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# Physicochemical Characteristics of Aerosol Particles Generated During the Milling of Beryllium Silicate Ores: Implications for Risk Assessment

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**Inhalation of beryllium dusts generated during milling of ores and cutting of beryl-containing gemstones is associated with development of beryllium sensitization and low prevalence of chronic beryllium disease (CBD). Inhalation of beryllium aerosols generated during primary beryllium production and machining of the metal, alloys, and ceramics are associated with sensitization and high rates of CBD, despite similar airborne beryllium mass concentrations among these industries. Understanding the physicochemical properties of exposure aerosols may help to understand the differential immunopathologic mechanisms of sensitization and CBD and lead to more biologically relevant exposure standards. Properties of aerosols generated during the industrial milling of bertrandite and beryl ores were evaluated. Airborne beryllium mass concentrations among work areas ranged from 0.001 μg/m$^3$ (beryl ore grinding) to 2.1 μg/m$^3$ (beryl ore crushing). Respirable mass fractions of airborne beryllium-containing particles were < 20% in low-energy input operation areas (ore crushing, hydroxide product drumming) and > 80% in high-energy input areas (beryl melting, beryl grinding). Particle specific surface area decreased with processing from feedstock ores to drumming final product beryllium hydroxide. Among work areas, beryllium was identified in three crystalline forms: beryl, poorly crystalline beryllium oxide, and beryllium hydroxide. In comparison to aerosols generated by high-CBD risk primary production processes, aerosol particles encountered during milling had similar mass concentrations, generally lower number concentrations and surface area, and contained no identifiable highly crystalline beryllium oxide. One possible explanation for the apparent low prevalence of CBD among workers exposed to beryllium mineral dusts may be that characteristics of the exposure material do not contribute to the development of lung burdens sufficient for progression from sensitization to CBD. In comparison to high-CBD risk exposures where the chemical nature of aerosol particles may confer higher bioavailability, respirable ore dusts likely confer considerably less. While finished product beryllium hydroxide particles may confer bioavailability similar to that of high-CBD risk aerosols, physical exposure factors (i.e., large particle sizes) may limit development of alveolar lung burdens.**

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Beryllium is a lightweight metal with unique physical, mechanical, and nuclear properties; the metal, its oxide, and alloys are used in a range of industries, including aerospace, telecommunications, defense, and automotive manufacturing (Stonehouse, 1986; Weston et al., 2005). Workers exposed to beryllium salts, mists, fumes, and particles may become sensitized, meaning that their immune systems respond to beryllium (Kreiss et al., 2007). According to a study by Newman et al. (2005), 30% of sensitized individuals developed chronic beryllium disease (CBD) within 4 yr on average (range: 1 to 10 yr), which corresponded to a conversion rate of 8% per year. CBD is a progressive respiratory disease characterized by the formation of granulomas (i.e., inflammatory injuries consisting of compactly grouped cells that replace normally functioning tissue). Development of CBD is associated with exposure to poorly soluble beryllium-containing particles (Sterner & Eisenbud, 1951; Kreiss et al., 1997; Eisenbud, 1998), i.e., materials whose

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clearance rate by chemical dissolution is slower than their mechanical clearance rate.

Sensitization appears to be a necessary precursor for development of disease (Newman et al., 2005); however, some beryllium exposure materials may produce sensitization without leading to CBD. For example, Curtis (1951) skin patch tested human volunteers with soluble beryllium salts and reported development of sensitization, but not CDB. Thus, a beryllium lung burden is needed for development of disease, but the exposure regime (intensity, time) and resultant mass of beryllium in the lung that are necessary to produce disease remain unknown. Autopsy studies revealed measurable masses of residual particulate beryllium in lungs of individuals with CBD (Freiman & Hardy, 1970). Beryllium particulate was identified in granulomas formed in the lungs of individuals with CBD years after exposure ceased (Williams & Wallach, 1989; Butnor et al., 2003; Sawyer et al., 2005). In these studies, the masses of beryllium represented residual particulate rather than the amount of beryllium that had dissolved via chemical dissolution during particle residence time in the lung and was made available to the immune system, which may help to explain why beryllium particle mass in the lung did not correlate with the severity of disease observed upon autopsy (Freiman & Hardy, 1970). Thus, a molecular/cellular model for development of the specific immune-type granuloma associated with CBD needs to include a local lung beryllium reservoir.

