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Chemical process based reconstruction of exposures for an epidemiological study III. Analysis of industrial hygiene samples

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Abstract

As part of an historical cohort study to investigate the mortality experience of industrial workers exposed to chloroprene (β-CD) and other substances, all available industrial hygiene exposure monitoring data were collected and summarized. From discussions with on-site industrial hygiene personnel, it was apparent that these data were not collected for epidemiological purposes and, therefore, their use in characterization of exposures was problematic as the data mostly pertained to samples collected to investigate the performance of specific tasks. These data were, however, informative for validating the exposure modeling process used to estimate historical exposures. The data summarized below clearly indicate that exposures to β-CD were lowered across the time period of this study. Typically, the exposures recorded were less than the occupational exposure limits of the periods in which the exposures were recorded. Additionally, exposure measurements recorded in the recent past do not represent the exposure actually experienced by the worker as a strict personal protective equipment use program has been in place for the facilities studied since the mid-1980s.

Keywords: Chloroprene; Cohort study; Industrial hygiene; Exposure

1. Introduction

β-Chloroprene (2-chloro-1,3-butadiene) (β-CD) is a monomer used exclusively for the production of synthetic rubber and latexes [1]. Because the chemical structure is similar to that of vinyl chloride, a known human carcinogen, a concern arose in the 1960s that chloroprene might have similar toxicologic properties [2]. Large-scale rodent bioassay and "in vitro" studies have demonstrated that in these test systems β-CD is both mutagenic and carcinogenic [3]. These studies indicate that β-CD is genotoxic and can disrupt normal cellular reproduction. The question of its carcinogenic potential in humans remains unanswered.

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Early studies of the chloroprene production facilities in Louisville, Kentucky were not able to adequately study the potential chronic health effects due to the short period between first exposure and the follow-up time for these studies [4,5].

More recently, studies conducted in eastern European countries have resulted in more questions than answers concerning the carcinogenic potential of β-CD. While indicating some weakly positive relationships between liver and lung cancer with β-CD exposures, the exposure metrics used were at best speculative and probably unreliable [6–8]. Recent reviews of these studies clearly demonstrate the weaknesses of these studies [9,10].

In 1999, the International Institute of Synthetic Rubber Producers (IISRP) initiated a four-plant, multinational epidemiologic study of workers with potential exposure to β-CD. As a component of this study, the historical industrial hygiene data from each plant were collected and analyzed. These data were then used to validate the exposure assessment methodology used to assign exposures to each worker. The analysis of the available industrial hygiene measurements that were used to validate the exposure assignment of β-CD is presented here.

2. Methods

2.1. Study sites and industrial hygiene data sources

The study sites consisted of two plants located within the boundaries of the United States of America, one plant in Northern Ireland and one plant in southern France. The two U.S. plants were the DuPont/Dow Elastomers LLC (DDE) plants in Louisville, KY and Pontchartrain, LA. The plant in Northern Ireland was located in Maydown and the French plant, Enichem Elastomers, was near Grenoble, France (FR). All four plants were integrated facilities in which β-CD monomer was produced from primary feedstocks and then polymerized to yield polychloroprene.

At the two oldest facilities in this study, Louisville and Maydown, β-CD synthesis was initially carried out through the acetylene dimerization process. Louisville synthesized β-CD from 1942 until this process was phased out during 1971–1976. The Maydown plant employed a similar process from 1960 to 1980, when the acetylene dimerization process was replaced by a process that employed butadiene as the primary feedstock. The Grenoble facility, which began operations in 1966, was the first commercial-scale plant in the world to produce chloroprene from butadiene. The Pontchartrain facility began production of β-CD using the butadiene process in 1969. With the development of the butadiene process, Pontchartrain served as the primary monomer synthesis site in the United States, shipping β-CD to the Louisville facility by train car for further processing.

2.2. Industrial hygiene records, retrieval, and development of exposure database

Each of the study sites were visited by the industrial hygiene investigators at least two times, except for the French plant which was visited once for this study. During these visits, interviews with plant industrial hygiene personnel assisted the research team in identifying all available industrial hygiene records. All hard copy records were scanned into a digital format and stored for further review and extraction. To insure that all available records were identified and retrieved, records storage inventories were also reviewed. This process resulted in the identification of a large number of historical records that were then collected from the corporation repositories and digitized for further analysis. This process resulted in the number of records identified and digitized shown in Tables 1–3.

