ORIGINAL ARTICLE

# Enhanced preventive programme at a beryllium oxide ceramics facility reduces beryllium sensitisation among new workers

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**Background:** A 1998 survey at a beryllium oxide ceramics manufacturing facility found that 10% of workers hired in the previous 6 years had beryllium sensitisation as determined by the beryllium lymphocyte proliferation test (BeLPT). In response, the facility implemented an enhanced preventive programme to reduce sensitisation, including increased respiratory and dermal protection and particle migration control.
**Aim:** To assess the programme's effectiveness in preventing sensitisation.
**Methods:** In 2000, the facility began testing newly hired workers for beryllium sensitisation with the BeLPT at time of hire and during employment. The sensitisation rate and prevalence for workers hired from 2000 to 2004 were compared with that for workers hired from 1993 to 1998, who were tested in the 1998 survey. Facility environmental conditions for both time periods were evaluated.
**Results:** Newly hired workers in both cohorts worked for a mean of 16 months. Of the 97 workers hired from 2000 to 2004 with at least one employment BeLPT result, four had abnormal results at time of hire and one became sensitised during employment. Of the 69 workers hired from 1993 to 1998 and tested in 1998, six were found to be sensitised. The sensitisation rate for the 2000–4 workers was 0.7–2.7/1000 person-months of employment, and that for the 1993–8 workers was 5.6/1000 person-months, at least 2.1 (95% confidence interval (CI) 0.6 to 8.4) and up to 8.2 (95% CI 1.2 to 188.8) times higher than that for the 2000–4 workers. The sensitisation prevalence for the 2000–4 workers was 1% and that for the 1993–8 workers was 8.7%, 8.4 (95% CI 1.04 to 68.49) times higher than that for the 2000–4 workers. Airborne beryllium levels for production workers for the two time periods were similar.
**Conclusions:** A comprehensive preventive programme reduced beryllium sensitisation in new workers during the first years of employment, despite airborne beryllium levels for production workers that were similar to pre-programme levels.

Workers with beryllium sensitisation are at higher risk of developing chronic beryllium disease (CBD), an immune-mediated granulomatous interstitial lung disease.[1 2] Beryllium sensitisation can be detected with the blood beryllium lymphocyte proliferation test (BeLPT). In a 1992 survey, 6% (8/136) of workers at a beryllium ceramics manufacturing facility were found to have beryllium sensitisation, and 4% (6/136) were diagnosed with CBD.[3] The facility responded by making targeted engineering changes designed to lower respiratory exposures, including enclosing additional machines and augmenting exhaust ventilation. Despite these modifications, a 1998 survey found that 10% (7/74) of workers hired after the 1992 survey were sensitised.[4] Two findings were particularly striking: these seven sensitised workers had been employed at the facility for <2 years, and more than half of them had mean respiratory exposures well below the permissible exposure limit.

CBD is primarily a pulmonary disease, and prevention at the facility during the first 18 years of operation had focused on reducing respiratory exposure to beryllium, primarily through engineering controls (table 1). The results of the 1998 survey, however, led to a re-evaluation of that approach. In designing an enhanced preventive programme, the facility expanded respiratory protection, and also added emphasis on skin exposure, clothing contamination, workplace cleanliness and control of dust migration. Table 2 shows the evolution of the enhanced preventive programme from 1999 to 2004.

After a freeze on hiring new workers in 1999, the facility resumed hiring for production positions in January 2000. Ongoing surveillance focused on newly hired workers, as previously hired workers may have had past beryllium exposures, conferring long-term CBD risk.[4] Frequent testing, early in employment tenure, provided data on the successes and failures of the preventive programme. We assessed the programme's effectiveness by comparing sensitisation for newly hired workers with that for workers hired from 1993 to 1998 and tested in the 1998 survey.

## METHODS

### BeLPT surveillance: 2000–4

Medical surveillance of new workers began in January 2000 and continued to end of December 2004. To establish baseline sensitisation status, each new worker had a BeLPT at time of hire. Periodic testing occurred at intervals of 3, 6, 12, 24 and 48 months of employment (interval BeLPT). Occasionally, the facility collected samples at 18 and 30 months of employment. Some workers submitted samples after leaving employment. The facility did not use test results to make decisions about

**Abbreviations:** BAL, bronchoalveolar lavage; BeLPT, beryllium lymphocyte proliferation test; CBD, chronic beryllium disease; ICP-AES, inductively coupled plasma atomic emission spectrometry; LOD, limit of detection; OSHA, Occupational Safety and Health Administration; PPE, personal protective equipment

