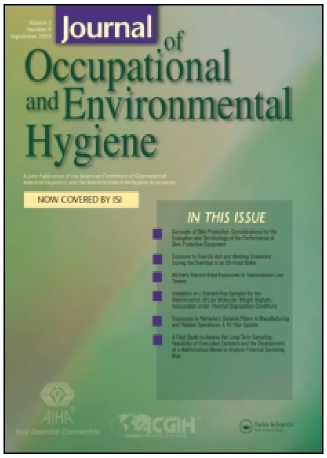

Journal of Occupational and Environmental Hygiene
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713657996

Exposure-Response Analysis for Beryllium Sensitization and Chronic Beryllium Disease Among Workers in a Beryllium Metal Machining Plant

To cite this Article: , 'Exposure-Response Analysis for Beryllium Sensitization and Chronic Beryllium Disease Among Workers in a Beryllium Metal Machining Plant', Journal of Occupational and Environmental Hygiene, 4:6, 448 - 466
To link to this article: DOI: 10.1080/15459620701354747
URL: http://dx.doi.org/10.1080/15459620701354747

Journal of Occupational and Environmental Hygiene, 4(6): 448–466
ISSN: 1545-9624 print / 1545-9632 online

DOI: 10.1080/15459620701354747

Exposure-Response Analysis for Beryllium Sensitization and Chronic Beryllium Disease Among Workers in a Beryllium Metal Machining Plant

Amy K. Madl,[1] Ken Unice,[2] Jay L. Brown,[2] Marc E. Kolanz,[3] and Michael S. Kent[4]

[1]ChemRisk, Inc., San Francisco, California
[2]ChemRisk, Inc., Pittsburgh, Pennsylvania
[3]Brush Wellman Inc., Cleveland, Ohio
[4]Brush Wellman Inc., Elmore, Ohio

The current occupational exposure limit (OEL) for beryllium has been in place for more than 50 years and was believed to be protective against chronic beryllium disease (CBD) until studies in the 1990s identified beryllium sensitization (BeS) and subclinical CBD in the absence of physical symptoms. Inconsistent sampling and exposure assessment methodologies have often prevented the characterization of a clear exposure-response relationship for BeS and CBD. Industrial hygiene (3831 personal lapel and 616 general area samples) and health surveillance data from a beryllium machining facility provided an opportunity to reconstruct worker exposures prior to the ascertainment of BeS or the diagnosis of CBD. Airborne beryllium concentrations for different job titles were evaluated, historical trends of beryllium levels were compared for pre- and postengineering control measures, and mean and upper bound exposure estimates were developed for workers identified as beryllium sensitized or diagnosed with subclinical or clinical CBD. Five approaches were used to reconstruct historical exposures of each worker: industrial hygiene data were pooled by year, job title, era of engineering controls, and the complete work history (lifetime weighted average) prior to diagnosis. Results showed that exposure metrics based on shorter averaging times (i.e., year vs. complete work history) better represented the upper bound worker exposures that could have contributed to the development of BeS or CBD. Results showed that beryllium-sensitized and CBD workers were exposed to beryllium concentrations greater than 0.2 $\mu g/m^3$ (95th percentile), and 90% were exposed to concentrations greater than 0.4 $\mu g/m^3$ (95th percentile) within a given year of their work history. Based on this analysis, BeS and CBD generally occurred as a result of exposures greater than 0.4 $\mu g/m^3$ and maintaining exposures below 0.2 $\mu g/m^3$ 95% of the time may prevent BeS and CBD in the workplace.

Keywords beryllium, beryllium sensitization, chronic beryllium disease, exposure assessment

Address correspondence to Amy Madl, ChemRisk, Inc., 25 Jessie Street at Ecker Square, Suite 1800, San Francisco, CA 94105; e-mail: amadl@chemrisk.com.

INTRODUCTION

Beryllium is a metal that has been used in a wide variety of applications for more than 75 years. There are four primary forms of beryllium: beryl ores, beryllium metal, beryllium oxide, and beryllium alloys. Copper beryllium alloy is the form of beryllium most widely used today. Because of its many unique characteristics, beryllium has been and continues to be used by a variety of strategic and vital industries, including aerospace, defense, energy, telecommunications, and medical equipment. It has been estimated that between 26,400 and 134,000 workers are currently exposed to beryllium in the United States.(1)

Beryllium was critical to the development of military defense weapons during the Cold War. Consequently, much of the history of beryllium as it relates to occupational disease and the development of an occupational exposure limit (OEL) was derived from the experience of the Department of Energy (DOE). In 1949, the U.S. Atomic Energy Commission (AEC), predecessor to the DOE, recommended the first OEL of 2 $\mu g/m^3$ for beryllium, a level measured as a quarterly daily weighted average (DWA), to protect beryllium workers against chronic beryllium disease (CBD). This recommended OEL was ultimately adopted by the AEC in 1956 based on 7 years of annual reviews by a panel of scientists led by Dr. Harriet Hardy.

Over the 50-year period that the 2 $\mu g/m^3$ OEL for beryllium has been in use, it has been reviewed and adopted by a number of occupational and governmental organizations, including the American Industrial Hygiene Association (AIHA) in 1956, the American Conference of Governmental Industrial Hygienists (ACGIH®) in 1959 as a threshold limit value (TLV®), the American National Standards Institute (ANSI) in 1970, and the Occupational Health and Safety Administration (OSHA) as a permissible exposure limit (PEL) in 1972. It was also adopted as the OEL in most developed countries

worldwide. In 2006, California OSHA adopted 0.2 $\mu g/m^3$ as its PEL for beryllium.[5]

Identification of CBD in the absence of physical symptoms and reports of CBD occurring as a result of mean or median exposures below 2 $\mu g/m^3$ have led to proposals to lower the ACGIH TLV to values ranging from 0.2 $\mu g/m^3$ to 0.02 $\mu g/m^3$.[2,3] The 0.02 $\mu g/m^3$ value is based on Kelleher et al.[4] wherein the authors observed increased cumulative and lifetime weighted average (LTW) exposures among beryllium-sensitized workers or those with CBD compared with controls. More specifically, it was reported in this study that 20 of 235 individuals in a beryllium machining plant with LTW average exposures between 0.024 $\mu g/m^3$ and 0.6 $\mu g/m^3$ were sensitized to beryllium. The authors also reported no beryllium sensitization (BeS) or CBD among 22 workers whose LTW average exposure was less than 0.02 $\mu g/m^3$.

With the goal of identifying an exposure metric that would best predict BeS and CBD, researchers have characterized occupational exposures to beryllium by a variety of methods.[4,6–11] These exposure metrics have included mean, median, and 95th percentile 8-hr TWA and DWA measurements, as well as cumulative exposure estimates for total airborne beryllium. Researchers have also looked at the influence of particle size, chemical form of beryllium, and type of operation on the prevalence of BeS and CBD.[4,7,9–13] Generally, researchers have found that particle size and operation type are important factors in the natural history of BeS and CBD; however, inconsistent findings have been reported for cumulative and DWA exposure estimates.[8,14]

Although there has not been a clear exposure-response relationship or an exposure metric that completely explains all of the beryllium-sensitized or CBD workers, most of these studies have not reconstructed individual worker exposures based on employment history. Rather, these studies have characterized beryllium-sensitized and CBD worker exposures based on broad job classifications and have not evaluated the beryllium exposures that may have contributed to BeS or CBD in individual workers.

With industrial hygiene and health surveillance data from a beryllium machining facility, the objective of this study was to reconstruct beryllium exposures of workers, who were identified as beryllium sensitized or diagnosed with subclinical or clinical CBD, and determine whether a threshold for BeS and CBD can be identified. This analysis involved an evaluation of airborne beryllium concentrations for different job titles, historical trends of personal and general area beryllium levels for pre- and postengineering control measures that were implemented in the 1990s, and mean and upper bound exposure estimates for workers identified as beryllium sensitized or CBD. Reconstructing historical beryllium exposures using several methods of analysis for each beryllium-sensitized or CBD-identified worker was expected to provide a better understanding of the range of plausible exposures to airborne beryllium that may have contributed to sensitization and disease.

METHODS

Description of Beryllium Machining Plant

According to plant personnel, since 1969, 98% of this plant's beryllium operations involved machining of beryllium metal and high beryllium content composite materials with occasional machining of beryllium oxide/metal matrix (<1%) and beryllium-containing alloys (<1%). Some beryllium oxide was handled in the grind department prior to the 1980s and beryllium oxide/metal matrix is currently processed in E-cell. Machining of metals other than beryllium is also performed. Plant representatives confirmed that the forms of beryllium processed at this location have not varied dramatically over time.

Machining processes have changed from primarily hand-controlled machining operations to more computer-controlled and fully-enclosed automated machining processes. Machining operations within the plant, including milling, grinding, lathing, lapping, deburring, and electrical discharge machining (EDM) were conducted in an open floor plan. Production support operations such as engineering sales and administration, management, shipping and receiving, tool making, inspection, and maintenance were located in separate but adjacent areas. The nonproduction employees had access to the machining operations areas.[4,13,15]

Since 1980, the industrial hygiene program at this plant has included the routine collection of personal lapel and high-volume general area samples throughout production and nonproduction areas to assess employee exposures to beryllium. Prior to the mid-1990s, the exposure assessment strategy focused on identifying high-exposure job categories and processes in order to implement effective hazard controls and maintain compliance with the OSHA PEL for beryllium. Following the mid-1990s, surveillance of airborne concentrations of beryllium involved all machining and nonmachining job categories.

The plant's hazard control program has given priority to the design, installation, and use of effective engineering and administrative controls to reduce employee exposures to beryllium rather than the utilization of personal protective equipment (i.e., respirators, etc.). Over the past 10 years, administrative and engineering controls were implemented at the plant with the focus on reducing beryllium exposures in machining operations. In 1995, pressurized air hoses were removed and dry sweeping was discouraged; in 1996, enclosures were built for all deburring processes; in 1997, uniforms were mandatory; and, in 1998, local exhaust ventilation was installed in EDM and updated in lap, deburr, and grind departments.[4]

Interviews with plant industrial hygiene personnel identified a number of other changes made during this time period that could have impacted historical exposures. Industrial hygiene and engineering control changes are summarized in Table I. Examples include modifying access to production areas via a clean/dirty transition room, installation of additional vacuum units, and a work shoe policy. This information shows

TABLE I. Administrative and Engineering Control Changes Made at a Beryllium Machining Plant (1996–1999)

Year of Change	Type of Change	Description
1996	Administrative	Pressurized air hoses used to blow beryllium dust off machines eliminated in all departments
1996–1997	Administrative	Dry sweeping of work surfaces discouraged and wet/vacuuming cleaning methods implemented
1996–1997	Administrative	Uniforms and dedicated work shoes policy implemented
1996–1997	Administrative	Access to production area is controlled via a clean room/dirty room to prevent secondary contamination in nonproduction areas
1996–1997	Engineering	Local exhaust ventilation (LEV) ductwork for Be dusts, fumes and mists separated from Be chips and sent to Torrit dust collector rather than Spencer baghouse
1996–1997	Engineering	Changed process layout so operations producing Be dusts, fumes, and mists in closer proximity to each other
1996–1997	Engineering	Installed enlcosures on lapping, deburring, grinding, EDM, and tool and die operations
1996–1997	Engineering	Installed vacuum systems for machining operations to aid in workplace clean-up and decontamination
1996–1997	Engineering	Installed Total Suspended Particulate (TSP) Mist Eliminators on some CNC milling machines
1999	Engineering	Replaced LEV ductwork for milling and lathe operations
1999	Engineering	Additional Donaldson vacuum systems added to some departments

that significant changes were made beginning in 1996 through 1999.

The population of workers at this machining plant provides a unique opportunity for the study of exposure-response relationships because respiratory protection was not routinely used by workers at this plant. Historically, respirators were used only when exposures were anticipated to be high, such as during sandblasting operations.[4,13,15] Because respiratory protection was used on a limited basis, the personal lapel measurements for workers at this facility are likely to be a true reflection of actual airborne exposures to beryllium and provide a potential opportunity to identify a threshold level of airborne beryllium at which BeS, subclinical CBD (sCBD), and clinical CBD (cCBD) is not observed. For these reasons, a respirator correction factor was not applied to this exposure analysis.