The digitized files from each site were reviewed and exposure data extracted into a database that would be used for further analysis. Information recorded included the file name and number, the page number of the file where the record was found, date of sample, facility, individual, occupation, work area, tasks (if identified), department, the cumulative time represented by the sample, the chemical name, the concentration of all substances monitored, and the units. For both of the U.S. facilities and the French facility the industrial hygiene exposure records were all in hard copy, while at the Northern Ireland facility, approximately 35% of available records were extracted from an electronic file provided to the research team.

When the data entry was complete for approximately 25% for any site, an internal review was conducted to assess the accuracy of entry and to correct any obvious entry errors. This process was repeated when 50% and 75% of data were abstracted and entered into the industrial hygiene exposure database. Observed data entry errors included non-numeric entries in numeric cells, duplicate entries, occupation identification errors, etc. This review process was continued until no further errors could be identified. The French data were abstracted from the available records and the abstracted data verified by francophone study personnel.

Personal exposure measurements for β-CD were first recorded in the industrial hygiene records of the Kentucky facility in 1975. The earliest personal exposure

Table 1
Kentucky facility (Louisville)—total number of β-chloroprene exposure measurements, number of chemical operator air samples (monomer), mean β-chloroprene 8-h

Year	Number of samples chem. oper. (monomer)	Mean (ppm)	Geometric mean (ppm)	G.S.D.	Maximum (ppm)	Number of samples chem. oper. (polymer)	Mean (ppm)	Geometric mean (ppm)	G.S.D.	Maximum (ppm)
1975	116	1.6	0.45	4.5	16	593	4.1	1.54	5.4	356
1976	515	1.6	0.45	5.1	58	1717	6.5	3.42	3.7	462
1977	247	2.2	0.63	3.8	50	2108	3.1	3.10	3.0	134
1978	388	1.4	0.41	4.5	35	2188	5.3	1.63	3.8	131
1979	284	1.3	0.38	3.7	33	895	2.1	1.12	3.3	51
1980	251	1.1	0.36	3.8	28	830	1.6	0.79	3.3	70
1981	182	0.8	0.30	3.1	21	727	1.1	0.52	3.1	21
1982	120	0.7	0.33	3.3	11	334	1.2	0.74	2.8	14
1983	235	3.0	0.21	4.0	236	278	0.9	0.43	3.7	12
1984	123	1.6	0.21	6.7	58	279	1.5	0.54	6.3	36
1985	–	–	–	–	–	16	2.8	0.91	5.1	17
1986	1	–	–	–	0.3	3	1.9	0.72	9.3	3.7
1987	–	–	–	–	–	7	3.1	0.92	4.6	17.2
1988	–	–	–	–	–	4	2.6	1.22	6.2	6.6
1989	77	1.7	0.35	6.4	33	39	3.1	1.91	3.6	9.4
1990	15	2.1	1.4	3.0	7	11	2.12	1.40	3.2	7.1

TWA exposure (ppm), Geometric mean β-chloroprene 8-h. TWA exposure (ppm), geometric standard deviation, maximum measured β-chloroprene 8-h. TWA exposure, number of chemical operator air samples (polymer), mean β-chloroprene 8-h. TWA exposure (ppm), geometric mean β-chloroprene 8-h. TWA exposure (ppm), geometric standard deviation, maximum measured β-chloroprene 8-h. TWA exposure.

Table 2
Louisiana facility (Pontchartrain)—total number of β-chloroprene exposure measurements, number of chemical operator air samples (monomer), mean β-chloroprene 8-h