**Table 1** History of the preventive programme from 1980 through 1998

| Year | Control type | Description of control |
|---|---|---|
| Baseline status of facility at opening | | |
| 1980 | Engineering | Exhaust ventilation for powder handling |
| 1980 | Engineering | Enclosed, ventilated wet machining operations |
| 1980 | Engineering | On-site laundry and locker rooms |
| 1980 | Engineering | HEPA-filtered central vacuum system |
| 1980 | Administrative | Compressed air for cleaning and dry sweeping in production areas prohibited |
| 1980 | Administrative | Dry vacuuming and wet mopping performed at least weekly |
| 1980 | Administrative | End-of-shift showering and change of clothing required |
| 1980 | PPE | Facility uniforms (short-sleeved jumpsuits) used |
| 1980 | PPE | Half-face negative pressure respirators required for powder handling |
| Changes made before the 1992 survey | | |
| 1984 | Engineering | Enclosures added around some machines |
| 1985–6 | Engineering | Building expanded. Additional local exhaust ventilation added |
| 1988 | Administrative | Smoking, eating and drinking in production areas banned |
| Changes made between 1992 and 1998 surveys | | |
| 1993–5 | Engineering | Additional exhaust ventilation and enclosures added around machines |
| 1995 | Engineering | Locker rooms fully segregated (clean/dirty sides) |
| 1995 | Engineering | Water spray added over hamper to keep uniforms wet before laundering |
| 1998 | Administrative | Free-standing man-cooling (high-velocity) fans prohibited in production areas |

HEPA, high-efficiency particulate air; PPE, personal protective equipment.

continuing or terminating a worker's employment. To assess participation, we compared the number of completed baseline and interval tests with the number of expected tests (based on each worker's full length of employment to end of December 2004).

A single commercial laboratory (lab 1) conducted the BeLPTs using standard criteria.[5] Tests were repeated for borderline or uninterpretable results using lab 1. Abnormal results were confirmed by sending split samples to lab 1 and to a second laboratory (lab 2). A worker with one abnormal test at lab 1, followed by a second abnormal test at either laboratory at any point, met the definition of beryllium sensitisation. Sensitised workers were offered further diagnostic testing for CBD, including chest *x* ray and bronchoscopy with bronchoalveolar lavage (BAL) BeLPT and transbronchial biopsy.

## Study subjects

We included workers hired from January 2000 to September 2004 who had undergone at least one interval BeLPT (2000–4 workers). The comparison group comprised all workers participating in the 1998 survey who had been hired during the 60 months (ie, 1993–8) before that survey (1993–8 workers), limiting the group to those with a similar length of employment as the 2000–4 workers. Before 2000, systematic, facility-wide BeLPT testing of workers occurred only in the 1992 and 1998 surveys, thus, routine periodic testing was not offered to the 1993–8 workers.

For the 1998 and 2000–4 BeLPTs, the facility used the same two laboratories. However, the facility used a different initial testing protocol in 1998: samples were split and sent to both labs 1 and 2. The protocols for confirming abnormal results were the same. Thus, 1993–8 workers and 2000–4 workers could meet the definition of sensitisation through abnormal results at both laboratories, or from sequential abnormal results at lab 1 only. A 1993–8 worker, but not a 2000–4 worker, could also meet the definition from sequential abnormal results at lab 2 only.

To assess the similarity of the two groups, we compared age at time of hire, length of employment at the time of the final interval BeLPT (for the 2000–4 workers) or the 1998 survey (for the 1993–8 workers), and work categories. Work categories were non-administration (production and production support) and administration. Production included complex machining, extruding, lapping, pressing, laser scribing, lasers, material preparation, and one operation (tape) eliminated in 2000. Production support included janitor/laundry operator, maintenance mechanic, and packaging and non-production workers who spent part of a typical day in the production area (eg, facility nurse). Administration workers spent little or no time in production areas (eg, front office workers). Workers who changed work categories were assigned to the category in which they spent most of their time; when the time spent in $\geqslant 2$ categories was similar, the category likely to have the higher beryllium exposure was used.

## Human subjects approval

As the BeLPT was a component of workplace medical surveillance, written informed consent was not obtained from the 2000–4 workers at the time of hire. We therefore analysed only de-identified data, under the terms of a confidentiality agreement between the National Institute for Occupational Safety and Health and Brush Wellman Incorporated (available on request), with Institutional Review Board waivers. We limited descriptive baseline characteristics to avoid identifying individuals. Additional personal data were included only with written permission from the worker.

## Airborne beryllium levels

From 1994 to 2003, the facility conducted routine environmental surveillance by collecting airborne beryllium full-shift personal samples. We grouped these data into two time periods: 1994–9 and 2000–3. Samples from 1999 were included as they pre-dated hiring of the 2000–4 workers and were likely to be similar to the 1994–8 samples. Personal lapel samplers were attached to workers' collars within the breathing zone, and were operated at a flow rate of approximately 2 l/min for approximately 8 h. Samples were analysed for the total mass of beryllium by either of two methods, flame atomic absorption spectrophotometry or inductively coupled plasma atomic emission spectrometry (ICP-AES). When results were reported below the limit of detection (LOD), a value equal to half the LOD was assigned. LODs were 0.2 $\mu g/m^3$ for flame atomic absorption samples (1994–8) and 0.02 $\mu g/m^3$ for ICP-AES samples (1999–2003). We grouped samples into work categories described above: non-administration (production, production support) and administration.