History of Medical Surveillance at the Plant

The machining plant evaluated in this study has employed 1166 workers since 1969 and currently has 208 active employees. Prior to 1994, annual medical surveillance (i.e., physicals) was conducted at the site and included work histories, chest X-rays, and pulmonary function testing. The identification of one worker with CBD in 1994 prompted plant-wide blood beryllium lymphocyte proliferation test (BeLPT) surveillance. Since that time, approximately 350 employees have been tested with the blood BeLPT. All current employees are tested with the blood BeLPT every 2 years, and newly hired employees are tested within 3 months of initial employment and every 2 years thereafter. No pre-exposure blood BeLPT is conducted at this plant.

The current criteria for establishing confirmed BeS is two positive blood BeLPTs. Workers identified as beryllium sensitized are offered further clinical evaluation, including bronchoscopy with bronchoalveolar lavage and transbronchial lung biopsy.[4] Follow-up testing to determine whether an employee has sCBD or cCBD is encouraged but not mandatory.

The current criteria for sCBD include two positive blood or one bronchoalveolar lavage BeLPT and the presence of pulmonary granulomas on lung biopsy without physical symptoms, or detection of X-ray or pulmonary function changes typically associated with cCBD pathology. Medical follow-up is offered to workers identified as BeS and CBD cases who leave the active work force. Information on work history including time worked in each job category and the date of BeS ascertainment or CBD diagnosis was obtained for all BeS and CBD workers.

Analysis of the Historical Plant Industrial Hygiene Data

Current and historical industrial hygiene (IH) air sampling data from 1980 to 2005 were provided by the beryllium precision machining plant. The plant maintains an IH database with sampling and analytical information for 3831 personal lapel samples for 16 different job titles, as well as 616 general area air samples for production and nonproduction areas of the plant. This data set also includes samples collected by researchers in prior investigations of this plant.[4,13]

Personal lapel air samples from 1980 to 2005 were collected by plant IH personnel using National Institute for Occupational Safety and Health (NIOSH) Method 7300. These samples were collected using closed-face, 0.8 μm pore-sized mixed cellulose ester filters (MCEF) in line with battery-operated pumps at

flow rates of approximately 2 L/min. High-volume, general area samples were collected in process and nonprocess areas of the plant using a closed-face, 0.8 μm MCEF in line with high-volume electric pumps at a flow rate of approximately 15 L/min and were analyzed at the plant chemical laboratory according to NIOSH Method 7300. Personal lapel and general area measurements were reported as low as 0.01 μg/sample or 0.01 μg/m^3 (based on a full-shift sample at 2 L/min), which is consistent with the limit of detection associated with the NIOSH Method 7300. All samples were analyzed by a graphite furnace atomic absorption spectrometer.

Electronic spreadsheets containing the results of all personal lapel and high-volume general area sampling from 1980 to June 2005 were obtained from the plant. Information and details about sample collection (i.e., time period, sample duration, locations, job categories, etc.) were entered into an Access database for further organization and analysis.

To assess the trend of airborne beryllium concentrations pre- and postimplementation of engineering controls in the mid-1990s, personal lapel and general area measurements were grouped according to distinct time periods when some engineering controls were in place (1980–1995) and when additional exposure controls were being implemented (1996–1999). Exposures between 2000 and 2005 were analyzed as a separate category to understand the current day environment of the plant. These samples reflect time periods with substantial differences in engineering and administrative control improvements.

Personal lapel samples were analyzed for 16 operational departments, including both machining and nonmachining departments, for time periods corresponding to changes in engineering controls, whereas the general area samples were analyzed for process (e.g., machining and nonmachining plant operations) and nonprocess (e.g., administrative) sample locations.

The mean, median, and 95th percentile concentrations were calculated for each grouping of personal and general area samples. The exceedance fraction for 0.02 μg/m^3, 0.2 μg/m^3, and 2 μg/m^3 were also calculated to evaluate trends in airborne beryllium concentrations over the various time periods as the different industrial hygiene controls were implemented.[16]

Exposure Reconstruction of BeS and CBD Workers

To assess the exposure-response relationship between beryllium exposure and disease at this plant location, health surveillance data for all persons identified as beryllium sensitized, sCBD, or cCBD were obtained and analyzed. Detailed work histories were provided by the plant for each of these persons, including job titles held, years worked in each job, and date of BeS ascertainment or CBD diagnosis. To develop an exposure profile for each of these persons, job titles held, and years worked for each was matched to personal lapel sampling data for the relevant job titles and duration.

When available, personal exposure data only from the job titles worked prior to and including initial ascertainment of BeS or diagnosis of CBD were used in defining the exposure profiles for these persons. However, in some circumstances, particularly in nonmachining job titles prior to the mid-1990s, air sampling data were limited. To avoid deriving exposure estimates that are heavily weighted by a few samples and to assess how different methods of reconstructing historical exposures may influence final exposure estimates, several approaches were used to estimate historical exposures for each worker.

In total, five approaches were considered in the reconstruction of historical exposures for workers identified as beryllium sensitized or diagnosed with CBD. For all approaches, mean, median, and 95th percentile beryllium time-weighted average (TWA) concentrations were calculated based on personal lapel samples collected over the 8-hour workday.

The IH data for years prior to BeS ascertainment or CBD diagnosis were evaluated by the following approaches: (1) TWA for highest year exposed based on available IH data (Approach 1, Table II); (2) TWA for highest year exposed based on supplemented IH data by era of engineering controls (Approach 2, Table II); (3) TWA for highest job title exposed based on available IH data (Approach 3, Table II); (4) TWA for all years and jobs worked pooled by era of engineering controls (Approach 4, Table II), and (5) lifetime weighted average (LTW) based on TWA exposures (supplemented with IH data by era) for all years worked for each job title and weighted according to work history (Approach 5, Table III).

In Approaches 1 and 2, IH data based on work history of each beryllium-sensitized and CBD worker were grouped for every year worked within a particular job title. Because studies have demonstrated that BeS and CBD occurred in some cases as a result of exposures less than 1 year, exposures for each worker were reported in terms of the highest exposed year for a particular job title. For years where no samples were collected for a job title, IH data from the next highest year with at least one sample were used in the exposure estimate.

Approaches 1 and 2 were conducted similarly, but Approach 2 involved a slightly different iteration by supplementing IH data for job titles, where the highest year exposed had less than 6 measurements, with data collected over the relevant era of engineering controls for a particular job title. This criterion is consistent with the guidelines published by AIHA, which recommend that 6–10 measurements provide a reasonable approximation of the exposure distribution.[16]

In Approach 3, IH data were grouped using only available data for all years for each job title prior to ascertainment of BeS or diagnosis of CBD. Approach 4 involved pooling airborne beryllium concentrations using all available data within an era to represent all years and jobs worked prior to BeS and CBD ascertainment. With this approach, IH data were grouped by era of similar engineering controls (1980–1995, 1996–1999, 2000–2005).

Approach 5 involved calculating the LTW for each beryllium-sensitized and CBD worker based on TWAs for all years worked in each job title (Table III). Exposure estimates

TABLE II. Exposure Estimates for Workers Identified as Beryllium Sensitized or Diagnosed with Chronic Beryllium Disease (2006)

						Approach 1						Approach 2						Approach 3				Approach 4			
						TWA for Highest Concentration Year (μg/m^3)						TWA for Highest Concentration Year with Supplemented Data (μg/m^3)						TWA for All Years Worked for Each Job Title (μg/m^3)*				TWA for All Years and Jobs Worked Pooled by Era (μg/m^3)			
Case No.	Status	Job Title Used from IH Database	Time Period Worked	Years Worked	DX Date	N^{A}	Mean	N^{A}	Median	N^{A}	95th Percentile	N^{A}	Mean	N^{A}	Median	N^{A}	95th Percentile	N	Mean	Median	95th Percentile	N	Mean	Median	95th Percentile
1	BeS	Grind	1980 to 1995	14.6	1997	2	36.77	2	36.77	2	69.71	13^{B}	8.48	13^{B}	1.05	13^{B}	40.00	13	4.56	3.84	8.73	44	4.17	0.29	17.75
		Grind	1995 to 2003	8.2		3	1.94	3	1.05	9	6.35	320^{B}	0.54	320^{B}	0.12	9	6.35	177	0.64	0.27	2.12				
		Flow Lines^{C}	2003 to 2005	2.1		10	0.09	10	0.10	10	0.16	10	0.09	10	0.10	10	0.16	87	0.07	0.06	0.15				
2	BeS	Grind	1986 to 1990	4.4	1996	3	1.94	3	1.05	3	3.98	13^{B}	8.48	13^{B}	1.05	13^{B}	40.00	3	1.94	1.05	3.98	33	3.40	0.12	10.59
		Flow Lines	1996 to 2000	4.0		10	0.12	44	0.09	10	0.27	10	0.12	44	0.09	10	0.27	64	0.08	0.07	0.18				
		Flow Lines^{C}	2000 to 2002	2.2		15	0.11	44	0.09	15	0.19	15	0.11	44	0.09	15	0.19	92	0.09	0.09	0.15				
3	BeS	Mill and NC Mill	1987 to 1988	1.1	1996	16	0.38	16	0.21	16	1.04	16	0.38	16	0.21	16	1.04	16	0.38	0.21	1.04	136	0.62	0.25	2.25
		Lathe	1995 to 1997	1.8		4	0.41	4	0.46	4	0.62	64^{B}	0.39	64^{B}	0.17	64^{B}	1.68	6	0.34	0.37	0.49				
4	BeS	Mill and NC Mill	1978	0.2	1995	9	0.45	9	0.36	9	1.15	9	0.45	9	0.36	9	1.15	9	0.45	0.36	1.15	73	0.81	0.29	2.59
		C-Grind	1978 to 1996	17.5		1	0.12	1	0.12	1	0.12	11^{B}	0.13	11^{B}	0.10	11^{B}	0.37	5	0.12	0.12	0.12				
5	BeS	Mill and NC Mill	1996	0.4	1996	1	0.92	1	0.92	1	0.92	128^{B}	0.67	128^{B}	0.18	128^{B}	1.41	1	0.92	0.92	0.92	128	0.67	0.18	1.41
6	sCBD	Mill and NC Mill	1973 to 1989	15.3	1995	13	1.65	7	0.46	13	6.98	13	1.65	7	0.46	13	6.98	72	0.55	0.32	1.73	72	0.82	0.30	2.60
		Admin	1989 to 1991	2.5		1	0.85	1	0.85	1	0.85	83^{B}	0.09	83^{B}	0.07	83^{B}	0.18	1	0.85	0.85	0.85				
		Admin	1991 to 1995	3.6		1	0.85	1	0.85	1	0.85	83^{B}	0.09	83^{B}	0.07	83^{B}	0.18	1	0.85	0.85	0.85				
		Admin	1995	0.6		1	0.85	1	0.85	1	0.85	83^{B}	0.09	83^{B}	0.07	83^{B}	0.18	1	0.85	0.85	0.85				
7	cCBD	Mill and NC Mill	1975 to 1996	21.0	1994	13	1.65	1	0.92	13	6.98	13	1.65	200^{B}	0.19	13	6.98	73	0.53	0.31	1.55	72	0.82	0.30	2.60
8	sCBD	Mill and NC Mill	1976 to 1987	11.0	1997	13	1.65	7	0.46	13	6.98	13	1.65	7	0.46	13	6.98	72	0.61	0.33	1.98	156	0.42	0.10	1.51
		Engineering/Est.	1987 to 1989	1.8		16	0.07	16	0.05	16	0.20	16	0.07	16	0.05	16	0.20	16	0.07	0.05	0.20				
		Engineering/Est.	1989 to 1994	5.0		16	0.07	16	0.05	16	0.20	16	0.07	16	0.05	16	0.20	16	0.07	0.05	0.20				
		Engineering/Est.	1994	0.9		16	0.07	16	0.05	16	0.20	16	0.07	16	0.05	16	0.20	16	0.07	0.05	0.20				
		Admin	1994 to 1995	0.9		1	0.85	1	0.85	1	0.85	83^{B}	0.09	83^{B}	0.07	83^{B}	0.18	1	0.85	0.85	0.85				
		Admin	1995 to 1999	3.9		1	0.85	1	0.85	1	0.85	83^{B}	0.09	83^{B}	0.07	83^{B}	0.18	83	0.54	0.53	0.58				
		Engineering/Est.^{C}	1999 to 2000	0.8		27	0.08	27	0.09	27	0.10	27	0.08	27	0.09	27	0.10	56	0.08	0.08	0.10				
		Admin^{C}	2004 to 2005	1.0		51	0.07	51	0.04	51	0.17	51	0.07	51	0.04	51	0.17	135	0.05	0.03	0.13				
9	sCBD	Grind	1970 to 2003	33.0	1997	2	36.77	2	36.77	2	69.71	320^{B}	0.54	320^{B}	0.12	320^{B}	0.85	187	2.73	2.33	5.44	44	2.90	0.24	9.10
		Inspection^{C}	2003 to 2005	2.5		68	0.06	68	0.05	68	0.16	68	0.06	68	0.05	68	0.16	159	0.05	0.03	0.12				
10	sCBD	P/C and I/C	1996 to 2000	3.7	1997	10	0.10	10	0.10	5	0.16	10	0.10	10	0.10	90^{B}	0.28	19	0.09	0.09	0.14	9	0.09	0.10	0.16
		Optics^{C}	2000 to 2005	5.0		7	0.12	7	0.13	21	0.31	7	0.12	7	0.13	21	0.31	66	0.10	0.09	0.18				
11	BeS	Mill and NC Mill	1996 to 1997	0.6	1997	34	2.04	1	0.92	34	4.32	34	2.04	128^{B}	0.18	34	4.32	35	1.48	0.64	2.62	128	0.67	0.18	1.41
12	sCBD	Lap	1982 to 1992	10.3	1995	3	0.18	3	0.09	3	0.36	9^{B}	0.15	9^{B}	0.09	9^{B}	0.37	3	0.18	0.09	0.36	9	0.15	0.09	0.39
		Chem. Finishing	1992 to 1993	0.3		2	12.73	2	12.73	2	23.71	19^{B}	1.54	19^{B}	0.21	19^{B}	3.37	2	12.73	12.73	23.71				
		Lap	1993 to 1994	0.9		3	0.18	3	0.09	3	0.36	9^{B}	0.15	9^{B}	0.09	9^{B}	0.37	3	0.18	0.09	0.36				
		Lap	1994 to 2005	10.1		1	0.86	1	0.86	26	1.06	257^{B}	0.16	257^{B}	0.09	26	1.06	251	0.22	0.17	0.44				