Year	Number of samples chem. oper. (monomer)	Mean (ppm)	Geometric mean (ppm)	G.S.D.	Maximum (ppm)	Number of samples chem. oper. (polymer)	Mean (ppm)	Geometric mean (ppm)	G.S.D.	Maximum (ppm)
1976	1098	0.12	0.09	2	0.2	1033	6.05	2.89	4.1	276
1977	918	0.61	0.11	6.9	45	1053	3.59	1.64	5.0	31.4
1978	123	1.41	0.26	7.1	20	344	3.09	1.16	5.5	23.9
1979	107	0.75	0.11	8.6	21	257	3.15	1.30	5.0	44.4
1980	318	0.69	0.11	8.1	21	231	2.80	1.13	5.3	38.8
1981	290	0.52	0.09	6.9	16	195	2.31	1.40	4.1	15.6
1982	217	0.54	0.13	6.3	9	185	2.71	1.56	3.4	24.6
1983	182	0.20	0.5	5.4	2.9	12	2.69	2.45	1.7	4.5
1984	299	0.35	0.04	7.6	17	47	2.90	0.52	11.5	11.6
1985	291	0.32	0.04	6.4	38	111	3.00	0.73	8.6	37.9
1986	632	0.21	0.05	7.2	4.2	134	2.45	1.64	1.1	11.4
1987	356	0.36	0.06	7.3	9.1	42	5.96	2.27	3.1	119.1
1988	580	0.13	0.04	5.1	4.2	45	2.62	1.58	2.5	18.8
1989	107	0.13	0.05	4.6	2.3	13	0.47	0.29	2.8	1.9
1990	94	0.23	0.10	3.8	2.3	43	4.31	2.63	2.8	33.5
1991	85	0.09	0.04	3.5	1.7	59	2.31	0.95	5.3	15.9
1992	68	0.09	0.03	4.7	0.5	66	1.17	0.53	5.4	5.5

TWA exposure (ppm), geometric mean β-chloroprene 8-h. TWA exposure (ppm), geometric standard deviation, maximum measured β-chloroprene 8-h. TWA exposure, number of chemical operator air samples (polymer), mean β-chloroprene 8-h. TWA exposure (ppm), geometric mean β-chloroprene 8-h. TWA exposure (ppm), geometric standard deviation, maximum measured β-chloroprene 8-h. TWA exposure.

Table 3
Northern Ireland (Maydown)—total number of β-chloroprene exposure measurements, number of chemical operator air samples (monomer), mean β-chloroprene 8-h

Year	Number of samples chem. oper. (monomer)	Mean (ppm)	Geometric mean (ppm)	G.S.D.	Maximum (ppm)	Number of samples chem. oper. (polymer)	Mean (ppm)	Geometric mean (ppm)	G.S.D.	Maximum (ppm)
1979	41	5.27	1.77	6.1	23	23	6.53	2.26	7.1	34
1980	42	3.64	1.36	5.3	27	84	5.30	2.66	4.0	27
1981	391	0.77	0.10	7.6	600	554	6.73	4.66	2.8	44
1982	315	1.99	0.51	5.3	380	398	4.51	1.65	5.6	58
1983	421	13.88	0.01	6.7	36	558	4.48	1.81	4.8	380
1984	442	3.87	0.70	7.3	296	783	3.70	0.87	5.8	152
1985	628	2.74	0.56	5.0	152	203	3.71	0.75	8.0	84
1986	262	2.75	0.46	5.9	156	359	2.51	0.41	6.0	156
1987	182	3.18	0.48	7.6	58	233	2.97	0.45	7.6	57
1988	162	0.69	0.15	5.4	8.8	248	0.69	0.16	5.3	9
1989	189	0.46	0.13	4.6	18.4	329	0.50	0.13	4.5	18
1990	133	0.82	0.21	5.4	19.3	257	0.66	0.47	4.9	19
1991	90	1.40	0.31	3.5	8.5	281	0.63	0.22	3.5	12.7
1992	97	1.88	0.86	3.2	30	347	0.88	0.37	3.5	17

TWA exposure (ppm), geometric mean β-chloroprene 8-h. TWA exposure (ppm), geometric standard deviation, maximum measured β-chloroprene 8-h. TWA exposure, number of chemical operator air samples (polymer), mean β-chloroprene 8-h. TWA exposure (ppm), geometric mean β-chloroprene 8-h. TWA exposure (ppm), geometric standard deviation, maximum measured β-chloroprene 8-h. TWA exposure.

measurements at the Louisiana and Northern Ireland facilities occurred in 1976 and 1979, respectively. Air sample results were available through the end of our study, however, annual sample numbers became very small after 1992 for all plants with the Northern Ireland plant closing in 1998 (Fig. 1). At the Grenoble plant, personal exposure sampling was first conducted in 1977, but the personal sampling data were sparse until 2000–2001, when a major campaign of personal exposure sampling was conducted.