## Dermal monitoring

The facility assessed the dermal protection components of the preventive programme in April and May of 2001. A total of 121 workers (70 (58%) in production, 37 (31%) in production support and 14 (11%) in administration) participated, including

**Table 2** Evolution of the enhanced preventive programme after the 1998 survey

| Year | Control type | Description of control |
|---|---|---|
| 1999 | Engineering | HEPA filters added to air handlers in non-production areas |
| 1999 | Engineering | Downdraught table added for respirator cleaning |
| 1999 | Engineering | Administrative offices physically separated from production areas |
| 1999–2001 | Engineering | Air showers added at all exits from production areas |
| 1999 | PPE | Half-face negative pressure respirators required in production areas |
| 1999 | PPE | Shoe covers worn over work shoes in non-respirator areas |
| 2000 | Engineering | Lapping area enclosed |
| 2000 | PPE | Facility uniform changed to long-sleeved jumpsuits |
| 2000 | PPE | Latex glove use required in production areas |
| 2000 | PPE | Aprons added for machining operations |
| 2000 | PPE | Water-resistant* garments added for wet operations |
| 2001 | Engineering | Reusable tacky mats installed at all production area exits |
| 2001 | Engineering | Enclosures installed around all mechanical presses |
| 2001 | Engineering | HEPA-filtered ventilation system for respirator storage room added |
| 2001 | PPE | Water-resistant coverall added to lapping area garments |
| 2001 | PPE | Respiratory protection standardised to loose-fitting PAPR† |
| 2002 | Administrative | Gloves required for handling work shoes and respirators |
| 2002 | Administrative | Production workers clean work areas 15 min/shift and 1 h/month |
| 2002 | PPE | Respirator belts replaced with non-woven belts for easier cleaning |
| 2002 | PPE | Waterproof* coveralls and shoe covers, taped gloves required for lapping |
| 2002 | PPE | Waterproof garments replaced water-resistant ones for other wet operations |
| 2002 | PPE | Aprons/smocks required for forming and dry machining operations |
| 2003 | Administrative | ''Transition shoes'' used between production and locker areas |
| 2003 | Administrative | Workers required to clean transition shoes monthly |

HEPA, high-efficiency particulate air; PPE, personal protective equipment.
*Water-resistant refers to materials such as Tyvek; waterproof refers to materials such as Saranex.
†Powered air-purifying respirator.

workers hired before 2000. After performing their regular duties for at least 1 h, workers answered questions about glove use, then removed their latex gloves and wiped both hands with a series of three moistened Ghost Wipes (Environmental Express, Mt Pleasant, South Carolina, USA). Wipe samples were sealed in plastic bags and later analysed for beryllium mass by ICP-AES. The limit of detection was 0.004 μg. We converted beryllium mass to beryllium dermal exposure loading (μg/100 $cm^2$) based on surface area estimates from hand tracings.

### Statistical analyses

We compared age at time of hire, length of employment and production categories for both groups of workers using $\chi^2$, Fisher's exact and Student's t tests. Because BeLPT collection was prospective in 2000–4 and cross sectional in 1998, we used two approaches to compare the data: sensitisation rate and sensitisation prevalence.

### Sensitisation rate comparison

We calculated a sensitisation incidence rate for the 2000–4 workers, using the sum of the months of sensitisation-free employment as the denominator. All interval and repeat BeLPT results were included for each worker, but not results of samples collected at unusual intervals (eg, 18 and 30 months of employment), as these intervals were not used for most workers. As the emphasis was on frequent testing early in employment tenure, we included only test results from the first employment period for workers rehired >18 months after initial termination of employment. We considered sensitised workers to be sensitisation-free until the time of the first abnormal result. For workers who were not found to be sensitised during the surveillance period, data were censored at the time of the BeLPT performed at the final interval (3, 6, 12, 24 or 48 months) of employment (final interval BeLPT). For workers tested after termination or rehired within 18 months of termination, the termination period was included in the calculation of sensitisation-free employment. Any worker with an abnormal baseline BeLPT result was excluded from the incidence calculation. When repeat tests for borderline tests were not obtained, we condsidered the result to be normal.

For 1993–8 workers, we were unable to calculate a true sensitisation incidence rate, as the baseline BeLPT status was unknown. Instead, we calculated the number of sensitised workers per person-time, using as sensitisation-free time the period from time of hire to the initial 1998 survey BeLPT. We did not consider 1993–8 workers who had abnormal results only at lab 2 to be sensitised, as these workers would not have been identified as sensitised by the 2000–4 testing protocol.

