) (continued)

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
Benign Neoplasms	1	3.0	33.3		0.8	185.6	0.2	247.5
Diabetes Mellitus	22	25.9	85.0		53.3	128.7	45.5	143.8
Cerebrovascular Disease	35	57.9	60.4	**	42.1	84.1	37.4	92.1
All Heart Disease	314	394.2	79.6	**	71.1	89.0	68.5	92.0
Rheumatic Heart Disease	5	4.2	119.2		38.7	278.2	25.7	337.4
Ischemic Heart Disease	239	294.5	81.2	**	71.2	92.1	68.3	95.7
Chronic Endocard. Dis.; Other Myocard. Insuff.	11	13.5	81.4		40.6	145.7	32.0	168.6
Hypertension with Heart Disease	1	12.2	8.2	**	0.2	45.6	0.0	60.8
All Other Heart Disease	58	69.8	83.1		63.1	107.4	57.7	115.5
Hypertension w/o Heart Disease	5	4.8	104.2		33.8	243.3	22.5	295.0
Non-malignant Respiratory Disease	49	87.9	55.7	**	41.2	73.7	37.4	79.7
Influenza & Pneumonia	14	26.5	52.9	*	28.9	88.7	23.5	101.4
Bronchitis, Emphysema, Asthma	13	24.2	53.8	*	28.6	91.9	23.1	105.4
Bronchitis	6	11.6	51.7		19.0	112.5	13.2	135.0
Emphysema	7	10.5	66.8		26.8	137.6	19.4	163.5
Asthma	0	2.1	N/A		0.0	176.1	0.0	252.9
Other Non-malignant Respiratory Disease	22	37.2	59.1	**	37.0	89.4	31.7	99.9
Ulcer of Stomach & Duodenum	0	3.6	N/A		0.0	103.4	0.0	148.5
Cirrhosis of Liver	9	29.9	30.1	**	13.8	57.1	10.5	66.8
Nephritis & Nephrosis	8	11.1	72.0		31.1	141.9	23.1	167.2
All External Causes of Death	45	129.7	34.7	**	25.3	46.4	22.8	50.4
Accidents	35	77.0	45.5	**	31.7	63.2	28.1	69.3
Motor Vehicle Accidents	23	38.2	60.3	*	38.2	90.5	32.8	100.9
All Other Accidents	12	38.8	30.9	**	16.0	54.0	12.7	62.2
Suicides	8	29.7	27.0	**	11.6	53.2	8.7	62.6
Homicides & Other External Causes	2	23.1	8.7	**	1.0	31.3	0.4	40.2
All Other Causes of Death	83	133.2	62.3	**	49.6	77.3	46.1	82.2
Certain Infectious and Parasitic Diseases	1	15.0	6.7	**	0.2	37.2	0.0	49.6
Unknown Causes (In All Causes Category Only)	0							
(*) SIGNIFICANT AT 5% LEVEL; (**) SIGNIFICANT AT 1% LEVEL								

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Appendix C
Washington Works vs West Virginia
All-Cause Mortality Surveillance Report: Males