All samples at the two plants in the U.S. were collected under the direction of professional industrial hygiene staff. Initially, personal air samples were collected under the direction of industrial hygienists from

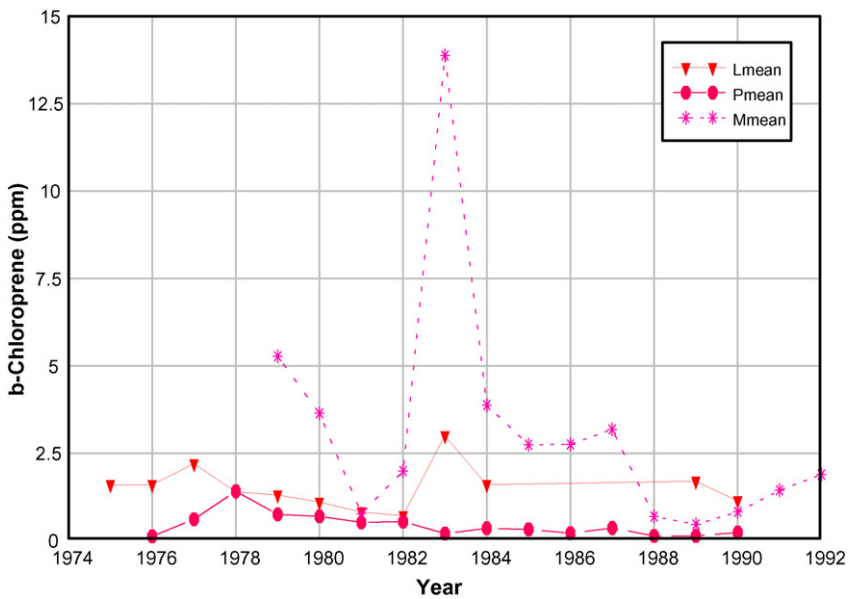

Fig. 1. Monomer operator geometric mean β-chloroprene exposure (ppm) for Kentucky, Louisiana, and Northern Ireland (Lmean = Kentucky, Pmean = Louisiana, Mmean = Northern Ireland).

the Haskell Laboratory, Newark, DE. Analysis of personal exposure estimates was also conducted at the company laboratory in Newark, DE, using standard gas chromatographic methods. The analytical method used for analysis was consistent with the accepted standard method of the time. The strategy employed for personal monitoring sought to monitor each potentially exposed employee at least once. Subsequent sampling was assumed to be a random selection within specific occupations where exposure to β-chloroprene monomer was thought to problematic, e.g. where exposure monitoring results indicated the potential for over-exposure.

The final complete database included more than 40,000 exposure records covering more than 200 distinct occupations. In addition to personal breathing zone air samples there were more than 1000 area samples that were collected at specific locations. While this type of sample is sometimes used to assess background exposures, that is exposures not related to personal activity, area samples are difficult to use to assess personal exposures [11–15]. For purposes of this study, we have only focused on those occupations that experienced continuous exposure to β-CD during the period of the epidemiologic study (1949–1992). Additionally, we have only evaluated personal breathing zone samples to assess exposure to β-chloroprene monomer. The focus of this effort then fell on four distinct occupations within each facility, chemical operators that were assigned either to the synthesis of β-CD or polymerization of β-CD and mechanics who worked in either the monomer or polymer areas.

All personal exposure estimates were assumed 8-h. TWAs unless otherwise labeled. Personal exposure estimates were adjusted to 8-h. TWA concentrations where sufficient information was available to make these adjustments. In the data presented, peak exposure levels refer to excursions and they are not necessarily the short term exposures experienced. While this depiction was useful in the validation of exposure equations [16], they should not be considered as estimates for the short term spikes in the exposure profile. Due to the scarcity of personal samples at the Grenoble facility during the study period, these data were not included in the analysis of historical data that follows.

Esmen et al. developed quantitative estimates of annual median exposure for vinyl chloride monomer (VCM) and β-CD that were used for exposure estimation for each occupational classification (job code) during each year the plants were in operation and the processes were used [16]. Esmen et al. were able to develop quantitative exposure estimates using physical/chemical models of the tasks where exposure to VCM or β-CD could occur. An essential element in estimating period-specific exposures was the identification of historical process modifications that would result in a change of exposure potential for that task. These changes were identified, described in detail and the resulting changes in exposure were computed for each process or task.

3. Results

Tables 1–3 show number of air samples collected, the arithmetic mean (AM), geometric mean (GM) and geometric standard deviation (G.S.D.) for the occupational title of chemical operator in both the monomer production and polymer areas of the three plants with sufficient data to be used in this analysis. For this study there were 15 years (1975–1990) where there were a relatively large number of samples collected on chemical operators in both the monomer and polymer sections of the studied facilities. A total 26,056 samples were available for this analysis. The majority of these samples (78%) were collected between 1975 and the mid-1980s. The sampling strategy used by Industrial Hygienists at the three plants that contribute the majority of the samples was focused on identifying those tasks that were the major determinants of exposure. Exposures occurring during these tasks were exhaustively evaluated and where necessary, control measures, e.g. engineering controls, personal protective equipment, etc. were instituted.