Our working hypothesis is that exposure aerosol physical properties, chemical properties, and physicochemical properties (properties that depend on interaction of physical and chemical properties) control development of beryllium lung burdens. In turn, these material properties and associated lung burden may distinguish development of sensitization from development of sensitization with progression to CBD. Physical properties of exposure aerosols such as aerodynamic particle size may influence deposition and distribution within the human respiratory tract. In particular, respirable particles having aerodynamic diameters <10 μm, with 50% aerodynamic cutoff diameters ($D_{50}$) of 4 μm, may contribute to development of an alveolar lung burden, whereas larger particles do not deposit in the alveoli (Stuart et al., 1986). The chemical properties of exposure aerosol materials that deposit in the alveolar region of the lung form the primary reactants in the inorganic/biochemical reaction that underlie the immunopathology that leads to CBD. The physicochemical properties of alveolar-deposited beryllium particles determine lung burden dynamics and particle dissolution kinetics. Lung burden dynamics account for the deposition of beryllium particles in the alveolar region of the lung and the clearance of beryllium particles removed from the lung via mechanical and chemical dissolution mechanisms. Particle dissolution kinetics limit the rate at which soluble beryllium becomes available to the immune system for inducing sensitization and pathological changes to lung tissue. Thus, in combination, these physical, chemical, and physicochemical exposure aerosol material factors may influence progression to CBD through development and regulation of a beryllium lung burden. Understanding how these exposure materials factors influence CBD is necessary for development of biologically based protective exposure standards for beryllium. In addition, the links between these exposure material factors and disease processes, together with understanding particle formation mechanisms, may help to elucidate opportunities for modifying industrial beryllium processes that might reduce hazard of beryllium exposures.

Beryllium is commercially extracted from two silicate minerals, bertrandite ($4BeO{\cdot}2SiO_2{\cdot}H_2O$) and beryl ($3BeO{\cdot}Al_2O_3{\cdot}6SiO_2$). In addition, high-purity beryl has commercial value as the gemstones emerald and aquamarine (Stonehouse, 1986). Wagner et al. (1969) reported that animals chronically exposed to bertrandite dust, but not to beryl, developed lesions consisting of tightly packed dust-laden macrophages. Thorat et al. (2003) reported that beryllium-containing particles generated during the extraction of ore had mass median aerodynamic diameters (MMAD) of 5 μm (leaching) to 8.8 μm (beryllium hydroxide filtration) and beryllium mass concentrations ranged from 0.1 μg/m$^3$ (leaching) to 1 μg/m$^3$ (jaw crushing sintered material). In humans, limited epidemiological evidence suggested that exposure to beryllium during the milling of ores and cutting and grinding aquamarine and emerald gemstones may induce sensitization. One of 57 gemstone cutters (among 100 eligible workers) was sensitized but declined follow-up clinical evaluation, precluding a determination of whether the subject had CBD (Wegner et al., 2000). Similarly, 3 of 75 miners and millers (among 87 eligible workers) were sensitized, one with CBD. The one subject with CBD previously worked in a beryllium primary production facility; the remaining two sensitized workers declined follow-up clinical evaluation and their health status remains unknown (Deubner et al., 2001). Further, Taiwo et al. (2008) reported that 2 of 734 aluminum smelter workers were sensitized (0.27%). Although there are weaknesses associated with these studies, such as small numbers of eligible participants, low participation rates, and/or small numbers of health events, the seemingly low prevalence of sensitization and CBD among these workers is of special interest because airborne beryllium mass concentrations encountered during these jobs are within the range reported for known high-sensitization- and high-CBD-risk processes such as primary production of beryllium metal powder, beryllium oxide powder, and copper–beryllium alloy. In addition, the number concentration of ultrafine particles in primary production work areas associated with high risk of CBD (Kreiss et al., 1997) ranged from $10^3$ to $10^7$ particles/cm$^3$ air (McCawley et al., 2001). Fine particle specific surface area varied by work area and beryllium was in the form of beryllium oxide, regardless of product line (beryllium metal, beryllium oxide, and copper-beryllium alloy) (Stefaniak et al., 2003, 2004). However, prevalence of beryllium sensitization among workers exposed to beryllium during primary production is 9–15% and prevalence of CBD is 5–8% (Kreiss et al., 2007). Thus, knowledge of the physicochemical properties of beryllium ore dusts and process-generated intermediary aerosols that have an apparently low association with CBD may lend insight to relevant exposure characteristics of beryllium-containing aerosols in known hazardous work areas.