(Continued on next page)

TABLE II. Exposure Estimates for Workers Identified as Beryllium Sensitized or Diagnosed with Chronic Beryllium Disease (2006) *(Continued)*

						Approach 1						Approach 2						Approach 3				Approach 4			
						TWA for Highest Concentration Year (μg/m³)						TWA for Highest Concentration Year with Supplemented Data (μg/m³)						TWA for All Years Worked for Each Job Title (μg/m³)*				TWA for All Years and Jobs Worked Pooled by Era (μg/m³)			
Case No.	Status	Job Title Used from IH Database	Time Period Worked	Years Worked	DX Date	N[A]	Mean	N[A]	Median	N[A]	95th Percentile	N[A]	Mean	N[A]	Median	N[A]	95th Percentile	N	Mean	Median	95th Percentile	N	Mean	Median	95th Percentile
13	sCBD	EDM	1996 to 1997	0.7	1996	3	0.08	3	0.02	3	0.18	12[B]	0.09	12[B]	0.03	12[B]	0.23	3	0.08	0.02	0.18	12	0.09	0.03	0.23
14	sCBD	Mill and NC Mill	1976 to 1992	15.9	1995	13	1.65	7	0.46	13	6.98	13	1.65	7	0.46	13	6.98	72	0.54	0.29	1.71	73	0.81	0.29	2.59
		Engineering/Est.	1992 to 2005	12.7		27	0.08	27	0.09	16	0.20	27	0.08	27	0.09	16	0.20	220	0.06	0.05	0.16				
15	sCBD	Lap	1982 to 1988	5.3	1997	3	0.18	3	0.09	3	0.36	9[B]	0.15	9[B]	0.09	9[B]	0.37	3	0.18	0.09	0.36	72	0.20	0.10	0.76
		Gas Bearings	1988 to 1993	5.5		25	0.09	25	0.09	25	0.13	25	0.09	25	0.09	25	0.13	25	0.09	0.09	0.13				
		P/C and I/C	1993 to 1996	3.2		4	0.08	4	0.08	4	0.14	10[B]	0.09	10[B]	0.08	10[B]	0.16	5	0.05	0.05	0.06				
		Lap	1996 to 2001	5.0		1	0.86	1	0.86	26	1.06	248[B]	0.16	248[B]	0.10	26	1.06	104	0.30	0.25	0.55				
		Inspection[C]	2001 to 2003	1.5		37	0.07	37	0.07	68	0.16	37	0.07	37	0.07	68	0.16	122	0.06	0.06	0.11				
		Inspection[C]	2003 to 2005	2.1		68	0.06	68	0.05	68	0.16	68	0.06	68	0.05	68	0.16	159	0.05	0.03	0.12				
16	BeS	Inspection	1997 to 1998	1.4	1997	13	0.12	13	0.06	13	0.39	13	0.12	13	0.06	13	0.39	13	0.12	0.06	0.39	28	0.11	0.09	0.27
17	sCBD	Mill and NC Mill	1981 to 1999	17.5	1997	34	2.04	1	0.92	13	6.98	34	2.04	200[B]	0.19	13	6.98	191	0.60	0.28	1.71	200	0.72	0.19	2.22
18	sCBD	Lap	1974 to 1991	17.2	1995	3	0.18	2	0.10	3	0.36	9[B]	0.15	9[B]	0.09	9[B]	0.37	9	0.17	0.09	0.33	9	0.15	0.09	0.37
		Chem. Finishing	1991 to 1999	7.9		2	12.73	2	12.73	2	23.71	19[B]	1.54	19[B]	0.21	19[B]	3.37	19	9.95	9.94	18.58				
19	sCBD	Maintenance	1969 to 1983	13.5	1995	2	3.10	2	3.10	2	3.28	15[B]	0.59	15[B]	0.16	15[B]	3.01	2	3.10	3.10	3.28	2	3.10	3.10	3.28
		Maintenance	1983 to 1999	16.2		2	3.10	2	3.10	2	3.28	15[B]	0.59	15[B]	0.16	15[B]	3.01	15	2.41	2.41	2.57				
20	sCBD	Mill and NC Mill	1984 to 1995	11.0	1995	7	0.66	7	0.46	7	1.87	7	0.66	7	0.46	7	1.87	23	0.40	0.23	1.11	72	0.82	0.30	2.60
		Inspection[C]	2003 to 2005	2.0		68	0.06	68	0.05	68	0.16	68	0.06	68	0.05	68	0.16	159	0.05	0.03	0.12				
21	sCBD	Mill and NC Mill	1986 to 1991	5.1	2005	16	0.38	16	0.21	16	1.04	16	0.38	16	0.21	16	1.04	16	0.38	0.21	1.04	452	0.14	0.05	0.36
		P/C and I/C	1991 to 1997	6.0		4	0.08	4	0.08	4	0.14	10[B]	0.09	10[B]	0.08	10[B]	0.16	5	0.05	0.05	0.07				
		Admin	1997 to 2004	6.9		1	0.85	1	0.85	1	0.85	370[B]	0.07	370[B]	0.05	370[B]	0.15	319	0.17	0.15	0.22				
		Admin	2004 to 2005	0.7		51	0.07	51	0.04	51	0.17	51	0.07	51	0.04	51	0.17	135	0.05	0.03	0.13				
22	sCBD	Grind	1979 to 1996	16.8	1999	2	36.77	2	36.77	2	69.71	44[B]	2.90	44[B]	0.24	44[B]	9.10	22	4.22	3.52	8.28	54	2.39	0.22	7.16
		C-Grind	1996 to 2005	9.3		6	0.19	6	0.17	6	0.38	6	0.19	6	0.17	6	0.38	152	0.09	0.09	0.15				
23	sCBD	Mill & NC Mill	1998 to 2000	2.4	2005	34	0.17	59	0.16	34	0.54	34	0.17	59	0.16	34	0.54	219	0.16	0.14	0.35	1346	0.16	0.09	0.28
		Grind	2000	0.3		35	0.14	35	0.12	35	0.25	35	0.14	35	0.12	35	0.25	35	0.14	0.12	0.25				
		Engineering/Est.	2000 to 2005	4.7		12	0.08	12	0.07	40	0.16	12	0.08	12	0.07	40	0.16	177	0.06	0.05	0.11				
24	BeS	Chem. Finishing	2002 to 2005	2.7	2004	40	0.17	40	0.15	40	0.49	40	0.17	40	0.15	40	0.49	110	0.12	0.11	0.25	153	0.13	0.12	0.27
25	BeS	Inspection	1972 to 1994	21.7	1999	13	0.12	13	0.06	13	0.39	13	0.12	13	0.06	13	0.39	13	0.12	0.06	0.39	28	0.11	0.09	0.27
		Inspection	1999 to 2005	6.3		15	0.10	15	0.09	15	0.20	15	0.10	15	0.09	15	0.20	261	0.06	0.06	0.12				
26	sCBD	P/C and I/C	1981 to 1982	1.8	1999	1	0.04	1	0.04	1	0.04	10[B]	0.09	10[B]	0.08	10[B]	0.16	1	0.04	0.04	0.04	84	0.09	0.07	0.18
		Chem. Finishing	1982 to 1994	11.7		2	12.73	2	12.73	2	23.71	19[B]	1.54	19[B]	0.21	19[B]	3.37	2	12.73	12.73	23.71				
		Admin	1994 to 1995	0.8		1	0.85	1	0.85	1	0.85	83[B]	0.09	83[B]	0.07	83[B]	0.18	1	0.85	0.85	0.85				
		Admin	1995 to 1998	3.2		1	0.85	1	0.85	1	0.85	83[B]	0.09	83[B]	0.07	83[B]	0.18	40	0.66	0.65	0.69				
		Admin	1998 to 1999	0.5		43	0.08	43	0.07	39	0.21	43	0.08	43	0.07	39	0.21	82	0.08	0.06	0.18				
		Admin	1999 to 2000	1.2		43	0.08	43	0.07	43	0.16	43	0.08	43	0.07	43	0.16	77	0.08	0.07	0.13				
27	cCBD	Mill and NC Mill	1999 to 2000	36.1	2005	34	2.04	1	0.92	13	6.98	34	2.04	965[B]	0.11	13	6.98	965	0.47	0.28	1.28	965	0.23	0.11	0.42

Note: BeS = beryllium sensitization; sCBD = subclinical chronic beryllium disease; cCBD = clinical chronic beryllium disease; IH = industrial hygiene; TWA = time-weighted average. Exposure estimates are based on available data for year and job title. Although, in some circumstances, fewer than three samples were available for the relevant job title and time period, summary statistics were presented for all cases for consistency. Status of each worker (BeS, sCBD, or cCBD) based on the status at the time of surveillance.

[A] N represents highest mean, median, 95th percentile for any given year within a job prior to diagnosis. N can differ if the highest mean, median, or 95th percentile are not represented in the same year.

[B] Began work at this job title after diagnosis.

[C] Supplemented with data from relevant eras of engineering controls for a corresponding job title because $n < 6$.