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
All Causes of Death	773	1331.3	58.1	**	54.0	62.3	52.8	63.7
Tuberculosis	0	2.1	N/A		0.0	176.8	0.0	253.9
All Malignant Neoplasms	222	325.2	68.3	**	59.6	77.9	57.0	81.0
Cancer of Buccal Cavity & Pharynx	4	6.4	62.1		16.9	159.0	10.4	195.5
Cancer of Digestive Organs & Peritoneum	49	68.6	71.5	*	52.9	94.5	47.9	102.2
Cancer of Esophagus	4	8.4	47.4		12.9	121.4	8.0	149.2
Cancer of Stomach	2	8.1	24.5	*	3.0	88.7	1.3	113.8
Cancer of Large Intestine	17	23.9	71.1		41.4	113.8	34.5	128.7
Cancer of Rectum	5	5.8	86.3		28.0	201.4	18.6	244.2
Cancer of Biliary Passages & Liver	7	6.7	104.2		41.9	214.6	30.3	254.9
Cancer of Pancreas	11	13.3	82.9		41.4	148.3	32.6	171.6
Cancer of All Other Digestive Organs	3	2.3	131.8		27.2	385.2	14.9	482.3
Cancer of Respiratory System	70	136.1	51.4	**	40.1	65.0	37.0	69.5
Cancer of Larynx	3	4.5	67.2		13.9	196.3	7.6	245.8
Cancer of Bronchus, Trachea, Lung	64	130.7	49.0	**	37.7	62.5	34.6	67.0
Cancer of All Other Respiratory	3	0.9	319.1		65.8	932.6	36.0	1167.7
Cancer of Breast	0	0.4	N/A		0.0	987.4	0.0	1418.0
Cancer of Prostate (Males only)	12	20.9	57.5		29.7	100.4	23.7	115.6
Cancer of Testes and Other Male Genital Organs	1	1.3	75.7		1.9	421.9	0.4	562.6
Cancer of Kidney	12	7.7	155.2		80.2	271.2	63.9	312.4
Cancer of Bladder and Other Urinary Organs	7	6.7	104.7		42.1	215.6	30.5	256.2
Malignant Melanoma of Skin	2	5.5	36.4		4.4	131.4	1.9	168.7
Cancer of Eye	0	0.2	N/A		0.0	2230.9	0.0	3203.9
Cancer of Central Nervous System	9	8.0	112.0		51.2	212.5	39.0	248.8
Cancer of Thyroid & Other Endocrine Glands	3	1.0	301.1		62.1	880.0	33.9	1101.9
Cancer of Bone	2	0.9	230.9		27.9	833.9	11.9	1070.5
Cancer of All Lymphatic, Haematopoietic Tissue	29	30.3	95.8		64.2	137.6	56.2	151.9
Hodgkins Disease	2	1.9	107.6		13.0	388.6	5.5	498.8
Non-Hodgkins Lymphoma	9	11.2	80.7		36.9	153.2	28.1	179.3
Leukemia & Aleukemia	12	12.0	100.2		51.8	175.1	41.3	201.6
Cancer of All Other Lymphopoietic Tissue	6	5.3	114.1		41.9	248.3	29.2	297.8
All Other Malignant Neoplasms	22	31.2	70.5		44.2	106.7	37.8	119.2

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Appendix C
Washington Works vs West Virginia
All-Cause Mortality Surveillance Report: Males (continued)

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
Benign Neoplasms	1	3.5	28.3		0.7	157.5	0.1	210.1
Diabetes Mellitus	20	29.8	67.0		41.0	103.5	34.7	116.2
Cerebrovascular Disease	34	56.6	60.1	**	41.6	83.9	36.9	92.1
All Heart Disease	309	465.8	66.3	**	59.1	74.2	57.0	76.7
Rheumatic Heart Disease	5	4.3	115.7		37.5	269.9	24.9	327.4
Ischemic Heart Disease	236	342.1	69.0	**	60.5	78.4	58.0	81.4
Chronic Endocard. Dis.; Other Myocard. Insuff.	11	15.7	70.1		35.0	125.5	27.6	145.2
Hypertension with Heart Disease	1	9.7	10.3	**	0.3	57.5	0.1	76.7
All Other Heart Disease	56	94.0	59.6	**	45.0	77.3	41.1	83.3
Hypertension w/o Heart Disease	5	4.2	117.8		38.2	274.8	25.4	333.3
Non-malignant Respiratory Disease	46	116.3	39.6	**	29.0	52.8	26.2	57.2
Influenza & Pneumonia	14	27.5	51.0	**	27.9	85.5	22.7	97.7
Bronchitis, Emphysema, Asthma	11	29.5	37.3	**	18.6	66.7	14.6	77.1
Bronchitis	5	16.8	29.8	**	9.7	69.5	6.4	84.3
Emphysema	6	11.1	54.1		19.9	117.8	13.9	141.2
Asthma	0	1.6	N/A		0.0	224.3	0.0	322.1
Other Non-malignant Respiratory Disease	21	59.2	35.4	**	21.9	54.2	18.7	60.7
Ulcer of Stomach & Duodenum	0	3.5	N/A		0.0	106.0	0.0	152.3
Cirrhosis of Liver	8	27.5	29.1	**	12.6	57.4	9.4	67.6
Nephritis & Nephrosis	8	13.5	59.2		25.6	116.7	19.0	137.5
All External Causes of Death	41	146.0	28.1	**	20.2	38.1	18.1	41.5
Accidents	31	94.6	32.8	**	22.3	46.5	19.6	51.2
Motor Vehicle Accidents	20	45.4	44.0	**	26.9	68.0	22.8	76.3
All Other Accidents	11	49.1	22.4	**	11.2	40.1	8.8	46.4
Suicides	8	33.1	24.2	**	10.4	47.6	7.8	56.1
Homicides & Other External Causes	2	18.3	10.9	**	1.3	39.4	0.6	50.6
All Other Causes of Death	78	138.1	56.5	**	44.6	70.5	41.4	75.1
Certain Infectious and Parasitic Diseases	1	3.2	30.9		0.8	172.1	0.2	229.5
Unknown Causes (In All Causes Category Only)	0							
(*) SIGNIFICANT AT 5% LEVEL; (**) SIGNIFICANT AT 1% LEVEL								