3.1. Monomer production operations

Air sampling to assess exposure to β-chloroprene started at the Kentucky facility in 1975, however only a limited (less than 5) number were collected until 1976 when an intensive exposure assessment campaign started. During the period from 1976 through 1984 12,410 air samples on chemical operators were collected in both the monomer (2461) and polymer areas (9949). More samples were collected in the polymer production area because exposure to β-chloroprene monomer was assumed a greater probability due to more tasks involving potential contact with solutions containing the β-chloroprene monomer. The mean value of β-chloroprene for monomer chemical operator exposures varied between 0.71 and 3.0 over this 15-year period, with overall average β-chloroprene monomer exposures at 1.14 ppm. The geometric means for the distribution of β-chloroprene monomer exposures by year varied from 0.21 to 0.63 ppm during this same period. The geometric standard deviation for the yearly β-chloroprene monomer exposure distributions ranged from 3.1 to 6.7 indicating a relatively large spread within the yearly data.

Air sampling to assess exposure to β-chloroprene monomer in the monomer production areas of the production facilities in the Pontchartrain plant began in 1976 and continued through the end date of this study, however, for study purposes, only the data through 1992 have been summarized. The annual mean of β-chloroprene exposures for monomer chemical operator exposures varied between 0.12 and 1.41 over this 15-year period, with overall average β-chloroprene monomer exposures at 0.38 ppm. The geometric means for the distribution of β-chloroprene monomer exposures by year varied from 0.09 to 0.26 ppm during this same period. The geometric standard deviation for the yearly β-chloroprene monomer exposure distributions ranged from 2.0 to 8.6 indicating right skewed distributions of the monitoring data.

Exposure monitoring began in the Maydown β-chloroprene monomer production facilities in 1979. Verifiable β-chloroprene monomer exposure measurements were available from 1979 through 1992. The mean annual β-chloroprene monomer exposure estimates ranged from a low of approximately 0.8 to 14 ppm with an overall mean of 3.3 ppm. The geometric mean exposures for this period ranged from 0.01 to 1.8 ppm. A sharp drop in the mean and geometric mean exposures for this population occurred between 1980 and 1981. Excursion values ranged from 9 and 600 ppm (1981) with a 10- to 20-fold reduction in the years following 1982.

3.2. Polymer production operations

In the Louisville plant, 1019 exposure measurements were collected for β-chloroprene monomer between 1976 and 1990. Between 1976 and 1978 approximately 1/3 of all air samples for β-chloroprene monomer were collected. The range of annual means for β-chloroprene monomer exposure estimates was from 0.9 to 6.5 (1976) with the largest annual means occurring in the mid-1970s to late 1970s. The geometric annual means for the distribution of exposures ranged from 0.4 to 3.4 ppm. Peak exposure values for β-chloroprene monomer ranged from 462 ppm (1976) to 7 ppm (1990). A significant downward trend in geometric mean exposures can be observed in Fig. 2 between 1976 and 1981.

Air sampling for β-chloroprene monomer at the Pontchartrain facility showed a similar trend with respect to the Louisville plant. Three thousand, seven hundred and forty-five air samples for β-chloroprene monomer collected between 1976 and 1990 with almost 2/3 between 1976 and 1977. The annual mean exposures ranged from 6.5 ppm (1976) to 0.5 ppm (1989) β-chloroprene monomer with sharp decline after 1977. The annual geometric mean exposures to β-chloroprene monomer ranged from 2.9 (1977) to 0.5 (1989). Typically, excursions to relatively high exposures values (276 in 1977) occurred more frequently in the early years of exposure monitoring these types of observations still occur in the later years (1990s).

At the Maydown facility, there were 4657 personal exposures estimates for β-chloroprene monomer on polymer operators between 1979 and 1992. The average annual mean exposure to β-chloroprene monomer was 3.13 ppm with a range of 0.5 (1989) to 6.3 (1979). These data demonstrate a distinct downward trend in exposures from 1979. This trend is also evident in the maximum measured exposures.