TABLE III. LTW Exposure Estimates for Workers Identified as Beryllium Sensitized or Diagnosed with Chronic Beryllium Disease

					Approach 5								Kelleher et al.[4] LTW ($\mu g/m^3$)
					TWA for All Years Worked for Each Job Title with Supplemented Data ($\mu g/m^3$)^A				LTW Based on All Years Worked for Each Job Title with Supplemented Data ($\mu g/m^3$)				
Case No.	Status	Job Title Used from IH Database	Years Worked Prior to Dx	DX Date	N	Mean	Median	95th Percentile	N	Mean	Median	95th Percentile	Median
1	BeS	Grind	14.6	1997	13	4.56	3.84	8.73	22	4.15	3.39	8.30	0.35
		Grind	2.3		12	1.58	0.52	5.56					
2	BeS	Grind	4.4	1996	13^B	8.48	1.05	40.00	23	7.89	0.98	37.19	0.35
		Flow Lines	0.3		10	0.07	0.06	0.18					
3	BeS	Mill and NC Mill	1.1	1996	16	0.38	0.21	1.04	80	0.38	0.19	1.32	0.60
		Lathe	0.9		64^B	0.39	0.17	1.68					
4	BeS	Mill and NC Mill	0.2	1995	9	0.45	0.36	1.15	20	0.14	0.10	0.37	0.035
		C-Grind	16.6		11^B	0.13	0.10	0.37					
5	BeS	Mill and NC Mill	0.3	1996	128^B	0.67	0.18	1.41	128	0.67	0.18	1.41	0.25
6	SubCBD	Mill and NC Mill	15.3	1995	72	0.55	0.32	1.73	155	0.41	0.24	1.26	0.45
		Admin	2.5		83^B	0.09	0.07	0.18					
		Admin	3.6		83^B	0.09	0.07	0.18					
		Admin	0.5		83^B	0.09	0.07	0.18					
7	CBD	Mill and NC Mill	19.8	1994	56	0.52	0.29	1.61	56	0.52	0.29	1.61	0.25
8	SubCBD	Mill and NC Mill	11.0	1997	72	0.61	0.33	1.98	171	0.35	0.20	1.12	0.17
		Engineering/Est.	1.8		16	0.07	0.05	0.20					
		Engineering/Est.	5.0		16	0.07	0.05	0.20					
		Engineering/Est.	0.9		16	0.07	0.05	0.20					
		Admin	0.9		83^B	0.09	0.07	0.18					
		Admin	1.7		83^B	0.09	0.07	0.18					
9	SubCBD	Grind	27.5	1997	22	3.28	2.79	6.52	22	3.28	2.79	6.52	0.35
10	SubCBD	P/C and I/C	0.9	1997	90^B	0.10	0.08	0.28	90	0.10	0.08	0.28	0.024
11	BeS	Mill and NC Mill	0.4	1997	35	1.48	0.64	2.62	35	1.48	0.64	2.62	0.25
12	SubCBD	Lap	10.3	1995	9^B	0.15	0.09	0.37	270	0.19	0.09	0.46	0.13
		Chem. Finishing	0.3		19^B	1.54	0.21	3.37					
		Lap	0.9		9^B	0.15	0.09	0.37					
		Lap	0.6		257^B	0.16	0.09	0.48					
13	SubCBD	EDM	0.2	1996	12^B	0.09	0.03	0.23	12	0.09	0.03	0.23	0.038
14	SubCBD	Mill and NC Mill	15.9	1995	72	0.54	0.29	1.71	88	0.47	0.26	1.48	0.53
		Engineering/Est	2.8		16	0.07	0.05	0.20					
15	SubCBD	Lap	5.3	1997	9^B	0.15	0.09	0.37	55	0.14	0.12	0.27	0.08
		Gas Bearings	5.5		25	0.09	0.09	0.13					
		P/C and I/C	3.2		10^B	0.09	0.08	0.16					

(Continued on next page)

TABLE III. LTW Exposure Estimates for Workers Identified as Beryllium Sensitized or Diagnosed with Chronic Beryllium Disease *(Continued)*

					Approach 5								
					TWA for All Years Worked for Each Job Title with Supplemented Data ($\mu g/m^3$)[A]				LTW Based on All Years Worked for Each Job Title with Supplemented Data ($\mu g/m^3$)				Kelleher et al.[(4)] LTW ($\mu g/m^3$)
Case No.	Status	Job Title Used from IH Database	Years Worked Prior to Dx	DX Date	N	Mean	Median	95th Percentile	N	Mean	Median	95th Percentile	Median
		Lap	1.1		11	0.56	0.48	0.75					
16	BeS	Inspection	0.2	1997	13	0.12	0.06	0.39	13	0.12	0.06	0.39	0.25
17	SubCBD	Mill and NC Mill	15.7	1997	98	0.65	0.30	1.86	98	0.65	0.30	1.86	0.25
18	SubCBD	Lap	17.2	1995	9	0.17	0.09	0.33	28	0.43	0.11	0.90	0.12
		Chem. Finishing	4.0		19[B]	1.54	0.21	3.37					
19	SubCBD	Maintenance	13.5	1995	15[B]	0.59	0.16	3.01	15	0.59	0.16	3.01	0.11
		Maintenance	12.2		15[B]	0.59	0.16	3.01					
20	SubCBD	Mill and NC Mill	10.7	1995	23	0.40	0.23	1.11	23	0.40	0.23	1.11	0.25
21	SubCBD	Mill and NC Mill	5.1	2005	16	0.38	0.21	1.04	396	0.20	0.14	0.42	
		P/C and I/C	6.0		10[B]	0.09	0.08	0.16					
		Admin	6.9		319	0.17	0.15	0.22					
		Admin	0.3		135	0.05	0.03	0.13					
22	SubCBD	Grind	16.8	1999	22	4.22	3.52	8.28	36	3.52	2.94	6.91	
		C-Grind	3.4		10	0.09	0.08	0.17					
23	SubCBD	Mill and NC Mill	2.4	2005	219	0.16	0.14	0.35	431	0.10	0.09	0.20	
		Grind	0.3		35	0.14	0.12	0.25					
		Engineering/Est.	4.3		177	0.06	0.05	0.11					
24	BeS	Chem. Finishing	1.9	2004	91	0.15	0.14	0.32	91	0.15	0.14	0.32	
25	BeS	Inspection	21.7	1999	13	0.12	0.06	0.39	28	0.12	0.06	0.39	
		Inspection	0.4		15	0.10	0.09	0.20					
26	SubCBD	P/C and I/C	1.8	1999	10[B]	0.09	0.08	0.16	112	1.11	0.26	2.29	
		Chem. Finishing	11.7		19[B]	1.54	0.21	3.37					
		Admin	0.8		83[B]	0.09	0.07	0.18					
		Admin	3.2		40	0.66	0.65	0.69					
		Admin	0.5		82	0.08	0.06	0.18					
		Admin	0.3		43	0.08	0.07	0.16					
27	CBD	Mill and NC Mill	36.1	2005	965	0.47	0.28	1.28	965	0.47	0.28	1.28	

Notes: LTW = lifetime weighted; TWA = time-weighted average.
[A]Similar to Approach 3 in Table II with the exception that exposure estimates were supplemented with additional data from the corresponding era worked when sample numbers were low (N < 6).
[B]Supplemented with data from relevant eras of engineering controls for a corresponding job title because n < 6.

derived from this approach involved grouping IH data for all years worked for each job title prior to ascertainment of BeS or diagnosis of CBD. When samples sizes were less than six, IH datasets were supplemented with data from the relevant era of engineering controls. LTW exposures were calculated by multiplying the airborne beryllium concentration by the years in each job title divided by the total years of employment. LTW estimates in our exposure analysis were also compared with those reported for Cases 1 through 20 in the original study by Kelleher et al.[4] of this machining plant (Table III).

Selection of the Best Descriptor of Exposure for BeS or CBD

Several studies of beryllium-sensitized or CBD workers have provided varying rationales which measures of central tendency are appropriate for use in estimating worker exposure.[4,8,9] Whereas some researchers have argued that arithmetic mean most accurately reflects cumulative exposure and the geometric mean is the best estimate for central tendency of log-normally distributed exposure data,[16] others have rationalized that the median is more appropriate for skewed data that may have a significant number of non-detectable measurements.[8,9] These issues are certainly important in considering the metric representing the best measure of central tendency for exposure in a group of individuals. However, a central tendency metric of exposure might not be the most appropriate measure for a chemical, such as beryllium, which has an immunological based pathology and has been shown to result in BeS or CBD in some workers with a relatively short work history (i.e., less than 1 year).

In identifying a protective level of exposure, it is critical to understand the dose-response relationship and the probability that a given level of exposure will not result in effects being observed in a known percentage of the population. Upper bound estimates of exposure, such as the 95th percentile concentration, allow one to define the upper distribution of exposure that is associated with disease and are important in the context of identifying a protective exposure level, particularly when effects can occur in less than 1 year.

The immunologic basis of CBD suggests that exposures less than 1 year can initiate the immune response or disease. Thus, understanding the upper bound exposure distribution associated with the highest exposed jobs is essential. Support for this is shown in studies of short-term exposures to beryllium that resulted in the detection of BeS or diagnosis of CBD in workers employed for as little as 3 months.[4,15,17] Studies have also reported that upper bound exposures, as defined by the 75th percentile or the number of self-reported accidental overexposures, are associated with CBD.[6,8,9,14] Further, work in higher potential exposure jobs such as in the machining of beryllium metal and beryllium oxide shows greater prevalence of BeS and CBD than lower exposure jobs,[4,8] and when upper bound air level exposures are well controlled, the incidence of CBD has been low or markedly decreased in some worker populations.[18] Although both mean and median beryllium exposures were considered in this analysis, particular emphasis was placed on understanding the relation between 95th percentile exposure concentration to beryllium and exceedance fractions as they relate to BeS and CBD.

RESULTS

Analysis of the Historical Plant Industrial Hygiene Data

Personal lapel and general area sampling results, grouped by the time periods before 1995 (1980–1995), during 1996–1999, and after 2000 (2000–2005) characterizing different levels of industrial hygiene control measures, are summarized in Table IV. Job categories with the highest personal lapel beryllium concentrations during 1980–1995 time period included Grinding, Lathe, Maintenance, and Mill/NC Mill. These operations showed mean beryllium concentrations ranging from 0.82 $\mu g/m^3$ to 8.48 $\mu g/m^3$ and 95th percentile concentrations ranging from 2.52 $\mu g/m^3$to 40.0 $\mu g/m^3$; these samples were collected during a time period when exposure characterization focused on high exposure tasks (i.e., changing of bag houses by maintenance workers). All other job categories during this period showed mean concentrations equal to or less than 0.25 $\mu g/m^3$ and 95th percentile concentrations equal to or less than 0.47 $\mu g/m^3$.

During the implementation of additional or improved exposure control measures (1996–1999), the highest exposures were measured in Chemical Finishing, Grinding, Lapping, and Mill/NC Mill operations. Mean exposures for these job categories ranged from 0.23 to 1.54 $\mu g/m^3$, where the 95th percentile concentrations ranged from 0.91 $\mu g/m^3$ to 3.37 $\mu g/m^3$. Mean and 95th percentile concentrations for all other job categories were equal to or less than 0.20 $\mu g/m^3$ and 0.64 $\mu g/m^3$, respectively.

During the 2000–2005 time period when control improvements were greatest, the mean and 95th percentile concentrations were equal to or less than 0.16 $\mu g/m^3$ and 0.61 $\mu g/m^3$, respectively. These results clearly show the effectiveness of engineering and administrative controls in reducing beryllium exposures for each job category by at least an order of magnitude from 1980 levels to those observed in 2005.

These data also clearly show that personal airborne concentrations of beryllium when grouped as a broad category for machining and nonmachining operations decreased substantially after additional control measures were implemented in the plant in 1996. Figure 1 shows a clear downward trend of airborne beryllium concentrations for personal lapel samples for machining and nonmachining job titles. Between 1980 and 1995, machining operations showed a mean airborne beryllium concentration of 1.63 $\mu g/m^3$ and a 95th percentile concentration of 3.81 $\mu g/m^3$. In 1996–1999, beryllium concentrations for these operations decreased substantially to a mean concentration of 0.45 $\mu g/m^3$ and a 95th percentile concentration of 0.93 $\mu g/m^3$. These levels were further reduced from 2000–2005 to mean levels of 0.11 $\mu g/m^3$ and a 95th percentile concentration of 0.24 $\mu g/m^3$.