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Appendix C
Washington Works vs West Virginia
All-Cause Mortality Surveillance Report: Females

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
All Causes of Death	33	45.0	73.4		50.5	103.1	44.7	113.2
Tuberculosis	0	0.0	N/A		0.0	9008.5	0.0	12937.7
All Malignant Neoplasms	12	15.1	79.4		41.0	138.7	32.7	159.8
Cancer of Buccal Cavity & Pharynx	0	0.1	N/A		0.0	3027.2	0.0	4347.6
Cancer of Digestive Organs & Peritoneum	2	2.3	87.0		10.5	314.1	4.5	403.2
Cancer of Esophagus	0	0.1	N/A		0.0	4248.5	0.0	6101.6
Cancer of Stomach	1	0.2	551.8		13.8	3074.9	2.8	4100.2
Cancer of Large Intestine	0	1.0	N/A		0.0	356.1	0.0	511.4
Cancer of Rectum	0	0.2	N/A		0.0	1992.8	0.0	2861.9
Cancer of Biliary Passages & Liver	1	0.2	441.4		11.0	2459.7	2.2	3279.9
Cancer of Pancreas	0	0.5	N/A		0.0	778.4	0.0	1117.9
Cancer of All Other Digestive Organs	0	0.1	N/A		0.0	3346.9	0.0	4806.8
Cancer of Respiratory System	2	3.6	55.2		6.7	199.3	2.8	255.8
Cancer of Larynx	0	0.1	N/A		0.0	5906.2	0.0	8482.2
Cancer of Bronchus, Trachea, Lung	2	3.5	56.6		6.8	204.3	2.9	262.3
Cancer of All Other Respiratory	0	0.0	N/A		0.0	13298.5	0.0	19098.8
Cancer of Breast	2	3.1	63.5		7.7	229.5	3.3	294.6
All Uterine Cancers (Females only)	0	1.2	N/A		0.0	319.3	0.0	458.6
Cancer of Cervix Uteri (Females only)	0	0.8	N/A		0.0	442.8	0.0	635.9
Cancer of Other Female Genital Organs	0	0.9	N/A		0.0	397.2	0.0	570.4
Cancer of Kidney	0	0.2	N/A		0.0	1690.2	0.0	2427.4
Cancer of Bladder and Other Urinary Organs	0	0.1	N/A		0.0	2837.0	0.0	4074.4
Malignant Melanoma of Skin	1	0.3	338.9		8.5	1888.5	1.7	2518.2
Cancer of Eye	0	0.0	N/A		0.0	48475.7	0.0	69618.9
Cancer of Central Nervous System	0	0.5	N/A		0.0	764.4	0.0	1097.9
Cancer of Thyroid & Other Endocrine Glands	0	0.1	N/A		0.0	6825.2	0.0	9802.0
Cancer of Bone	0	0.0	N/A		0.0	7639.3	0.0	10971.2
Cancer of All Lymphatic, Haematopoietic Tissue	3	1.3	235.1		48.5	687.2	26.5	860.4
Hodgkins Disease	0	0.1	N/A		0.0	3287.9	0.0	4721.9
Non-Hodgkins Lymphoma	0	0.5	N/A		0.0	804.2	0.0	1155.0
Leukemia & Aleukemia	1	0.5	187.6		4.7	1045.3	0.9	1393.8
Cancer of All Other Lymphopoietic Tissue	2	0.2	1165.6	*	141.0	4210.9	60.0	5405.1
All Other Malignant Neoplasms	2	1.3	151.5		18.3	547.4	7.8	702.6

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Appendix C
Washington Works vs West Virginia
All-Cause Mortality Surveillance Report: Females (continued)