To compare the sensitisation rates of the 2000–4 and 1993–8 workers, we established a range of rates for the 2000–4 workers, using both the incidence rate and an adjusted rate. The adjusted rate included those 2000–4 workers with an abnormal baseline BeLPT result, to account for the unknown baseline status of the 1993–8 workers. The sensitisation rate comparisons were performed by calculating incidence rate ratios of the 1993–8 workers' rate and the values at the extremes of the 2000–4 workers' rate range. The corresponding 95% mid-p confidence limits were determined using a binomial probability model.[6]

### Sensitisation prevalence comparison

We calculated the prevalence of sensitisation for the 1993–8 workers, using the number of sensitised workers divided by the total number of 1993–8 workers tested in the 1998 survey. Again, we did not consider 1993–8 workers who had abnormal results only at lab 2 to be sensitised. For the 2000–4 workers, to approximate a cross-sectional survey, we included only the results available from the final interval BeLPT. Thus, for sensitised 2000–4 workers, results were not censored at the time of the first abnormal result, as in the rate calculations. Instead, the BeLPT result from the worker's last testing interval in the surveillance period was used to determine sensitisation status. We used the number of 2000–4 workers who would have been identified as sensitised based on the final interval BeLPT, divided by the total number of 2000–4 workers with an interval BeLPT result, to determine the sensitisation prevalence for this group. The prevalence comparison was performed by calculating a prevalence ratio. The 95% confidence intervals (CIs) were derived using a cohort study method that accounts for the variance of both the numerator and the denominator.[7]

**Table 3** Beryllium lymphocyte proliferation test results of 2000–4 workers included in calculation of sensitisation incidence*

| | Time of hire | Interval (months) | | | | |
|---|---|---|---|---|---|---|
| | | 3 | 6 | 12 | 24 | 48 |
| Normal | 90 | 88 | 80 | 52 | 30 | 11 |
| Abnormal† | 0 | 0 | 1 | 0 | 3 | 0 |
| Uninterpretable‡ | 3 | 1 | 0 | 1 | 0 | 0 |
| Missed§ | 0 | 4 | 0 | 0 | 0 | 0 |
| Total workers | 93 | 93 | 81 | 53 | 33 | 11 |

*Incidence calculation excludes the four workers with abnormal results at time of hire; results for these four workers are shown in table 4.
†Initial (not confirmatory) results shown; any results after confirmation of sensitisation are not shown.
‡In most cases, uninterpretable tests were repeated, and those repeat results are shown; in the five cases indicated, repeat tests were not performed.
§The worker was not tested in this interval, but was tested in the following interval.

### Airborne beryllium comparisons

For airborne beryllium samples, under the assumption of lognormality,[8] we calculated the upper 95% confidence limit around the 95th centile of the distribution (the upper tolerance limit), and around exceedances of two occupational exposure limits,[9] the Occupational Safety and Health Administration (OSHA) permissible exposure limit[10] of 2.0 $\mu g/m^3$ and the Department of Energy action level of 0.2 $\mu g/m^3$.[11] We used the upper 95% confidence limit to account for the uncertainty around each exceedance point estimate. An area is generally considered to be well controlled to a specified level when the exceedance fraction for that level is $\leqslant 5\%$.[12] Exceedances were not calculated for sample sizes $<15$.

For all analyses, $p \leqslant 0.05$ was considered significant. We performed analyses using SAS V.9.1 software.

## RESULTS

### Study subjects

Between January 2000 and September 2004, the facility hired 126 workers. Overall, 95% (404/425) of expected BeLPTs were completed (100% of baseline and 93% of interval tests). We excluded 28 (22%) newly hired workers because they left employment in their first 3 months, and thus completed only the baseline BeLPT. We excluded one other worker who was employed for 7 months but was not available for interval testing because of medical leave. None of the excluded workers had abnormal BeLPT results at time of hire. Of the remaining 97 workers with interval BeLPT results (2000–4 workers), 24 BeLPTs were not used in the analysis, as they were collected at unusual intervals (n = 18) or at >18 months after termination of employment (n = 6). None of these excluded BeLPTs was abnormal.

Of the 199 workers hired between 1993 and the 1998 survey, 69 were employed in 1998 and participated in the survey, and thus served as the comparison group (1993–8 workers). Most of the remaining 130 workers had left employment before the survey. The mean age at time of hire for the 2000–4 workers was 37 years (range 18–65), and that for the 1993–8 workers was 35 years (range 18–59). Both groups had a mean length of employment of 16 months (range 3–48 for 2000–4 workers and 3–55 for 1993–8 workers); for 86% of the 2000–4 workers and 80% of the 1993–8 workers, the length of employment was <24 months. There were no significant differences in the means and distributions of these characteristics. Of the 2000–4 workers, 63 (65%) were in production, 28 (29%) in production support and 6 (6%) in administration. For the 1993–8 workers, the corresponding figures were 57 (83%), 10 (14%) and 2 (3%). There was no significant difference between the two groups when comparing non-administration with administration; however, when non-administration was further divided into production and production support, the difference was significant ($p = 0.04$).