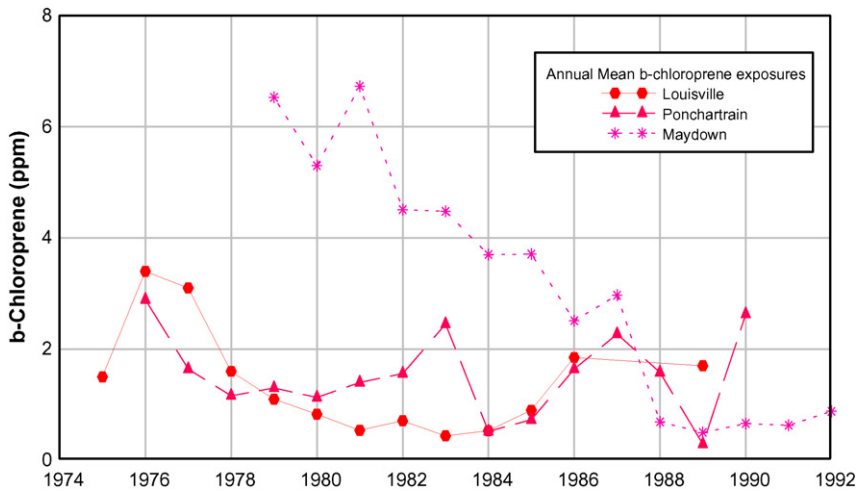

Fig. 2. Polymer operator geometric mean β-chloroprene exposure (ppm) for Kentucky, Louisiana, and Northern Ireland (Lmean = Kentucky, Pmean = Louisiana, Mmean = Northern Ireland).

4. Discussion

Extensive personal exposure monitoring for β-chloroprene monomer began at each of these facilities in the 1970s due to concerns about the potential carcinogenicity of small highly bioactive chemicals. Interest in the results of exposure to human populations still is high due to the results of the National Toxicological Program rodent bioassay of β-chloroprene monomer that, as stated earlier, was positive for the test species.

Monitoring at these facilities was not conducted for epidemiologic purposes. Discussions with on-site hygiene personnel clearly indicated that exposure monitoring was conducted to determine what tasks were the dominant determinants of exposure. These tasks were then the focus of improved engineering controls and the mandatory use of personal protective equipment. In this respect, comparison of exposures between facilities depends on the tasks sampled at each facility and the tasks defined in each job class at any given year. Therefore, between the facilities, the sample based comparison of overall averages or even the sample based comparison of exposure for similar sounding job classes might lead to fallacious conclusions.

It is clear that exposures, both average and maximum, were significantly reduced across time and that the more recent mean exposures were well within the OSHA Permissible Exposure Limits. It should be noted that these data indicate some recent apparent increases in both the average and maximum exposures (Pontchartrain 1991–1992). These increases are related to a few, <10%, excursion exposures and all operators were wearing personal protective equipment which included a half or full face respirator. This is reflected in the drastic reduction of the number of samples collected in the latter years, as the measured exposure values for the tasks thought to be the highest contributors to exposures started to fall well below recommended exposure limits. The uneven distribution of collected samples with respect to time and tasks resulted in the difficulties with respect to the direct use of the observed values in the epidemiological investigation. However, the detailed information available in some samples that encompassed some tasks was very useful in the validation of the exposure estimation process [16].

Ideally, the type and number of exposure estimates available in this study might lead an investigator to utilize these measurements as estimates of group or occupational exposure means. The use of historical exposure data collected for purposes other than characterization of the exposed population can be observed in a wide variety of studies [13,14]. It should be made clear that while there are a large number of measurements per occupational title were available for this cohort, the selection of who was monitored, how many personal samples were collected per individual and why the particular individual was chosen was unclear. The initial strategy was to collect at least one exposure estimate from each individual. Once that goal was reached the selection strategy was based on observation of what tasks or occupations had the potentially highest exposures. In epidemiologic studies the selection of subject to be monitored should be conducted in a random manner to insure that exposure parameters describing the distribution of exposures within the population are unbiased. The exposure monitoring data collected and available for this study cannot be expected to fulfill that criterion because of the exposure monitoring strategy employed. The available exposure data did, however, play an important role in assuring that the exposure assignment model used accurately portrayed the exposure of the differing occupational groups. Esmen et al. [17] compared the assigned exposures for the Louisville polymer operator cohort against the median exposures developed from the years where sufficient monitoring data exists, 1976–1995. This comparison showed that the assigned exposures and those estimated from the actual exposure measurements were remarkably consistent [17].

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