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
Benign Neoplasms	0	0.2	N/A		0.0	2200.4	0.0	3160.2
Diabetes Mellitus	2	1.6	121.7		14.7	439.6	6.3	564.2
Cerebrovascular Disease	1	2.0	49.7		1.2	277.2	0.2	369.6
All Heart Disease	5	9.8	51.1		16.6	119.3	11.0	144.6
Rheumatic Heart Disease	0	0.3	N/A		0.0	1272.7	0.0	1827.8
Ischemic Heart Disease	3	6.0	49.7		10.3	145.3	5.6	182.0
Chronic Endocard. Dis.; Other Myocard. Insuff.	0	0.5	N/A		0.0	792.8	0.0	1138.5
Hypertension with Heart Disease	0	0.3	N/A		0.0	1239.2	0.0	1779.7
All Other Heart Disease	2	2.7	74.1		9.0	267.7	3.8	343.6
Hypertension w/o Heart Disease	0	0.2	N/A		0.0	1940.3	0.0	2786.5
Non-malignant Respiratory Disease	3	3.1	95.7		19.7	279.7	10.8	350.2
Influenza & Pneumonia	0	0.7	N/A		0.0	526.5	0.0	756.2
Bronchitis, Emphysema, Asthma	2	1.2	173.9		21.0	628.2	9.0	806.3
Bronchitis	1	0.7	146.8		3.7	817.7	0.7	1090.4
Emphysema	1	0.3	383.1		9.6	2134.5	1.9	2846.2
Asthma	0	0.2	N/A		0.0	1776.0	0.0	2550.7
Other Non-malignant Respiratory Disease	1	1.3	77.9		1.9	434.0	0.4	578.7
Ulcer of Stomach & Duodenum	0	0.1	N/A		0.0	5737.2	0.0	8239.5
Cirrhosis of Liver	1	0.7	150.1		3.8	836.6	0.8	1115.5
Nephritis & Nephrosis	0	0.5	N/A		0.0	806.0	0.0	1157.5
All External Causes of Death	4	5.8	69.4		18.9	177.8	11.7	218.6
Accidents	4	3.6	109.9		30.0	281.5	18.5	346.1
Motor Vehicle Accidents	3	2.5	118.0		24.3	344.7	13.3	431.7
All Other Accidents	1	1.1	91.3		2.3	508.6	0.5	678.1
Suicides	0	1.1	N/A		0.0	340.4	0.0	488.9
Homicides & Other External Causes	0	1.0	N/A		0.0	355.2	0.0	510.1
All Other Causes of Death	5	5.9	85.0		27.6	198.5	18.3	240.7
CERTAIN INFECTIOUS AND PARASITIC DISEASES	0	0.1	N/A		0.0	2506.3	0.0	3599.4
Unknown Causes (In All Causes Category Only)	0							
(*) SIGNIFICANT AT 5% LEVEL; (**) SIGNIFICANT AT 1% LEVEL								

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Appendix C
Washington Works vs West Virginia
All-Cause Mortality Surveillance Report: Totals (Males and Females)

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
All Causes of Death	806	1376.3	58.6	**	54.6	62.8	53.4	64.1
Tuberculosis	0	2.1	N/A		0.0	173.4	0.0	249.0
All Malignant Neoplasms	234	340.3	68.8	**	60.2	78.2	57.7	81.2
Cancer of Buccal Cavity & Pharynx	4	6.6	60.9		16.6	156.0	10.2	191.8
Cancer of Digestive Organs & Peritoneum	51	70.9	72.0	*	53.6	94.6	48.7	102.2
Cancer of Esophagus	4	8.5	46.9		12.8	120.1	7.9	147.7
Cancer of Stomach	3	8.3	36.0		7.4	105.3	4.1	131.8
Cancer of Large Intestine	17	25.0	68.1		39.7	109.1	33.1	123.4
Cancer of Rectum	5	6.0	83.6		27.1	195.1	18.0	236.7
Cancer of Biliary Passages & Liver	8	6.9	115.2		49.7	226.9	37.0	267.4
Cancer of Pancreas	11	13.7	80.0		39.9	143.2	31.4	165.7
Cancer of All Other Digestive Organs	3	2.4	125.7		25.9	367.4	14.2	460.0
Cancer of Respiratory System	72	139.7	51.5	**	40.3	64.9	37.2	69.3
Cancer of Larynx	3	4.5	66.2		13.7	193.6	7.5	242.4
Cancer of Bronchus, Trachea, Lung	66	134.2	49.2	**	38.0	62.5	35.0	67.0
Cancer of All Other Respiratory	3	1.0	310.0		64.0	905.9	34.9	1134.2
Cancer of Breast	2	3.5	56.8		6.9	205.1	2.9	263.3
All Uterine Cancers (Females only)	0	1.2	N/A		0.0	319.3	0.0	458.6
Cancer of Cervix Uteri (Females only)	0	0.8	N/A		0.0	442.8	0.0	635.9
Cancer of Other Female Genital Organs	0	0.9	N/A		0.0	397.2	0.0	570.4
Cancer of Prostate (Males only)	12	20.9	57.5		29.7	100.4	23.7	115.6
Cancer of Testes and Other Male Genital Organs	1	1.3	75.7		1.9	421.9	0.4	562.6
Cancer of Kidney	12	7.9	151.0		78.0	263.7	62.2	303.8
Cancer of Bladder and Other Urinary Organs	7	6.8	102.7		41.3	211.5	29.9	251.3
Malignant Melanoma of Skin	3	5.8	51.8		10.7	151.4	5.8	189.5
Cancer of Eye	0	0.2	N/A		0.0	2132.7	0.0	3063.0
Cancer of Central Nervous System	9	8.5	105.6		48.3	200.5	36.8	234.7
Cancer of Thyroid & Other Endocrine Glands	3	1.1	285.6		58.9	834.7	32.2	1045.2
Cancer of Bone	2	0.9	218.7		26.5	789.9	11.3	1013.9
Cancer of All Lymphatic, Haematopoietic Tissue	32	31.5	101.5		69.4	143.3	61.2	157.5
Hodgkins Disease	2	2.0	101.4		12.3	366.5	5.2	470.4
Non-Hodgkins Lymphoma	9	11.6	77.5		35.4	147.1	27.0	172.2
Leukemia & Aleukemia	13	12.5	103.9		55.3	177.7	44.6	203.9
Cancer of All Other Lymphopoietic Tissue	8	5.4	147.3		63.6	290.3	47.3	342.1
All Other Malignant Neoplasms	24	32.5	73.8		47.3	109.8	40.7	122.2