### Beryllium sensitisation, 2000–4

Table 3 presents the time of hire and interval BeLPT results for the 2000–4 workers included in the calculation of sensitisation incidence. Three workers who had uninterpretable BeLPT results at baseline did not have repeat baseline tests available. All three were subsequently tested at ⩾2 employment intervals, and none of those tests was abnormal.

Eight workers had at least one abnormal BeLPT during surveillance (table 4). Worker A (production) had an abnormal BeLPT result at 24 months of employment, which was confirmed with repeat tests. Workers B (production support), C (production) and D (production) each had a single abnormal result at 24, 6 and 24 months of employment, respectively, which could not be confirmed on repeat testing performed during the interval. Workers E, F, G and H had their first abnormal results at time of hire. Worker E's abnormal result was confirmed at time of hire, worker F's at 6 months of employment and worker G's at 3 months of employment; worker H's single abnormal result was not confirmed with repeat testing. Further diagnostic testing of worker A showed a normal BAL BeLPT and no granulomas on transbronchial biopsy.

After the confirmation of sensitisation in worker A, the facility reviewed this worker's history. At the time of hire, the BeLPT result was normal (table 4). During the first 22 months of employment, worker A worked as a small press operator for 4 months (producing unfired parts on mechanical presses), in lapping for 12 months (smoothing the surface of fired beryllium products using grit in a water-soluble organic fluid) and in laser machining for 6 months (wet-machining fired ceramic components). The interval BeLPTs at 3, 6 and 12 months of employment were normal. At 22 months of

**Table 4** Beryllium lymphocyte proliferation test (BeLPT) results of 2000–4 workers who had at least one abnormal BeLPT result during surveillance*

| Worker | Time of hire | 3 months | 6 months | 12 months | 24 months | 48 months |
|---|---|---|---|---|---|---|
| A | Normal | Normal | Normal | Normal | **Abnormal (4/4)†** | Abnormal |
| B | Normal | Normal | Normal | Normal | Abnormal (1/5) | Normal |
| C | Normal | Normal | Abnormal (1/5) | | | |
| D | Normal | Normal | Normal | Normal | Abnormal (1/4) | |
| E | **Abnormal (3/3)** | Abnormal | Normal | | | |
| F | Abnormal (1/3) | Normal | **Abnormal (1/1)** | Normal | | |
| G | Abnormal (1/3) | **Abnormal (1/1)** | Normal | | | |
| H | Abnormal (1/3) | Normal | Normal | Normal | Normal | |

*If initial results were uninterpretable, interpretable repeat results are shown.
†Numbers in parentheses indicate the number of abnormal results/total number of interpretable results (including confirmatory results) associated with the interval; bold lettering indicates that sensitisation was confirmed in the interval.

employment, worker A returned to lapping. The interval BeLPT at 24 months of employment was abnormal. In an interview conducted after confirmation of sensitisation, worker A noted using all required personal protective equipment (PPE), including the respirator. However, at times, despite taping of gloves to sleeves, a gap developed between the sleeves and gloves, and on several occasions lapping fluid had dripped on to the skin in the area of this gap. Worker A described a rash, approximately 4 cm in diameter, which had developed on the ulnar aspect of the right wrist after one such occasion.

### Sensitisation rate comparison

Among the 2000–4 workers, one developed sensitisation during a total of 1480 months of employment, for a sensitisation incidence rate of 0.7/1000 person-months of employment. Including the 2000–4 workers with at least one abnormal BeLPT result at time of hire yielded four sensitised workers during a total of 1504 months of employment, or an adjusted sensitisation rate of 2.7/1000 person-months of employment. Thus, for the 2000–4 workers, we estimate a sensitisation rate range of 0.7 (the incidence rate) to 2.7 (the adjusted rate) per 1000 person-months of employment. Seven of the 1993–8 workers (all in production) met the definition of sensitisation, none of whom had an abnormal BAL BeLPT or granulomas on transbronchial biopsy at the time of the 1998 survey. One of these seven had abnormal BeLPT results only at lab 2. Thus, we classified six of the 1993–8 workers as sensitised, over a total of 1081 months of employment, giving a sensitisation rate of 5.6/1000 person-months. This sensitisation rate for the 1993–8 workers is thus at least 2.1 (95% CI 0.6 to 8.4) and up to 8.2 (95% CI 1.2 to 188.8) times greater than that of the 2000–4 workers.