TABLE IV. Summary of Historical Personal Lapel (PL) and General Area (GA) Industrial Hygiene Data Collected During Different Time Periods

		1980–1995							1996–1999							2000–2005						
						Exceedance Frac.							Exceedance Frac.							Exceedance Frac.		
Department	Category	N	Mean	Median	95th Percentile	0.02	0.2	2	N	Mean	Median	95th Percentile	0.02	0.2	2	N	Mean	Median	95th Percentile	0.02	0.2	2
Personal Lapel Samples																						
Admin	N	—	—	—	—	—	—	—	83	0.09	0.07	0.18	97%	5%	0.0%	287	0.06	0.04	0.12	83%	2%	0.0%
C-Grind**^{A}	M	1	0.12	0.12	0.12	—	—	—	10	0.14	0.09	0.37	83%	23%	0.7%	142	0.08	0.08	0.16	94%	7%	0.0%
Chem. finishing	N	—	—	—	—	—	—	—	19	1.54	0.21	3.37	92%	49%	7.1%	153	0.13	0.12	0.27	97%	20%	0.0%
EDM**	M	2	0.06	0.06	0.11	62%	14%	0.8%	12	0.09	0.03	0.23	61%	16%	1.2%	89	0.11	0.11	0.19	100%	10%	0.0%
Engineering/est.**^{A}	N	1	0.07	0.07	0.07	—	—	—	43	0.08	0.08	0.15	98%	3%	0.0%	177	0.06	0.06	0.10	86%	2%	0.0%
Flow lines**^{A}	N	3	0.25	0.12	0.47	100%	47%	0.3%	20	0.09	0.06	0.25	88%	14%	0.0%	179	0.08	0.07	0.16	97%	4%	0.0%
Gas bearings	M	—	—	—	—	—	—	—	—	—	—	—	—	—	—	158	0.05	0.05	0.12	85%	2%	0.0%
Grind	M	13	8.48	1.05	40.00	99%	86%	44%	31	0.56	0.18	1.04	98%	50%	2.2%	276	0.16	0.11	0.61	96%	24%	0.1%
Inspection	N	—	—	—	—	—	—	—	28	0.11	0.09	0.27	92%	13%	0.0%	246	0.06	0.05	0.14	84%	3%	0.0%
JWST	M	—	—	—	—	—	—	—	–	—	—	—	—	—	—	10	0.02	0.02	0.03	24%	0%	0.0%
Lap	M	9	0.15	0.09	0.37	100%	22%	0.0%	53	0.23	0.10	0.91	93%	33%	1.0%	195	0.14	0.09	0.33	97%	18%	0.0%
Lathe	M	18	0.88	0.35	2.52	100%	79%	11%	46	0.20	0.13	0.64	95%	31%	0.5%	288	0.10	0.08	0.21	98%	9%	0.0%
Maintenance**^{A}	N	2	3.10	3.10	3.28	100%	100%	100%	13	0.20	0.16	0.42	100%	40%	0.0%	102	0.11	0.10	0.22	96%	13%	0.0%
Mill and NC Mill	M	72	0.82	0.30	2.60	99%	66%	6.7%	128	0.67	0.18	1.41	96%	45%	2.1%	765	0.10	0.09	0.21	98%	11%	0.0%
Optics	N	—	—	—	—	—	—	—	—	—	—	—	—	—	—	66	0.09	0.06	0.16	92%	7%	0.0%
P/C and I/C**	N	1	0.04	0.04	0.04	—	—	—	9	0.09	0.10	0.16	93%	10%	0.0%	81	0.10	0.08	0.28	94%	11%	0.0%
Machining PL		115	1.63	0.33	3.81	98%	66%	11%	280	0.45	0.16	0.93	93%	38%	1.8%	1913	0.11	0.09	0.24	96%	12%	0.0%
Nonmachining PL		7	1.01	0.12	3.18	93%	58%	14%	215	0.22	0.08	0.30	94%	15%	0.0%	1301	0.08	0.06	0.18	89%	6%	0.0%
General Area Samples																						
Process GA**^{A}		2	0.20	0.20	0.38	59%	31%	11%	102	0.06	0.06	0.16	73%	9%	0%	445	0.08	0.04	0.19	86%	3%	0%
Nonprocess GA		10	0.04	0.05	0.07	75%	2%	0%	18*	0.04	0.04	0.10	49%	7%	0%	38	0.04	0.04	0.07	91%	0%	0%

Note: Department/Sample Type: N = nonmachining; M = machining; PL = personal lapel; GA = general area; C-Grind = cutter grind; EDM = electrical discharge machining; JWST = James Webb Space Telescope; NC Mill = numerical controlled mill; P/C and I/C = product control and inventory control. *Nonprocess GA Sample #2-11-17-F (4.42 $\mu g/m^3$) was excluded as an outlier from the 1996-1998 time period in Table IV.^{A} Although, in some circumstances, fewer than three samples were available for a particular job title and time period, summary statistics were presented for all jobs for consistency. Exceedance fraction is an estimate of the proportion of the exposure distribution that describes the probability that an exposure will exceed a specified concentration.

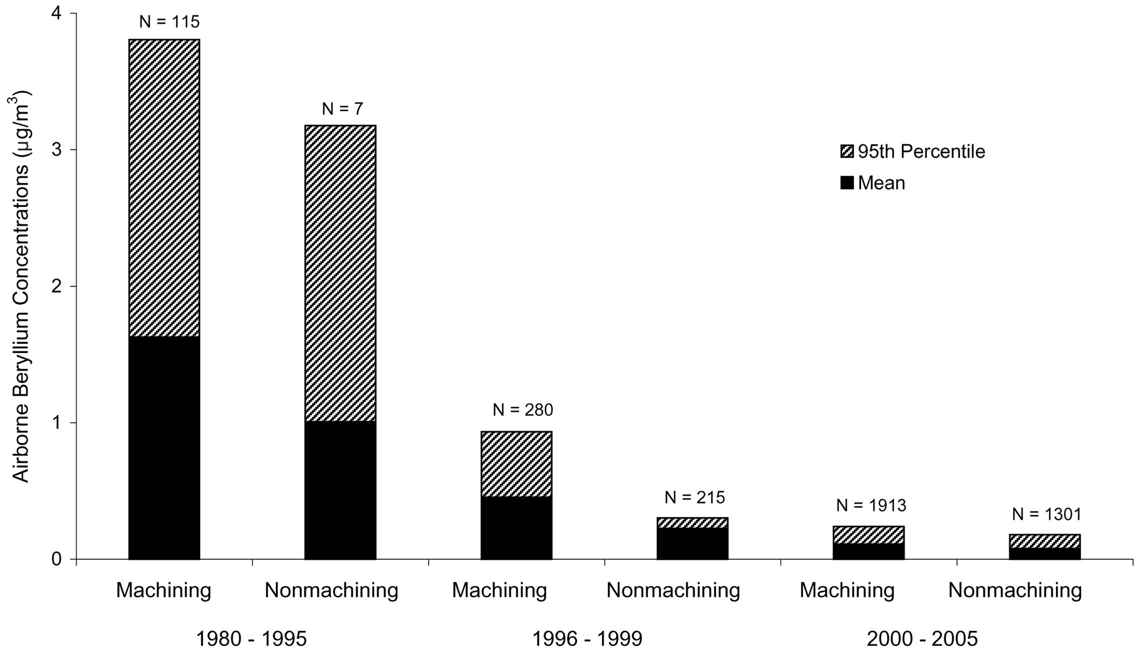

FIGURE 1. Personal lapel beryllium concentrations (mean and 95th percentile) in machining and nonmachining operations at a beryllium machining plant during different time periods

The probability that personal samples exceeded 2.0 μg/m^3, 0.2 μg/m^3, or 0.02 μg/m^3 also decreased over the time periods evaluated. The exceedance fraction above 2 μg/m^3 for samples collected in machining operations in 1980–1995, 1996–1999, and 2000–2005 were 11%, 1.8%, and 0%, respectively, whereas exceedance fractions above 0.2 μg/m^3 were 66%, 38%, and 12%, respectively (Table IV). All exceedance fractions for samples greater than 0.02 μg/m^3 were greater than 93%, meaning that all personal lapel measurements had a greater than 93% probability of exceeding 0.02 μg/m^3.

Based on the exposure trends observed in the personal air samples, worker exposures were approximately four times higher in the period before significant IH improvements were implemented in the 1990s. Further, based on the most recent data (2000–2005), the current exposures have been reduced nearly fifteenfold since the 1980s.

The general area samples showed airborne concentrations lower than the personal lapel samples. Although the data are very limited for the process areas in 1980–1995 (N = 2), the general area air concentrations have been relatively stable over time (Figure 2). General area samples collected in the process areas of the plant showed mean and 95th percentile beryllium concentrations of 0.06 μg/m^3 and 0.16 μg/m^3 in 1996–1999 and 0.08 μg/m^3 and 0.19 μg/m^3 in 2000–2005, respectively (Table IV, Figure 2). The general area samples collected in nonprocess areas were also consistent over time showing mean beryllium concentrations of 0.04 μg/m^3 for each era of engineering controls (e.g., 1980–1995, 1996–1999, 2000–2005). The 95th percentile concentrations for these same time periods ranged from 0.07 μg/m^3 to 0.10 μg/m^3. General area samples collected for process and nonprocess areas had a 49% or greater probability of exceeding 0.02 μg/m^3.

Exposure Reconstruction of Beryllium Sensitized and CBD Workers

Twenty-seven beryllium-sensitized and CBD workers have been identified at the plant since 1995 and include 9 BeS, 16 sCBD, and 2 cCBD cases. The occupational tenure of beryllium-sensitized workers prior to ascertainment of BeS ranged from 0.2 year to 22.1 years with a mean and median of 7.3 years and 2.0 years, respectively. The occupational tenure for the sCBD cases prior to diagnosis ranged from 0.2 year to 27.5 years with a median of 18.3 years prior to diagnosis, whereas cCBD cases worked between 19.8 years and 36.1 years with a median of 28 years prior to diagnosis. Combined (sCBD and cCBD), CBD cases had a mean and median occupational tenure of 17.6 years and 18.5 years, respectively. Eleven percent of CBD cases (both sCBD and cCBD) worked less than 5 years at the plant.

Historical exposures for all 27 workers identified as beryllium sensitized or diagnosed with sCBD or cCBD were reconstructed based on plant IH data. A summary of the work history; employment duration; and mean, median, and 95th percentile TWA concentration of airborne beryllium based on highest exposed year, job title, and era of engineering controls for all years worked is summarized for each worker identified as beryllium sensitized, sCBD, or cCBD in Table II. LTWs based on TWA airborne beryllium concentrations for all years worked for each job title prior to ascertainment of BeS or diagnosis of CBD is shown for each case in

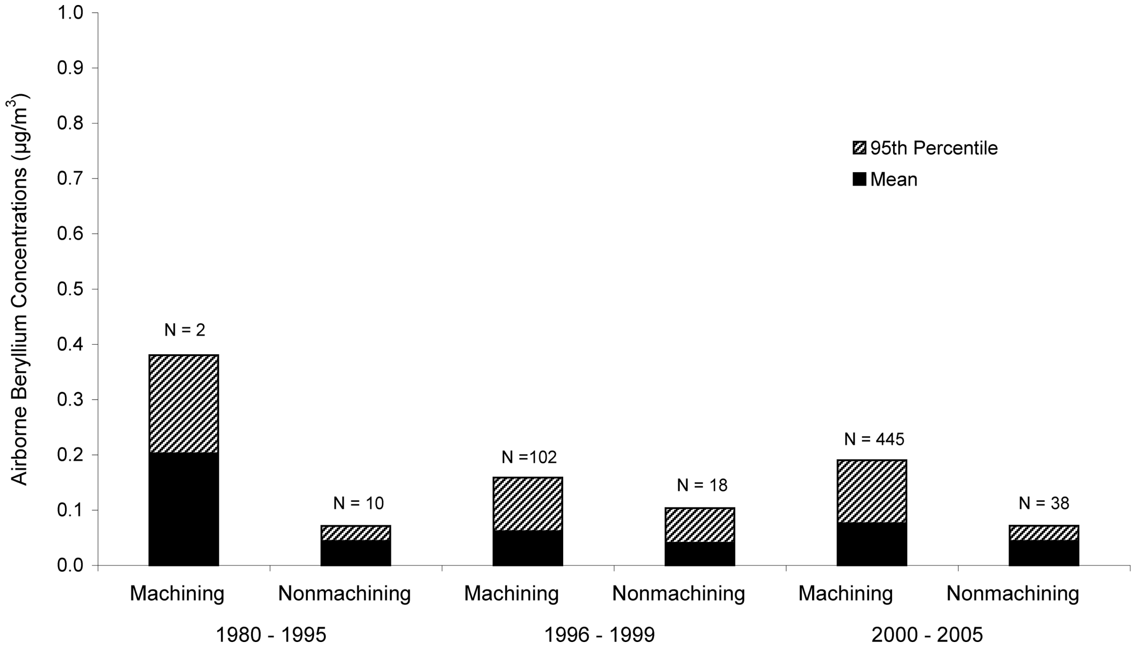

FIGURE 2. General area beryllium concentrations (mean and 95th percentile) in machining and nonmachining operations at a beryllium machining plant during different time periods

Table III. Of the 5 approaches (Tables II and III) that were used to reconstruct individual worker exposures, the magnitude of these exposure estimates depended on whether the IH data were grouped by small or larger units of time (e.g., by year vs. pooled for all years) (Table II, Figures 3a–b, 4a–b). The shorter and more historical period of time from which exposures were derived, the higher the exposure estimates generally were for a particular worker. For example, higher exposures were identified when data were grouped on an annual basis (Approach 1) vs. by all years worked within a particular job title (Approach 3) or by era of engineering controls (Approach 4). Furthermore, exposure estimates were generally lower when more recent data were used and higher when exposures estimates were derived primarily from more historical data.