The goal of this study was to characterize the physicochemical properties of aerosols generated during the industrial milling of bertrandite and beryl mineral ores. Using a suite of air sampling and analytical techniques, the following research questions were investigated:

a. What are the exposure characteristics (number and mass concentration, and particle size distribution) of aerosols generated during milling of beryllium ores?
b. What are the physical characteristics (morphology, specific surface area, and density) of aerosols generated during milling?
c. What is the chemical composition of aerosols generated during milling?
d. Do the physicochemical properties of beryllium-containing aerosols produced during milling differ from those of beryllium-containing aerosols generated during primary production?

## MATERIALS AND METHODS

Two types of samples were collected in this study: ambient airborne work environment particles and process-sampled airborne particles. Airborne particles from the ambient environment were collected from general work room air in the vicinity of manufacturing processes, thus representing aerosols to which workers may potentially be exposed. Process-sampled particles were collected from the local exhaust ventilation of manufacturing processes themselves, representing the source term for aerosols to which workers may be potentially exposed. Estimates of process-related risk for beryllium sensitization at this mill facility are unavailable, due in part to the small number of cases (Deubner et al., 2001). As such, work areas were selected for sample collection based on considerations of where changes in particle physicochemical properties were likely to occur because of process conditions (e.g., crushing, heating).

Figure 1 is a flow diagram of the beryllium extraction process (adapted from Stonehouse, 1986). Asterisks denote the sampling locations in this study. The extraction process begins with input materials of either bertrandite (0.32% beryllium by mass on average for the period during which samples were collected) or beryl ore (4.18% beryllium by mass on average for the period during which samples were collected). The masses of beryllium in feedstock ore materials were determined using a lithium metaborate fusion method similar to that described by Panteeva et al. (2003). Bertrandite was crushed outdoors to break up the ore, wet ground into slurry, wet screened, and acid leached with sulfuric acid to make a water-soluble beryllium sulfate. The aqueous solution containing beryllium sulfate was separated