### Sensitisation prevalence comparison

Using only the final interval BeLPT results would have identified just one of the 2000–4 workers (worker A) as sensitised. Workers E, F and G would not have been identified as sensitised, as their final interval BeLPTs were not abnormal. This analysis yields a sensitisation prevalence estimate for the 2000–4 workers of 1.0% (1/97). For the 1993–8 workers, sensitisation prevalence was 8.7%, or 8.4 (95% CI 1.04 to 68.49) times greater than that of the 2000–4 workers.

### Airborne beryllium levels

Between 1994 and 1999, 412 full-shift personal lapel samples were taken (table 5). The median beryllium levels were 0.20 μg/m$^3$ in production and 0.10 μg/m$^3$ in production support; all administration samples were below the LOD. Upper 95% exceedance fractions were 2% for 2.0 μg/m$^3$ and 55% for 0.2 μg/m$^3$ in production, and <1% for 2.0 μg/m$^3$ and 29% for 0.2 μg/m$^3$ in production support. The upper tolerance limit was 1.25 μg/m$^3$ in production and 0.51 μg/m$^3$ in production support. In lapping, the upper 95% exceedance fractions were 8% for 2.0 μg/m$^3$ and 66% for 0.2 μg/m$^3$, and the upper tolerance limit was 2.67 μg/m$^3$ (data not shown).

Between 2000 and 2003, 791 full-shift personal lapel samples were collected. The median beryllium levels were 0.18 μg/m$^3$ in production, 0.04 μg/m$^3$ in production support and 0.02 μg/m$^3$ in administration. Upper 95% exceedance fractions were 4% for 2.0 μg/m$^3$ and 50% for 0.2 μg/m$^3$ in production (similar to the fractions for the 1994–9 period), <1% for 2.0 μg/m$^3$ and 12% for 0.2 μg/m$^3$ in production support, and <1% for both 2.0 and 0.2 μg/m$^3$ in administration. The upper tolerance limit was 1.66 μg/m$^3$ in production, 0.36 μg/m$^3$ in production support and 0.10 μg/m$^3$ in administration. In lapping, the upper 95% exceedance fractions were 16% for 2.0 μg/m$^3$ and 81% for 0.2 μg/m$^3$, and the upper tolerance limit was 4.88 μg/m$^3$ (data not shown).

### Dermal monitoring

All workers participating in the 2001 dermal monitoring reported wearing latex gloves when working in production areas. Nearly all (120/122) hand wipe samples had quantifiable levels of beryllium, ranging from 0.05 to 46 μg/sample. The beryllium dermal exposure loading ranged from <0.01 to 7.7 μg/100 cm$^2$. The geometric mean was 0.27 μg/100 cm$^2$ (95% CI 0.20 to 0.36 μg/100 cm$^2$).

## DISCUSSION

Prior efforts at this company to prevent beryllium sensitisation and CBD focused on maintaining airborne levels of beryllium below the 2.0 μg/m$^3$ OSHA standard. The 1998 survey at this facility showed the overall ineffectiveness of that approach.[4] The enhanced preventive programme begun in 1999 appears to have been more effective. Specifically, comparing the workers hired after the establishment of the enhanced preventive programme with those hired in the years preceding, we found a reduction in sensitisation during the early years of employment, despite little change in airborne beryllium levels in production areas.

**Table 5** Airborne beryllium personal sample total mass exposure concentration by work category, 1994–9 and 2000–3

| Work category | < LOD (%)* | Range (μg/m$^3$) | Median (μg/m$^3$) | GM (μg/m$^3$) | GSD | 95th UTL† (μg/m$^3$) | OEL exceedance UCL (%)‡ 2.0 μg/m$^3$ | 0.2 μg/m$^3$ |
|---|---|---|---|---|---|---|---|---|
| Production | | | | | | | | |
| 1994–9 (n=352) | 86 (24) | <0.02–62.4 | 0.20 | 0.21 | 2.71 | 1.25 | 2 | 55 |
| 2000–3 (n=550) | 17 (3) | <0.02–53.2 | 0.18 | 0.18 | 3.54 | 1.66 | 4 | 50 |
| Production support | | | | | | | | |
| 1994–9 (n=57) | 34 (60) | <0.02–0.80 | 0.10 | 0.11 | 2.12 | 0.51 | <1 | 29 |
| 2000–3 (n=178) | 35 (20) | <0.02–7.70 | 0.04 | 0.04 | 3.30 | 0.36 | <1 | 12 |
| Administration | | | | | | | | |
| 1994–9 (n=3) | 3 (100) | <0.20 | ** | ** | ** | ** | ** | ** |
| 2000–3 (n=63) | 27 (43) | <0.02–0.35 | 0.02 | 0.02 | 2.18 | 0.10 | <1 | <1 |

GM, geometric mean; GSD, geometric standard deviation; OEL, occupational exposure limit; LOD, limit of detection; UCL, upper confidence limit; UTL, upper tolerance limit.
*Number (%) of samples that were below the limit of detection (the LOD for 1994–8 was 0.2 μg/m$^3$, and that for 1999–2003 was 0.02 μg/m$^3$).
†95th centile upper tolerance limit, indicates upper 95% confidence limit around the 95th centile of the distribution.
‡OEL exceedance fraction upper confidence limit, indicates the upper 95% confidence limit for the fraction of samples that exceed a given OEL.
**Calculation was not performed due to small numbers of samples.