When exposure estimates were based on all years worked within a particular job title (Approach 3, Table II), median exposures for the highest exposed job title ranged from 0.02 μg/m^3 to 12.73 μg/m^3 with 95th percentile concentrations ranging from 0.14 μg/m^3 to 23.71 μg/m^3. Exposure estimates based on all years and jobs worked pooled by era of engineering controls (Approach 4, Table II) resulted in median beryllium concentrations ranging from 0.03 μg/m^3 to 3.10 μg/m^3 with 95th percentile concentrations ranging from 0.16 μg/m^3 to 17.75 μg/m^3. When exposure estimates were weighted by time worked within a particular job title (LTW), median exposure estimates ranged from 0.03 μg/m^3 to 3.39 μg/m^3 with 95th percentile concentrations ranging from 0.20 μg/m^3 to 37.19 μg/m^3 (Approach 5, Table III).

Of the 27 workers identified as beryllium sensitized or diagnosed with CBD, 22 were involved with machining operations at some point in their career. Workers (three BeS, three sCBD) not involved with machining operations worked in Production Control and Inventory Control (PC&IC), Maintenance, Chemical Finishing, and Inspection. For these six workers, upper bound exposures (95th percentile) based on the highest year exposed (Approach 2, Table II) ranged from 0.28 μg/m^3 (PC&IC) to 3.37 μg/m^3 (Chemical Finishing).

Exposure-Response Analysis of BeS and CBD

To evaluate whether any exposure-response pattern was apparent for workers identified as beryllium sensitized or diagnosed with CBD, the four of the five approaches used to reconstruct historical exposures were ranked by the percentage of total cases from lowest to highest exposed. Figures 3a and 4a show median exposures, whereas Figures 3b and 4b illustrate 95th percentile concentrations of beryllium derived for each case using the four different approaches (e.g., highest year [non supplemented]–Approach 1; job title–Approach 3; era of engineering controls–Approach 4; LTW–Approach 5). These figures show that exposures vary not only depending on the approach that is used but also depending on whether the worker is at the high or low end of the exposure-response curve. In general, the greater the time period that exposures were averaged, the lower the exposures were for a particular case.

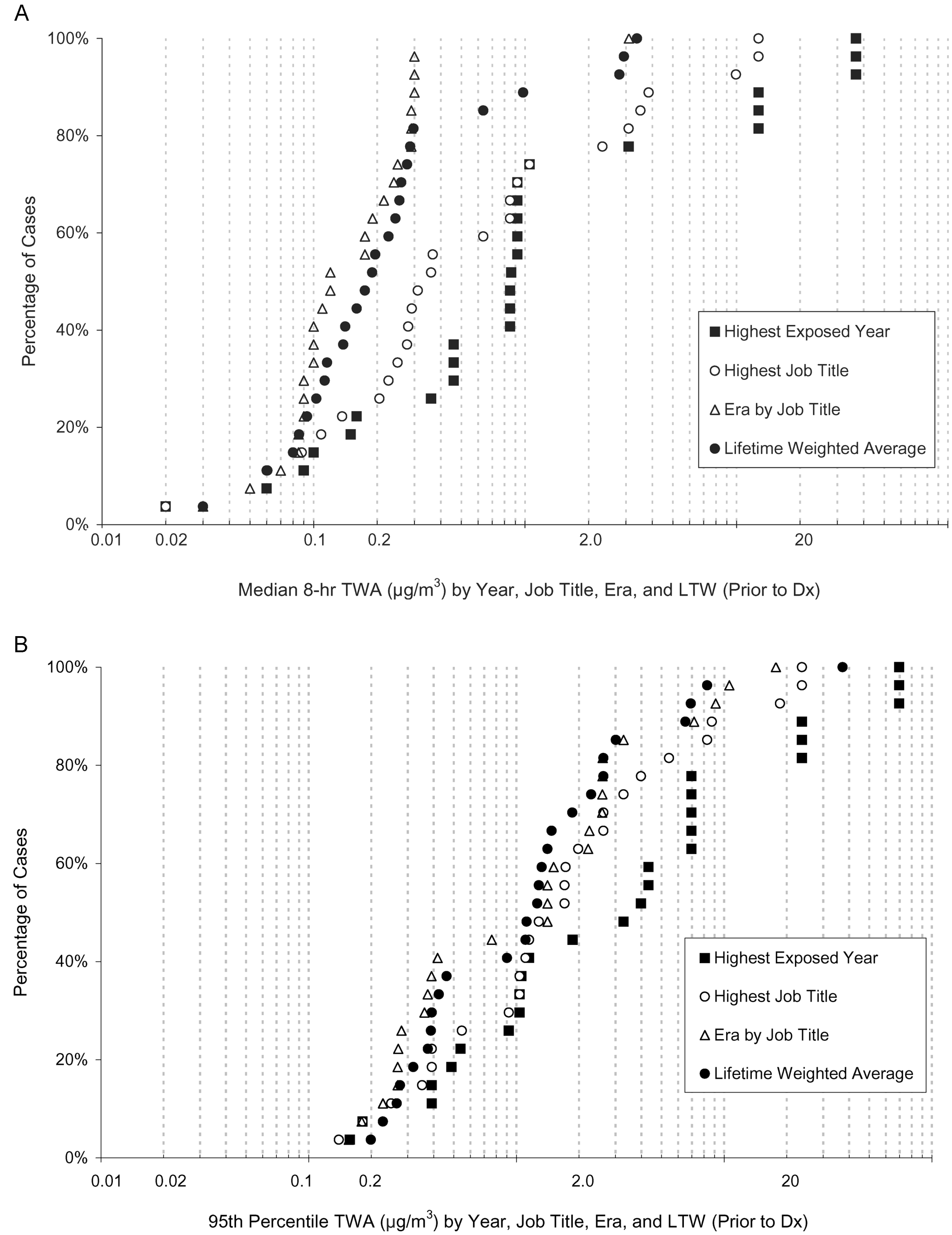

FIGURE 3. (A) Median 8-hr TWA exposures for beryllium sensitized and CBD cases based on different exposure reconstruction methods (ranked lowest to highest for each approach). (B) 95th percentile 8-hr TWA exposures for beryllium sensitized and CBD cases based on different exposure reconstruction methods (ranked lowest to highest for each approach). *Note:* Exposure estimates are based on Approaches 1, 3, 4, 5 from Tables II and III and are ranked from lowest to highest.

In both Figures 3a and 3b, exposure-response curves for LTW exposures (Approach 5) or estimates based on IH data pooled by era of engineering controls (Approach 4) were generally positioned to the left, whereas exposures estimates based on highest exposed year (Approach 1) or highest job title (Approach 3) were located to the right. The LTW estimate was most often the lowest exposure calculated of all the methods used to reconstruct historical exposures for the beryllium-sensitized and CBD workers (Figures 4a and 4b).

A broader range of exposures were observed for workers at the high end of the exposure-response curve compared with those at the lower end of the curve. Differences between methods were greatest for median exposure estimates compared with the 95th percentile (Figures 4a and 4b). Although not

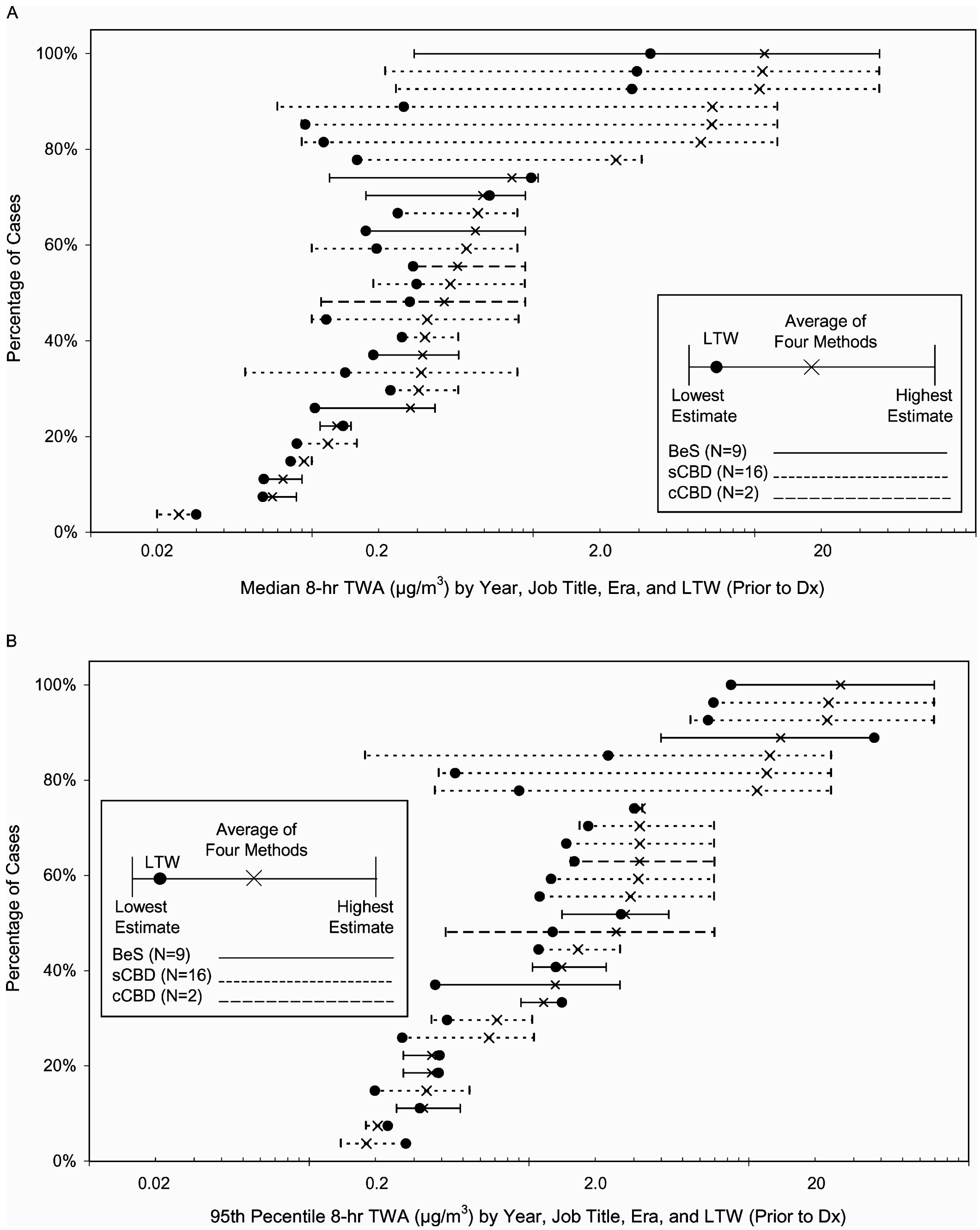

FIGURE 4. (A) Range of median 8-hr TWA exposures estimated for each beryllium sensitized and CBD case using different exposure reconstruction methods. (B) Range of 95th Percentile 8-hr TWA exposures estimated for each beryllium-sensitized and CBD case using different exposure reconstruction methods. *Note:* Exposure estimates are based on approaches 1, 3, 4, 5 from Tables II and III and are ranked by each beryllium sensitized and CBD case

shown, the shape and position of the exposure-response curves for mean exposures for the four different methods were generally between that observed for median and 95th percentile exposure-response curves.