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Appendix C
Washington Works vs West Virginia
All-Cause Mortality Surveillance Report: Totals (Males and Females) (continued)

Cause of Death	Observed	Expected	SMR		95% Lower	95% Upper	99% Lower	99% Upper
Benign Neoplasms	1	3.7	27.0		0.7	150.4	0.1	200.6
Diabetes Mellitus	22	31.5	69.9		43.8	105.8	37.5	118.2
Cerebrovascular Disease	35	58.6	59.7	**	41.6	83.1	36.9	91.0
All Heart Disease	314	475.6	66.0	**	58.9	73.7	56.8	76.3
Rheumatic Heart Disease	5	4.6	108.4		35.2	253.0	23.4	306.8
Ischemic Heart Disease	239	348.1	68.7	**	60.2	77.9	57.7	81.0
Chronic Endocard. Dis.; Other Myocard. Insuff.	11	16.1	68.1		34.0	121.9	26.8	141.1
Hypertension with Heart Disease	1	10.0	10.0	**	0.3	55.8	0.1	74.4
All Other Heart Disease	58	96.7	60.0	**	45.5	77.5	41.6	83.4
Hypertension w/o Heart Disease	5	4.4	112.7		36.6	263.0	24.3	319.0
Non-malignant Respiratory Disease	49	119.4	41.0	**	30.4	54.3	27.5	58.7
Influenza & Pneumonia	14	28.2	49.7	**	27.2	83.4	22.1	95.2
Bronchitis, Emphysema, Asthma	13	30.7	42.4	**	22.6	72.5	18.2	83.1
Bronchitis	6	17.5	34.3	**	12.6	74.7	8.8	89.6
Emphysema	7	11.4	61.7		24.8	127.1	17.9	150.9
Asthma	0	1.9	N/A		0.0	199.1	0.0	286.0
Other Non-malignant Respiratory Disease	22	60.5	36.3	**	22.8	55.0	19.5	61.5
Ulcer of Stomach & Duodenum	0	3.5	N/A		0.0	104.1	0.0	149.5
Cirrhosis of Liver	9	28.1	32.0	**	14.6	60.7	11.1	71.1
Nephritis & Nephrosis	8	14.0	57.3		24.7	112.8	18.4	133.0
All External Causes of Death	45	151.8	29.7	**	21.6	39.7	19.5	43.1
Accidents	35	98.2	35.6	**	24.8	49.6	22.0	54.3
Motor Vehicle Accidents	23	48.0	47.9	**	30.4	71.9	26.1	80.2
All Other Accidents	12	50.2	23.9	**	12.3	41.7	9.8	48.1
Suicides	8	34.2	23.4	**	10.1	46.1	7.5	54.3
Homicides & Other External Causes	2	19.4	10.3	**	1.2	37.3	0.5	47.9
All Other Causes of Death	83	144.0	57.6	**	45.9	71.5	42.6	76.0
CERTAIN INFECTIOUS AND PARASITIC DISEASES	1	3.4	29.5		0.7	164.6	0.1	219.5
Unknown Causes (In All Causes Category Only)	0							
(*) SIGNIFICANT AT 5% LEVEL; (**) SIGNIFICANT AT 1% LEVEL								