The facility's preventive programme included multiple components, each of which may have contributed to its success. Certainly, the mandatory use of powered air-purifying respirators in production areas may have been important, reducing respiratory exposure from measured airborne levels by an estimated factor of 25, yet, prior surveys have shown that sensitisation can occur despite low production area air levels.[4 13] The recognition that respiratory exposures might also occur in production support areas, based on settled dust on clothing or skin coming into contact with the respiratory tract, was the basis for several of the programme's innovations. These changes included air showers to remove easily resuspendable dust from clothing and shoes as workers left production areas (and subsequently removed respirators). The air showers also functioned as an air lock, preventing beryllium from migrating to production offices, meeting rooms and break rooms.

Several new components of the preventive programme stemmed from consideration of the possible role of dermal exposure in sensitisation. Although skin exposure to soluble beryllium salts had previously been shown to induce sensitisation experimentally,[14] localisation of the primary disease process to the lungs and barrier properties of the skin to insoluble particles were arguments against the role of skin exposure in occupationally induced beryllium sensitisation. The suggestion that respiratory protection alone may not prevent sensitisation, however, led to the implementation of dermal protection measures. A recent laboratory study explored the biological plausibility of beryllium sensitisation via skin exposure. The authors showed that fine (non-beryllium) particles can penetrate the stratum corneum of intact cadaveric skin, when combined with skin flexing motion. They also showed that topical application of relatively insoluble fine beryllium oxide particles (such as those used in ceramics manufacturing) induced sensitisation in mice.[15] Thus, in light of these findings, elements of the preventive programme aimed at reducing skin exposures might also have contributed to the observed decrease in sensitisation.

The skin protection efforts also highlight the evolving nature of the enhanced preventive programme. The 2001 under-glove skin wipe samples showed that nearly all workers had measurable amounts of beryllium on their hands after working for at least 1 h, despite the universal use of latex gloves in production areas. This unexpected finding led to a reconsideration of the proper use of gloves. As a result, the preventive programme was modified to include the mandatory use of gloves when handling work shoes and potentially contaminated PPE before entering production areas. Similarly, the facility considered the possibility that worker A's skin contact with machining fluids containing beryllium oxide particles led to sensitisation. To prevent further skin contact with lapping fluids, the facility expanded lappers' PPE.

Our analysis has several notable strengths. Because BeLPT results were collected at time of hire and over time in the 2000–4 workers, we were able to calculate a sensitisation incidence rate for these workers. Furthermore, BeLPT data from an earlier cohort, the 1993–8 workers, were available for comparison, arguably a unique opportunity in workplace intervention evaluations. The 1993–8 workers were similar to the 2000–4 workers in important ways. Age at time of hire, length of employment and work categories were comparable, and the 1993–8 workers were the immediate predecessors to the 2000–4 workers, limiting differences in workplace experience that might be based on changes in job description or responsibility due to technological advances. Although testing protocols were different for the two groups, the same laboratories were used, which allowed us to identify (and recategorise) the 1993–8 workers found to be sensitised by the 1998 protocol who would not have been classified as sensitised by the 2000–4 protocol. Specifically, we found that only one of the seven workers identified as sensitised by the 1998 protocol would not have been recognised as sensitised by the 2000–4 testing protocol, suggesting that the calculated sensitisation incidence rate for the 2000–4 workers is unlikely to be a significant underestimate. Furthermore, we included airborne beryllium levels for both time periods, which were not dissimilar.