Although not shown, the exposure-response curves based on Approach 2 more closely resembled the LTW curve for median TWA exposures (Figure 3a) and highest job title for 95th percentile TWA exposures (Figure 3b). In general, exposure estimates derived from Approach 2 had very little impact on the 95th percentile exposures but substantially shifted the position of the median exposure-response curve to the left compared with those derived from Approach 1.

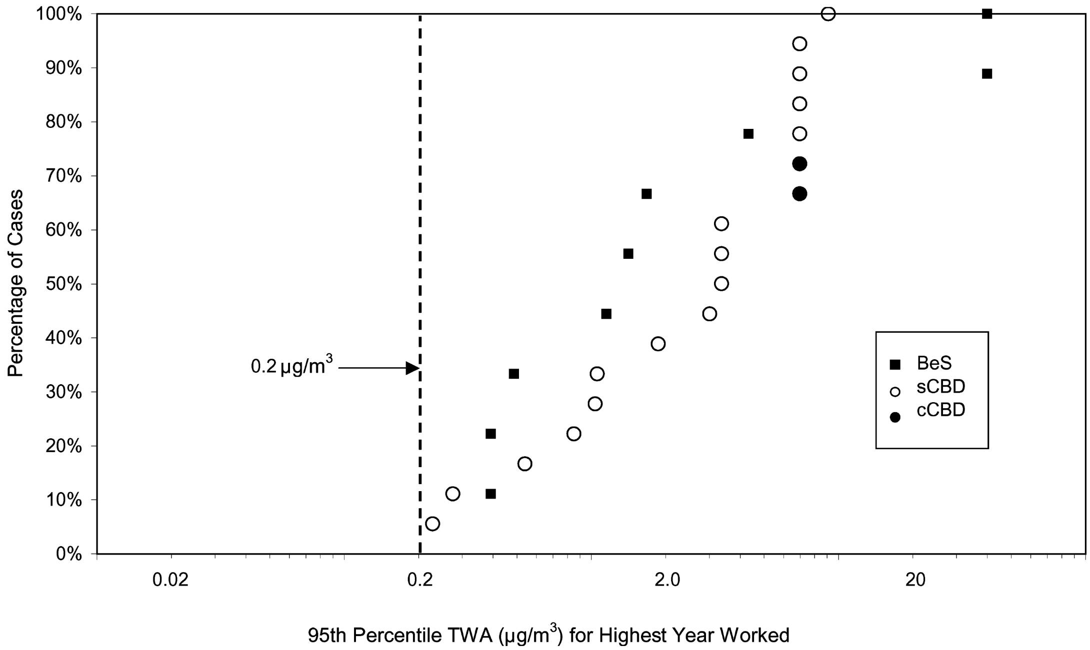

FIGURE 5. TWA beryllium exposures for beryllium-Sensitized and CBD cases (95th percentile based on highest exposed year w worked). *Note:* Exposure estimates are based on Approach 2 (Table II, 95th percentile based on highest exposed year worked with supplemented data when N $<$ 6) and are ranked by each beryllium-sensitized and CBD case.

Potential Threshold for Beryllium Sensitization and Chronic Beryllium Disease

Exposure-response curves for workers identified as beryllium sensitized or diagnosed with CBD demonstrate that historical exposures for these two groups can be differentiated (Figure 5). The exposure-response curve for workers identified as beryllium sensitized were generally to the left of the CBD exposure-response curve, suggesting that higher exposures are required for the development of CBD. Exposure-response curves also showed that beryllium-sensitized and CBD workers experienced upper bound exposures (95th percentile for the highest exposed year with supplemented data) of greater than 0.2 $\mu g/m^3$ (Figure 5).

Data from Approach 2 were used in this exposure-response graph because these data represented the most robust dataset while still capturing upper bound exposures. The results showed that approximately 90% of the beryllium-sensitized and CBD workers were exposed to a 95th percentile concentration of 0.4 $\mu g/m^3$ or greater within a given year of employment (Figure 5).

Based on IH data pooled by era of engineering controls (1980–1995, 1996–1999, 2000–2005) (Approach 4), 26 of the 27 BeS and CBD workers had at least a 10% probability of being exposed to beryllium concentrations exceeding 0.2 $\mu g/m^3$ during their career (Figure 6), whereas all cases had a greater than 5% probability of exceeding this level. There seemed to be no apparent difference in the probability of beryllium-sensitized vs. CBD workers exceeding an exposure of 0.2 $\mu g/m^3$ during their career. Although not shown, all cases had at least a 27% probability of being exposed to beryllium concentrations greater than 0.1 $\mu g/m^3$ prior to their ascertainment of BeS or diagnosis of CBD.

Similarly, all cases had at least a 41% probability of being exposed to 0.05 $\mu g/m^3$ prior to ascertainment of BeS or diagnosis of CBD. This type of analysis was possible only for data in which multiple years were pooled (i.e., by job title, era of engineering controls) because exceedance fractions could not be calculated in circumstances of limited sample sizes.

Based on the different methods used in this assessment to reconstruct and understand historical exposures that may have contributed to the identification of BeS or CBD, all workers showed exposure-response curves converging to a 95th percentile beryllium concentration of about 0.2 $\mu g/m^3$ and 90% of beryllium-sensitized and CBD workers were exposed above a 95th percentile concentration of 0.4 $\mu g/m^3$ within the highest exposed year prior to diagnosis (Figure 5).

DISCUSSION

This analysis provides a better understanding about individual worker exposures that may have been experienced and contributed to BeS and diagnosis of CBD in a beryllium metal machining plant. There are general conclusions one can draw from this analysis about different methods for reconstructing historical occupational exposures, as well as more specific conclusions about the exposure-response relationship between beryllium exposures and the prevalence of BeS and CBD. First, when grouped as a broad category for machining and

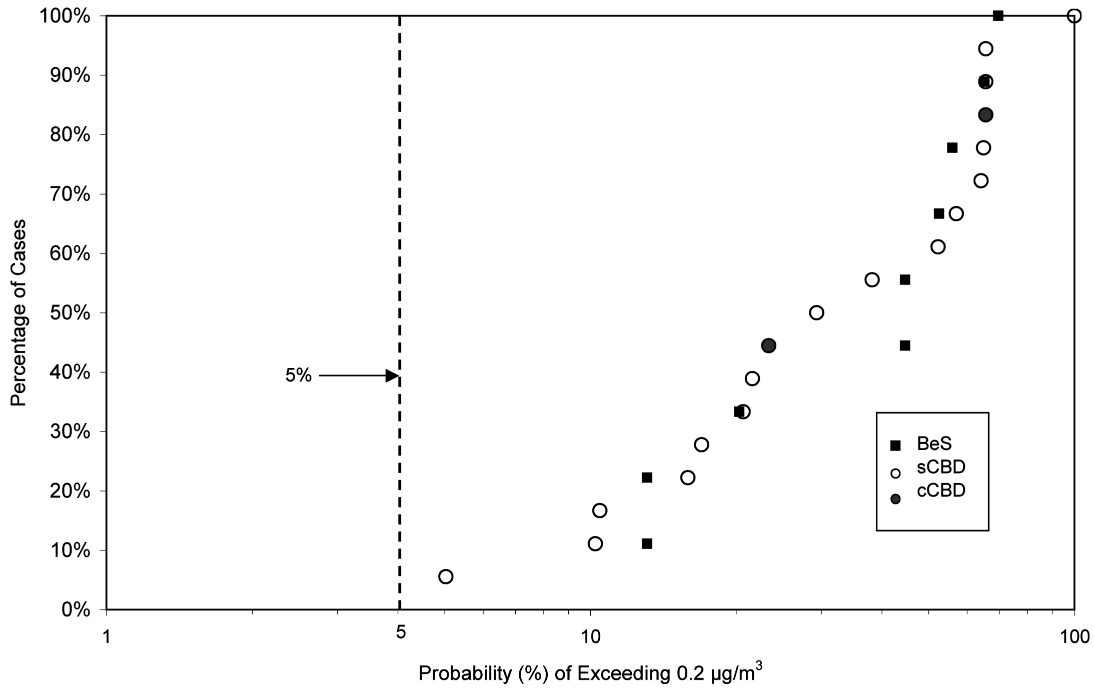

FIGURE 6. Probability of exceeding 0.2 mg/m^3 for each beryllium-sensitized and CBD case based on historical exposures pooled by era of engineering controls

nonmachining operations, personal airborne concentrations of beryllium decreased substantially after additional control measures were implemented in the plant in 1996. It was observed that worker exposures were approximately four times higher in the period before additional IH improvements were made in the 1990s, and, based on the most recent data (2000–2005), current exposures have been reduced nearly fifteenfold since the 1980s.

The decreasing trend of airborne beryllium concentrations over time as additional engineering controls were implemented in this beryllium metal machining plant suggests that exposure estimates should be based on contemporaneous IH data. Reconstructing individual worker exposures is more informative than grouping exposures and health outcome information by job title; however, it is important to note that IH measurements on which exposures are derived need to represent time periods relevant to employee work history and common eras of engineering controls.

Second, different approaches used to reconstruct historical exposures prior to the ascertainment of BeS or diagnosis of CBD resulted in varying exposure estimates. Five different approaches were used to reconstruct historical exposures of each worker's complete work history by pooling industrial hygiene data by year, job title, era of engineering controls, and the lifetime weighted average prior to diagnosis. Results showed that exposure metrics based on shorter averaging times (i.e., year vs. complete work history) were more likely to show higher upper bound exposures that could have contributed to the development of BeS or CBD. The results of this study show that cumulative exposure estimates (i.e., LTW) do not reflect the upper bound measurements that potentially led to BeS and CBD. In general, the greater the time period over which exposures were averaged, the lower the exposures were for a particular case. The exposure reconstruction method also influenced whether the exposure-response curve was shifted to the left or the right.

Third, estimates of central tendency exposures do not reflect the upper bound exposures that may have contributed to the development of BeS and CBD. In addition, median exposure estimates were more sensitive or showed greater variation with the different approaches used to derive historical exposures than metrics based on the 95th percentile. Twenty-six of the 27 beryllium-sensitized and CBD workers had at least a 10% probability of being exposed to beryllium concentrations exceeding 0.2 μg/m^3 during their career, and all cases had a greater than 5% probability of exceeding this level.

Furthermore, no beryllium-sensitized and CBD workers were exposed to a median concentration greater than 2 μg/m^3, but approximately 50% of the beryllium-sensitized and CBD workers were exposed to a 95th percentile concentration greater than 2 μg/m^3 when looking at supplemented data for only the highest exposed year. The upper bound exposures are not generally reflected in exposure estimates based on LTW, mean, or median concentrations for a particular job title or an individual worker.

Fourth, the exposure-response curve for workers identified as beryllium sensitized were generally to the left of the CBD exposure-response curve, suggesting that higher upper bound

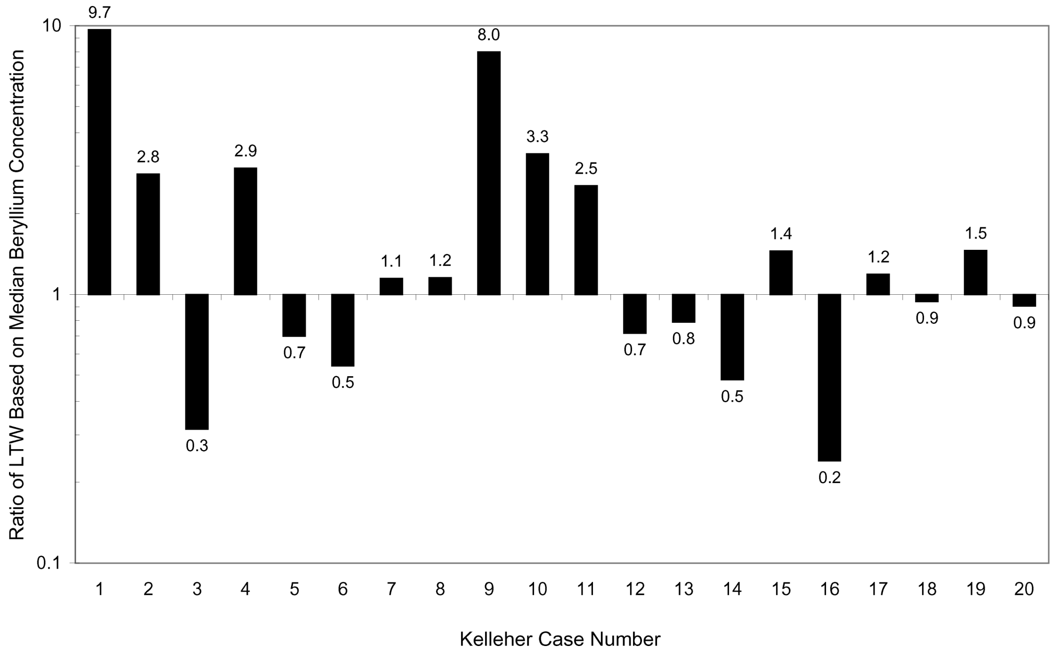

FIGURE 7. Ratio of lifetime weighted average exposure (Plant Industrial Hygiene Data/Kelleher Sampling Data)

exposures are required for the development of CBD. This assessment is the first in which the exposure-response curve for BeS could be differentiated from CBD. This difference in upper bound exposures for beryllium-sensitized and CBD workers may be a reflection of the greater length of employment of CBD cases, who worked when engineering controls were not as extensive and higher airborne beryllium concentrations were observed.