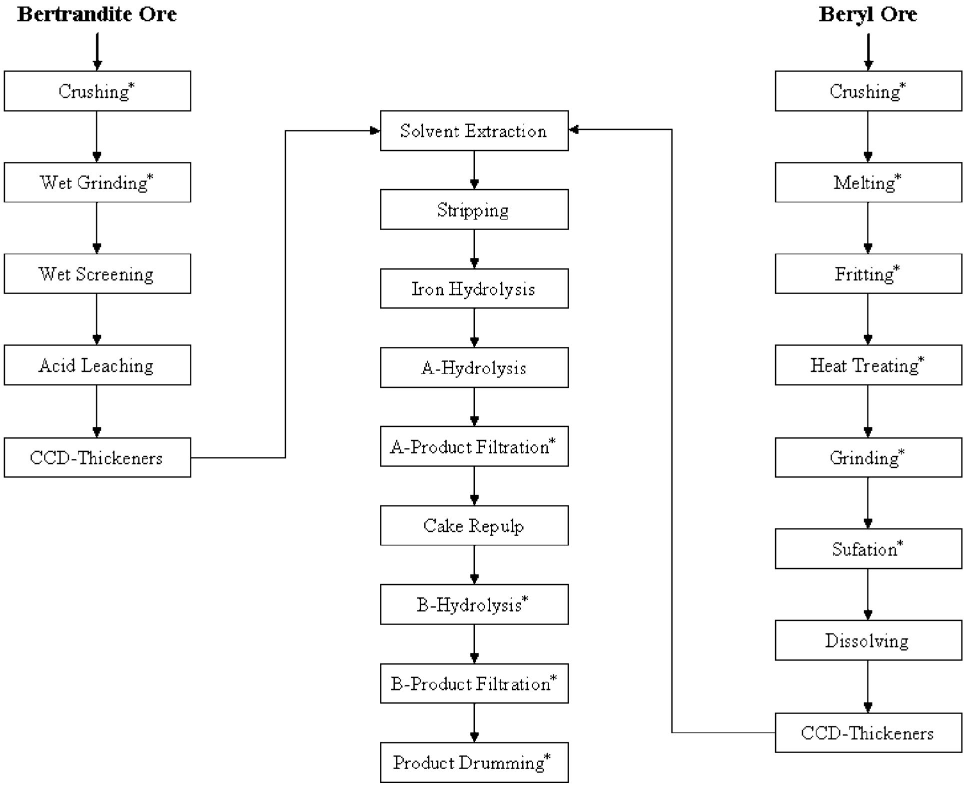

**FIG. 1.** Beryllium extraction process (adapted from Stonehouse, 1986). Asterisks denote the sampling locations in this study. Detailed descriptions of the work areas are provided in the Materials and Methods section.

from the solids by countercurrent decantation (CCD) thickener operations and sent to the solvent extraction plant. The silicate structure of beryl ore is not readily acid soluble; as such, the ore must first be crushed, melted in an arc furnace, and then quenched in water (fritted) to destroy the original silicate structure. The resulting fritted material is then heat-treated to increase its reactivity with sulfuric acid, ground (ball milled), made into a slurry of powdered frit and sulfuric acid (sulfation), and heated to convert the beryllium content to a water-soluble beryllium sulfate. The aqueous solution containing beryllium sulfate is then separated from the solids by CCD thickener operations and introduced to the solvent extraction plant. Once introduced to the solvent extraction plant, the bertrandite and beryl feed streams are combined and from this point forward, the ore from which the beryllium came loses its identity in the solution (Stonehouse, 1986). The aqueous solutions containing beryllium sulfate are concentrated by organic solvent extraction. Beryllium is then stripped from the organic solution with aqueous ammonium carbonate. The strip solution is heated to precipitate iron and filtered, the solution is further heated to precipitate basic beryllium carbonate, filtered (A-product filtration), the cake is repulped in deionized water to make a slurry, the slurry is heated (B-hydrolysis) to yield beryllium hydroxide powder, and the powder is filtered (B-product filtration), drummed, then shipped off-site for primary processing into beryllium metal, beryllium oxide, or beryllium alloys (typically copper–beryllium alloy).

## Characterization of Work Environment Aerosols

Airborne particles in the ambient work environment were characterized using a real-time optical particle counter (OPC) and filter sampling techniques. During specific work activities such as crushing ore and drumming finished hydroxide powder, airborne particles were counted independent of chemical composition using a GRIMM OPC (model 1108, GRIMM Technologies, Douglasville, GA) to characterize particle number concentration. The OPC measured particle number concentration in 18 channels that covered the diameter range of 0.3 μm to greater than 20 μm and logged measurements in 1-min intervals. “Total” particle mass concentrations were measured using 37-mm closed-face cassette samplers. To characterize total mass concentrations, particles were collected on preweighed 37-mm, 5-μm pore size, polyvinyl chloride (PVC) substrates (Omega Specialty Products Division, SKC, Inc., Eighty Four, PA) loaded into two-piece plastic closed-face cassettes. Air was drawn through each filter at 2 L/min using a calibrated (Gillibrator, Gillian, Clearwater, FL) personal air sampling pump (Gillian). Both particle mass concentrations and particle size distributions were measured using multi-orifice uniform deposit impactor (MOUDI) samplers (MSP Corp., Shoreview, MN). To characterize aerosol size distributions, particles were collected on preweighed PVC substrates (47-mm, 0.5-μm pore size for the inlet stage through stage 8; 37-mm, 5-μm pore size for the final filter) (Omega Specialty Products Division) using eight-stage MOUDI samplers. All MOUDI substrates, except the final filter, were sprayed with silicone (product number 07041, MSP Corp.) to minimize particle bounce during sampling. Air was drawn through each MOUDI sampler at 30 L/min using a high-volume pump (Gast, Benton Harbor, MI) that was calibrated at the sampling location using a primary flow device (model 4046, TSI, Inc., Shoreview, MN). The $D_{50}$ for the individual stages of the MOUDI samplers were >18 for the inlet, 10, 5.6, 3.2, 1.8, 1.0, 0.56, 0.32, and 0.18 for stages 1 to 8, respectively, and <0.18 μm for the final filter.