An important limitation is that the 1993–8 workers' testing was cross sectional in nature, while that of the 2000–4 workers was prospective. These differences in testing yield sensitisation measures, prevalence and incidence, respectively, which are not directly comparable. To address this limitation, we used two analyses designed to make the data from the two groups as similar as possible for the purposes of comparison. The first approximated a sensitisation incidence for the 1993–8 workers, whereas the second estimated a point prevalence for the 2000–4 workers. For the sensitisation rate comparison, we accounted for the unknown baseline sensitisation status of the 1993–8 workers by using a range of possible sensitisation rates for the 2000–4 workers. Had baseline testing been carried out for the 1993–8 workers, abnormal BeLPT results might have been found in as few as zero (analogous to the 2000–4 workers' incidence rate) or in as many as the proportion of 2000–4 workers with abnormal results at time of hire (analogous to the 2000–4 workers' adjusted rate). This approach allowed us to deal with the uncertainty of the 1993–8 workers' baseline status while still adjusting for time (length of employment). For the prevalence comparison, we used the 2000–4 workers' final interval BeLPT to create a cross-sectional assessment. This approach forced us to ignore the 2000–4 workers' baseline and serial results, data that were not available for the 1993–8 workers. Both approaches suggest that sensitisation was more common before the introduction of the enhanced preventive programme than afterwards. Although we cannot completely eliminate the possibility that the observed differences in sensitisation are due to the differences in data collection, the fact that multiple analyses led to the same conclusion is evidence that the difference in sensitisation is real.

Another limitation of the cross-sectional data collection for the 1993–8 workers is that it might have underestimated sensitisation compared with prospective testing. There is evidence that some individuals identified as sensitised may not always have abnormal BeLPT results on subsequent testing. In one study, over an average follow-up period of $<5$ years, 40% of sensitised individuals who did not develop CBD and 12% of sensitised individuals who did develop CBD did not maintain an abnormal BeLPT.[2] With serial testing, a hypothetical worker with abnormal BeLPT results at 3 months but with normal results at 12 months would be identified as sensitised. In a cross-sectional survey, that same worker might not be identified as sensitised if the survey took place at 12 months of employment. Indeed, when we created a cross section of the 2000–4 workers using the final interval BeLPT, we found that three of the workers with confirmed sensitisation by serial testing were not identified as sensitised. Thus, the difference in sensitisation between the 1993–8 and 2000–4 workers may be greater than that estimated from the available data.

For both cohorts, BeLPT results are not available for all workers hired during the employment periods. For the 2000–4 period, 29 newly hired workers were not tested during employment, whereas for the 1993–8 period, 130 were not tested. This reduced our sample size, limiting the statistical power to detect a difference between the two groups. It might also have reduced the total number of sensitised workers identified. For 2000–4, most (28/29) of those not tested worked for $<3$ months; one worked for 7 months. The short period of

## Main messages

- Prior efforts to prevent beryllium sensitisation and chronic beryllium disease by focusing on engineering airborne beryllium levels below the permissible exposure limit of 2.0 μg/m$^3$ and task-based use of respiratory protection were ineffective.
- An enhanced preventive programme that expanded respiratory protection and added emphasis on controlling skin exposure, clothing contamination, workplace cleanliness and dust migration reduced beryllium sensitisation in new workers during the first years of employment.

## Policy implications

- A follow-up of these workers is necessary to determine the long-term effectiveness of this programme in preventing chronic beryllium disease.
- Pending follow-up, consideration should be given to the adoption of the components of this preventive programme in other manufacturing facilities with potentially hazardous beryllium exposures.

employment makes it unlikely that these workers were sensitised, particularly when we consider that all other 2000–4 workers with normal baseline results also had normal results at 3 months of employment. For 1993–8, the length of employment of the 130 untested workers was not available. On the basis of general trends at the facility, it is probable that many left early in employment, but some might have worked for >3 months, increasing the chance of sensitisation. Given the larger number of workers not tested in 1998 and the possibility that some of these worked for longer than 3 months, it is possible that testing in 1998 might have missed more sensitised workers than did testing in 2000–4. Thus, had all workers hired during the two periods been tested, the difference in sensitisation between the two cohorts might have been found to be greater.

Most of the 1993–8 and 2000–4 workers had been employed for <2 years at the time of the 1998 survey or the final interval BeLPT. The absence of CBD among workers found to be sensitised may therefore reflect disease latency. Some of the 1993–8 workers have been followed up since 1998; our preliminary data show that one non-sensitised worker has subsequently developed sensitisation, and one sensitised worker has progressed to CBD (National Institute for Occupational Safety and Health, unpublished data). Thus, it is possible that, with time, additional sensitisation and cases of CBD may be found among the 2000–4 workers, warranting further follow-up of this group. Despite these limitations, our findings remain an encouraging example of primary prevention in the beryllium industry.

## CONCLUSIONS

Past experience has shown that implementation of protective measures based solely on the 2.0 μg/m$^3$ airborne beryllium OSHA standard does not prevent beryllium sensitisation. An enhanced preventive programme, incorporating novel interventions to minimise beryllium particle migration and both respiratory and dermal exposures, has reduced beryllium sensitisation in newly hired workers in the first years of employment. Ongoing follow-up of these workers will be necessary to determine the long-term effectiveness of this programme in preventing CBD. In the meantime, the adoption of the components of this preventive programme should be considered in other manufacturing facilities with potentially hazardous beryllium exposures.

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