Fifth, various approaches should be considered to maximize the number of historical measurements used in the exposure assessment. For example, because early IH sampling efforts at the plant focused on high-exposure operations, measurements collected during this time period represented upper bound exposures that a worker may experience intermittently but most likely not on a daily basis. Therefore, limited measurements ($N < 6$) could overestimate or underestimate worker exposure during this time period. In many cases, supplemented data reflect a more realistic estimate of historical exposures because data are based on adequate sample numbers and are reflective of measurements during the relevant era of engineering controls.

A way to increase the robustness of the dataset while maintaining relevance to the job and time period of interest is to pool measurements representative of similar engineering controls and operations for the relevant time periods. Further, the manner in which the historical IH data are pooled (i.e., averaging time period) will influence how reflective the exposure estimates are of central tendency or upper bound exposures. Overall, one must understand the history of the plant, operations, and the employee to adequately characterize and reconstruct exposures representative of historical times. Multiple approaches should be used to maximize the use of historical measurements and to best characterize the upper bound, average, or cumulative exposures that are consistent with the dose-response and latency of the health outcome.

Comparisons with Kelleher et al.

The previously published job-specific air concentrations and worker-specific exposure estimates by Kelleher et al.[4] were compared with those in this analysis (Table III, Figure 7). The Kelleher et al. study provides a considerable amount of information that advances our understanding of the hazards posed by beryllium. However, the Kelleher et al. analysis underestimated historical exposures of beryllium-sensitized and CBD workers because contemporaneous data were not used to estimate historical exposures, and a limited number of samples were collected for each job category. Of the 17 job titles for which cascade impactor samples were collected, 11 jobs had only 4 samples on which to characterize representative exposures, 1 job had only 1 sample, and the remaining 5 jobs had between 7 and 15 samples collected for each job title. In comparing exposures derived from the plant IH data of specific job titles over time, the plant IH data gave higher mean and median values compared with samples ($N = 4$) for some job titles that Kelleher et al. used in their study (Figure 7).

Kelleher et al.[4] also grouped plant exposure data for machinist and nonmachinist job categories when evaluating whether cascade impactor sampling would be representative of historical exposures. A comparison was made based on the plant IH data between the exposures for machinists, nonmachinists, and general area over different distinct time periods (1981–1984, 1995–1997, 1998–1999) to determine whether these operations substantially changed over time.

Given the assumption that nonmachinists and general area air beryllium concentrations did not change and that machinists' exposures remained the same prior to 1997, Kelleher and colleagues concluded that their airborne measurements of beryllium from personal cascade samples were representative of those historically experienced in the plant. This conclusion is not supported by our analysis of the plant IH data presented in Table I and Figure 1, which show that worker exposures measured by personal lapel samplers substantially decreased over time as a result of improved engineering and work practice controls.

Lastly, the Kelleher et al.[4] reliance on the LTW underestimated exposure and did not capture the upper bound distribution of exposures that most likely initiates the immunologic response observed with BeS and CBD. This is illustrated in Figures 3a and 4a, where the LTW exposure estimates were consistently to the left of the exposure-response curves for the highest year or job title exposed. The limited sample size combined with the reliance on recent air sampling data, when engineering controls were increased, likely had a substantial influence on the LTW exposures estimated by Kelleher et al.

Implications for an Occupational Exposure Limit for Beryllium

Because the LTW exposure places greatest weight on the job title of longest employment even when there is brief employment in high-exposure jobs and the fact that BeS can occur within a relatively short duration of exposure (weeks to months), it is biologically plausible that the LTW exposures may not be the best descriptor of BeS and CBD. Due to the impact of employment duration on the LTW exposure estimate, any past high-exposure job may be diluted by long-duration, low-exposure jobs and may not be reflective of a true workplace exposure profile that may be responsible for causing BeS and CBD. Provided that an adequate number of samples have been collected to define the variability of exposure, an upper bound concentration estimate (i.e., 95th percentile) or exposures within the first few months to first year of employment may provide a better reflection of exposures which contribute most to the identification of BeS or CBD.

An effective OEL is one that reduces or eliminates the risk of an adverse health effect or outcome in the majority of the working population. Unlike many other chemicals, identifying the exposure metric on which to derive the OEL is particularly difficult for beryllium due to its immunologic pathogenesis.

Historically, epidemiologic studies have studied BeS and CBD prevalence in relation to the mean or median beryllium concentration for the longest or most recent job title held. In general, these studies have found that certain job titles or operations may pose an increased or lesser risk of BeS and CBD, but none have shown an exposure-response pattern for these endpoints. Most of these studies reconstructed worker exposures based on broad job classifications and have not evaluated the beryllium exposures that may have contributed to the identification of BeS or diagnosis of CBD in each worker.

Our analysis is not only the first to reconstruct worker exposures to beryllium based on individual work history, but it also is the first to evaluate a variety of exposure reconstruction methods and their influence on the exposure-response patterns for BeS and CBD. The results of our analyses show that the magnitude of the upper bound exposures, which may have led to the development of BeS and CBD, is typically not reflected in historical exposure estimates that are averaged over several years (e.g., LTW). Given the immunologic basis of BeS and CBD and that these endpoints have been documented, in some cases, as a result of relatively short-term exposures (e.g., <1 year), it is important not only to understand central tendency estimates of exposure but also upper bound exposures.

In addition to understanding the plausible range of exposures that may contribute to the identification of BeS and diagnosis of CBD, for purposes of deriving an OEL, it is important to characterize the level of exposure below which the risk of disease is not substantially increased. The majority of studies conducted to date have involved cross-sectional studies that have not included adequate control comparison groups or an evaluation of worker-specific exposures.

Although our analysis evaluated only workers identified as BeS or diagnosed with CBD, this analysis provides a better understanding of the range of exposures to airborne beryllium that is associated with BeS or CBD. Based on the different approaches used in this assessment to reconstruct and understand historical exposures, it was also observed that most workers diagnosed with CBD were exposed to beryllium concentrations of 0.4 $\mu g/m^3$ (95th percentile) or greater within a given year of their work history. Most beryllium-sensitized and CBD workers had at least a 10% probability of experiencing beryllium exposures exceeding 0.2 $\mu g/m^3$, and all of these workers had at least a 5% probability of exceeding this level. Thus, maintaining exposures below 0.2 $\mu g/m^3$ 95% of the time may prevent BeS and CBD in the workplace.

ACKNOWLEDGMENTS

Special appreciation is extended to the machining company who provided the data for this study and previous studies. This study was supported by Brush Wellman as part of ongoing research on beryllium sensitization and chronic beryllium disease.

REFERENCES

1. **Henneberger, P.K., S.K. Goe, W.E. Miller, B. Doney, and D.W. Groce:** Industries in the United States with airborne beryllium exposure and estimates of the number of current workers potentially exposed. *J. Occup. Environ. Hyg. 1*:648–659 (2004).
2. **American Conference of Governmental Industrial Hygienists (ACGIH):** *Notice of Intended Change, Documentation of the Threshold Limit Value for Beryllium and Compounds*. Cincinnati, Ohio: ACGIH, 1999.
3. **American Conference of Governmental Industrial Hygienists (ACGIH):** *Notice of Intended Change, Documentation of the Threshold*

Limit Value for Beryllium and Compounds. Cincinnati, Ohio: ACGIH, 2005.

4. **Kelleher, P.C., J.W. Martyny, M.M. Mroz, et al.:** Beryllium particulate exposure and disease relations in a beryllium machining plant. *J. Occup. Environ. Med. 43*:238–249 (2001).
5. **California OSHA:** *Permissible Exposure Limits for Chemical Contaminants*. Chapter 4, Subchapter 7, Article 107, Section 5155. Sacramento, Calif.: California Occupational Safety and Health Standards Board (OSHSB), California Occupational Safety and Health Administration, 2006.
6. **Henneberger, P.K., D. Cumro, D.D. Deubner, M.S. Kent, M. McCawley, and K. Kreiss:** Beryllium sensitization and disease among long-term and short-term workers in a beryllium ceramics plant. *Int. Arch. Occup. Environ. Health 74(3)*:167–176 (2001).
7. **Kent, M.S., T.G. Robins, and A.K. Madl:** Is total mass or mass of alveolar-deposited airborne particles of beryllium a better predictor of the prevalence of disease? A preliminary study of a beryllium processing facility. *Appl. Occup. Environ. Hyg. 16*:539–558 (2001).
8. **Kreiss, K., M.M. Mroz, L.S. Newman, J. Martyny, and B. Zhen:** Machining risk of beryllium disease and sensitization with median exposures below 2 $\mu g/m^3$. *Am. J. Ind. Med. 30(1)*:16–25 (1996).
9. **Kreiss, K., M.M. Mroz, B. Zhen, H. Wiedemann, and B. Barna:** Risks of beryllium disease related to work processes at a metal, alloy, and oxide production plant. *Occup. Environ. Med. 54(8)*:605–612 (1997).
10. **Schuler, C.R., M.S. Kent, D.C. Deubner, et al.:** Process-related risk of beryllium sensitization and disease in a copper-beryllium alloy facility. *Am. J. Ind. Med. 47(3)*:195–205 (2005).
11. **Stanton, M.L., P.K. Henneberger, M.S. Kent, D.C. Deubner, K. Kreiss, and C.R. Schuler:** Sensitization and chronic beryllium disease among workers in copper-beryllium distribution centers. *J. Occup. Environ. Med. 48*:204–211 (2006).
12. **Deubner, D., M. Kelsh, M. Shum, L. Maier, M. Kent, and E. Lau:** Beryllium sensitization, chronic beryllium disease, and exposures at a beryllium mining and extraction facility. *Appl. Occup. Environ. Hyg. 16*:579–592 (2001).
13. **Martyny, J.W., M.D. Hoover, M.M. et al.:** Aerosols generated during beryllium machining. *J. Occup. Environ. Med. 42*:8–18 (2000).
14. **Kreiss, K., M.M. Mroz, B. Zhen, J.W. Martyny, and L.S. Newman:** Epidemiology of beryllium sensitization and disease in nuclear workers. *Am. Rev. Respir. Dis. 148(4 Pt 1)*:985–991 (1993).
15. **Newman, L.S., M.M. Mroz, L.A. Maier, E.M. Daniloff, and R. Balkissoon:** Efficacy of serial medical surveillance for chronic beryllium disease in a beryllium machining plant. *J. Occup. Environ. Med. 43*:231–237 (2001).
16. **Mulhausen, J.R., and J. Damiano (eds.):** *A Strategy for Assessing and Managing Occupational Exposures*, Second Edition. Fairfax, Va.: AIHA Press, 1998. pp. 105–110.
17. **Shima, S.:** Beryllium hazards and the sensitization phenomenon due to beryllium exposure, with special reference to the patch test. In *Proceedings of the 15th International Congress Occupational Health*, September 19–24, 1966 (208:901–904). Vienna: Verlag der Wiener Medizinischen Akademie, 1966.
18. **Johnson, J.S., K. Foote, M. McClean, and G. Cogbill:** Beryllium exposure control program at the Cardiff Atomic Weapons establishment in the United Kingdom. *Appl. Occup. Environ. Hyg. 16*:619–630 (2001).