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Appendix D

Job Exposure Category Development based on Division and Job

Division	Job	Median	Min	Max	<0.1	<0.5	<1.0	<5.0	<10.0	Total	Cat
TECHNICAL	PROJECT COORD	0.008	0.008	0.008	1					1	1
TEFLON@ POLYMERS PROD	SYSTEMS ANALYST	0.024	0.024	0.024	1					1	1
RESEARCH	HR SPEC	0.025	0.025	0.025	1					1	1
TEFLON@ POLYMERS PROD	BUSINESS ANALYST	0.034	0.034	0.034	1					1	1
MANUFACTURING		0.037	0.037	0.037	1					1	1
RESEARCH	DIVISION CHEMIST	0.041	0.04	0.043	2					2	1
TEFLON@ POLYMERS PROD	RES SUPERVISOR	0.056	0.056	0.056	1					1	1
POLY ENG DESIGN		0.067	0.012	0.139	2	2				4	1
CONT ADM/BUS SVC/SAFETY		0.072	0.026	0.149	8	2				10	1
RESEARCH	4423 NL ANALYST	0.072	0.036	0.605	6	4	1			11	1
RESEARCH	4421 LAB ANALYST	0.073	0.073	0.073	1					1	1
TEFLON@ POLYMERS PROD	ENGINEER	0.084	0.037	0.131	1	1				2	1
SPECIALTY COMPOUND PROD		0.084	0.023	0.377	14	4				18	1
TEFLON@ POLYMERS PROD	ADMIN ASSISTANT	0.089	0.051	0.127	1	1				2	1
BUSINESS SERVICES		0.092	0.007	0.183	11	8				19	1
TEFLON@ POLYMERS PROD	PROJECT ENGINEER	0.093	0.049	0.136	1	1				2	1
RESEARCH	STAFF ENGINEER	0.095	0.026	0.462	2	1				3	1
TEFLON@ COPOLYMERS PROD	PROD'N COORDINATOR	0.1	0.1	0.1	1					1	1
HUMAN RESOURCES		0.103	0.033	0.173	1	1				2	1
TEFLON@ POLYMERS PROD	MASTER SCHEDULER	0.104	0.104	0.104		1				1	1
TEFLON@ COPOLYMERS PROD	ENGINEER	0.105	0.083	0.118	1	2				3	1
TECHNICAL	AREA SPECIALIST	0.106	0.106	0.106		1				1	1
BUTACITE@ PRODUCTION		0.107	0.019	0.23	23	21				44	1
RESEARCH	SYSTEMS ANALYST	0.116	0.116	0.116		1				1	1
RESEARCH	TECHNOLOGY MANAGER	0.118	0.031	0.204	1	1				2	1
TECHNICAL	AREA SUPT TECH	0.119	0.119	0.119		1				1	1
RESEARCH	ADMIN ASSISTANT	0.119	0.076	0.171	1	2				3	1
TEFLON@ POLYMERS PROD	SPECIAL ASSIGNMENT	0.12	0.12	0.12		1				1	1
E. P. COMPOUNDING PROD		0.12	0.026	0.652	21	11	1			33	1
RESEARCH	4422 LE ANALYST	0.127	0.127	0.127		1				1	1
TECHNICAL	PROD'N COORDINATOR	0.128	0.128	0.128		1				1	1
BUTACITE@ MAINTENANCE		0.128	0.128	0.128		1				1	1
TECHNICAL	DIVISION ENGINEER	0.131	0.107	0.154		2				2	1
TEFLON@ COPOLYMERS PROD	SPECIAL ASSIGNMENT	0.131	0.032	0.297	2	1				3	1
RESEARCH	SR ENGINEER	0.134	0.081	2.07	1	2		1		4	1
TEFLON@ COPOLYMERS PROD	SENIOR SPECIALIST	0.136	0.032	0.239	1	1				2	1
FILAMENT PRODUCTION		0.136	0.005	0.657	18	25	1			44	1
SHE&EA		0.137	0.018	0.279	3	8				11	1
TEFLON@ POLYMERS PROD	STAFF BUS ANALYST	0.138	0.138	0.138		1				1	1
RESEARCH	SPECIALIST	0.138	0.038	0.261	1	2				3	1
SPECIALTY COMPOUND MAINT		0.139	0.067	0.211	1	1				2	1
ZYTEL@ PRODUCTION		0.14	0.006	0.746	22	22	3			47	1
ACRYLICS		0.145	0.052	0.481	6	4				10	1
Division	Job	Median	Min	Max	<0.1	<0.5	<1.0	<5.0	<10.0	Total	Cat

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Division	Job	Median	Min	Max	<0.1	<0.5	<1.0	<5.0	<10.0	Total	Cat
TECHNICAL	SR TECH ASSOC	0.147	0.146	0.148		2				2	1
TEFLON@ POLYMERS PROD	MFG SERVICE REP	0.15	0.15	0.15		1				1	1
TECHNICAL	SR CHEMIST	0.153	0.153	0.153		1				1	1
TEFLON@ POLYMERS PROD	SPECIALIST	0.153	0.025	0.272	1	4				5	1
TEFLON@ POLYMERS PROD	PLANT SUPT	0.157	0.157	0.157		1				1	1
TEFLON@ COPOLYMERS PROD	STAFF ENGINEER	0.159	0.017	0.35	1	2				3	1
TEFLON@ POLYMERS PROD	DIVISION ENGINEER	0.161	0.078	0.242	1	2				3	1
RESEARCH	TECH ASSOC	0.164	0.028	0.426	3	6				9	1
FILAMENT MAINTENANCE		0.167	0.104	0.213		4				4	1
RESEARCH	AREA SUPT	0.17	0.104	0.191		3				3	1
TECHNICAL	SENIOR TECHNICIAN	0.171	0.053	0.377	1	4				5	1
POLY ENG CONSTRUCTION		0.172	0.172	0.172		1				1	1
RESEARCH	TECHNICIAN	0.181	0.042	0.275	1	3				4	1
TEFLON@ COPOLYMERS PROD	AREA SUPT PROD	0.184	0.184	0.184		1				1	1
RESEARCH	STORES COORDINATOR	0.184	0.184	0.184		1				1	1
TEFLON@ COPOLYMERS PROD	PROCESS DESIGNER	0.19	0.181	0.198		2				2	1
DELRIN@ MAINTENANCE		0.194	0.078	0.43	2	7				9	1
ZYTEL@ MAINTENANCE		0.194	0.069	0.43	1	3				4	1
TECHNICAL	ADMIN ASSISTANT	0.197	0.054	0.34	1	1				2	1
TEFLON@ COPOLYMERS PROD	SENIOR TECHNICIAN	0.198	0.198	0.198		1				1	1
RESEARCH	4420 LABORATORIAN	0.201	0.055	1.38	3	37	5	2		47	1
DELRIN@ PRODUCTION		0.203	0.044	0.457	5	31				36	1
B&ES MAINTENANCE		0.209	0.063	0.464	3	10				13	1
TECHNICAL	CERT COORDINATOR	0.219	0.185	0.252		2				2	1
POWER & SERVICES-MAINT		0.221	0.221	0.221		1				1	1
TECHNICAL	4420 LABORATORIAN	0.225	0.07	0.352	3	12				15	1
E. P. COMPOUND MAINTENANCE		0.234	0.107	0.476		3				3	1
TEFLON@ POLYMERS PROD	SR PROJECT SUPVR	0.24	0.24	0.24		1				1	1
EMPLOYEE RELATIONS		0.24	0.106	0.38		3				3	1
TEFLON@ MAINTENANCE	AREA SUPT MAINT	0.242	0.242	0.242		1				1	1
RESEARCH	TECH FELLOW	0.244	0.174	0.314		2				2	1
POWER & SERVICES		0.245	0.045	0.963	6	14	2			22	1
RESEARCH	SR CHEMIST	0.246	0.246	0.246		1				1	1
RESEARCH	DIVISION ENGINEER	0.247	0.125	0.581		2	1			3	1
TEFLON@ POLYMERS PROD	DIVISION CHEMIST	0.248	0.248	0.248		1				1	1
TECHNICAL	SPECIAL ASSIGNMENT	0.249	0.249	0.249		1				1	1
TEFLON@ COPOLYMERS PROD	AREA SPECIALIST	0.255	0.255	0.255		1				1	1
RESEARCH	SUPERVISOR	0.258	0.159	0.357		2				2	2
TEFLON@ COPOLYMERS PROD	SR CHEMIST	0.265	0.171	0.359		2				2	2
TEFLON@ COPOLYMERS PROD	SPECIALIST	0.273	0.134	1.28		4		1		5	2
TEFLON@ COPOLYMERS PROD	AREA SUPT	0.279	0.137	0.369		3				3	2
TEFLON@ POLYMERS PROD	TECH FELLOW	0.282	0.282	0.282		1				1	2
TECHNICAL	SR ENGINEER	0.282	0.097	0.316	1	2				3	2
TEFLON@ COPOLYMERS PROD	RES ENGINEER	0.286	0.133	0.439		2				2	2
TEFLON@ POLYMERS PROD	TECH ASSOC	0.288	0.131	0.471		6				6	2
TECHNICAL	TECHNICIAN	0.289	0.099	0.562	1	1	1			3	2
RESEARCH	MFG SUPT	0.292	0.292	0.292		1				1	2

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TEFLON@ COPOLYMERS PROD.	SR TECH ASSOC	0.292	0.197	0.387		2				2	2
RESEARCH	AREA SUPT TECH	0.296	0.296	0.296		1				1	2
TEFLON@ COPOLYMERS PROD.	SUPERVISOR	0.307	0.123	2.39		6	2	3		11	2
RESEARCH	SENIOR TECHNICIAN	0.31	0.31	0.31		1				1	2
TEFLON@ COPOLYMERS PROD.	DIVISION ENGINEER	0.33	0.33	0.33		1				1	2
TEFLON@ POLYMERS PROD.	ENVIR CONT CONSULT	0.34	0.329	0.35		2				2	2
RESEARCH	SR TECH ASSOC	0.344	0.058	0.559	2	3	3			8	2
TEFLON@ COPOLYMERS PROD.	6810 OPERATOR I	0.349	0.349	0.349		1				1	2
TEFLON@ MAINTENANCE	6720 STC/SPS MECH	0.35	0.159	0.54		1	1			2	2
TEFLON@ POLYMERS PROD.	SR CHEMIST	0.356	0.308	0.405		2				2	2
TEFLON@ POLYMERS PROD.	MAINT SUPT	0.363	0.363	0.363		1				1	2
TEFLON@ COPOLYMERS PROD.	SR ENGINEER	0.363	0.101	0.576		4	1			5	2
TECHNICAL	TECH ASSOC	0.369	0.148	0.589		1	1			2	2
TEFLON@ COPOLYMERS PROD.	4420 LABORATORIAN	0.382	0.166	0.708		7	2			9	2
TEFLON@ POLYMERS PROD.	AREA SUPT	0.39	0.112	0.837		3	2			5	2
TEFLON@ COPOLYMERS PROD.	PROCESS ENGINEER	0.427	0.28	0.574		1	1			2	2
TEFLON@ POLYMERS PROD.	SENIOR TECHNICIAN	0.427	0.244	0.61		1	1			2	2
TEFLON@ POLYMERS PROD.	QUALITY COORD	0.444	0.444	0.444		1				1	2
TEFLON@ COPOLYMERS PROD.	TECH ASSOC	0.459	0.196	0.715		2	1			3	2
TEFLON@ COPOLYMERS PROD.	ADMIN ASSISTANT	0.488	0.488	0.488		1				1	2
TEFLON@ POLYMERS PROD.	PROD'N COORDINATOR	0.55	0.528	0.572			2			2	2
TEFLON@ POLYMERS PROD.	SR TECH ASSOC	0.581	0.17	1.57		3		1		4	2
TECHNICAL	SPECIALIST	0.635	0.61	0.659			2			2	2
TEFLON@ COPOLYMERS PROD.	SPECIALIST	0.763	0.134	2.39		4		2		6	2
TEFLON@ POLYMERS PROD.	SR ENGINEER	0.765	0.412	1.59		2	1	1		4	2
TECHNICAL	TECH SPEC	0.783	0.783	0.783			1			1	2
TEFLON@ POLYMERS PROD.	6810 ADVM OPR II	0.805	0.299	1.53		2	17	4		23	3
TEFLON@ POLYMERS PROD.	6810 TRNC OPR II	1.07	1.07	1.07				1		1	3
TEFLON@ COPOLYMERS PROD.	6810 OPERATOR II	1.136	0.188	5.015		18	12	19	1	50	3
TEFLON@ POLYMERS PROD.	SUPERVISOR	1.21	0.233	3.18		1	3	4		8	3
TEFLON@ POLYMERS PROD.	6810 STC/SPS OP II	1.3	1.3	1.3				1		1	3
TEFLON@ COPOLYMERS PROD.	TECH SPEC	1.46	1.46	1.46				1		1	2
TEFLON@ MAINTENANCE	6720 MECHANIC	1.726	0.155	6.81		4	6	7	2	19	3
TEFLON@ POLYMERS PROD.	6810 OPERATOR II	3.311	0.199	9.55		4	2	18	8	32	3

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