In each work area sampled, the 37-mm cassette and the MOUDI samplers were positioned side by side, generally at breathing zone height and near processes for durations ranging from 16 to 48 h. One pair of samples was collected in each of 12 work areas that span the extraction processes. Size distributions of dust and beryllium-containing particles in air were estimated for each MOUDI sample. Estimates of size distributions (MMAD and GSD) of beryllium-containing particles and dusts were calculated using methods described by Hinds (1986). For the purpose of calculating size distributions of beryllium-containing particles and dusts, mass values below analytical detection limits (described later) were assigned values equal to one-half the limit (Hornung & Reed, 1990).

All MOUDI and 37-mm cassette substrates and field and lab blank substrates were submitted to a commercial lab for quantification of total dust. Total dust was quantified in accordance with a modified NIOSH Method 0500: Total Particulates Not Otherwise Regulated (NIOSH, 2003). The method was modified as follows: (1) Filters were stabilized in a temperature- and humidity-controlled room (20 ± 1°C, 50 ± 5% relative humidity [RH]) for at least 2 h prior to tare and gross readings, (2) two measurements were taken of the tare and gross weights, and (3) averages of these measurements were used to determine total masses. The analytical limit of detection (LOD) was determined to be 20 μg/filter for Method 0500 during this study.

Beryllium content was quantified by a commercial laboratory in accordance with a modified NIOSH Analytical Method 7300: Elements by Inductively Coupled Plasma-Atomic Emission Spectroscopy (ICP-AES) (NIOSH, 2003). Recognizing the limitations of many common analytical methods to digest poorly soluble particles (Stefaniak et al., 2007, 2008), the method was modified to digest beryllium contained in a poorly soluble silicate matrix: Each filter sample was first transferred to a Teflon beaker, 5 ml hydrofluoric acid was added to each beaker, and the beakers were covered with a Teflon watch glass and placed on a hotplate to reflux for 2 h. The covers were then removed and the solutions each reduced to ~1 ml volume. This step of acid addition, reflux, and solution volume reduction was repeated. Next, 5 ml nitric acid was added to each beaker, and the beakers were covered with a Teflon watch glass and placed on a hotplate to reflux for 2 h. The covers were then removed and the solutions each reduced to ~1 ml volume. To continue the digestion, the digestates and filters were transferred to separate glass beakers, 5 ml nitric acid and 1 ml perchloric acid were added to each beaker, the samples were placed back on the hotplate and reduced in volume to ash the filters, and then the solutions were further reduced until the liquid was clear. Finally, the samples were removed from the hotplate and cooled, 2 ml nitric acid was added to each beaker, and then the digestates were transferred and rinsed into separate 50-ml centrifuge tubes and each sample was diluted to a final volume of 25 ml with American Society for Testing and Materials (ASTM) Type II water. Filter samples were collected and analyzed in two batches; the analytical LOD was 0.005 μg beryllium/filter and the limit of quantification (LOQ) was 0.02 μg beryllium/filter for samples collected during milling of bertrandite and production of beryllium hydroxide. The LOD was 0.008 μg beryllium/filter and the LOQ was 0.03 μg beryllium/filter for samples collected during milling of beryl. All MOUDI and 37-mm cassette sample results were blank-corrected as appropriate.

### Characterization of Process-Sampled Particles

Process-sampled particles were collected from the ventilation ductwork of the beryl ore crushing, melting, heat treating, and grinding processes and from the product drumming process using an aerosol cyclone, then characterized using a suite of analytical techniques, including transmission electron microscopy, surface area measurement, and density measurement (Stefaniak et al., 2003, 2004; Rouleau et al., 2005). One cyclone sample was collected from each work area, with the exception of product drumming where two samples were collected. Cyclone samples were not collected from the outdoor process that lacked ventilation ductwork (bertrandite ore crusher) or from wet processes (fritting, sulfation, wet grinding, A-product filtration, B-hydrolysis, and B-product filtration). For comparison with these process-collected particles, bulk samples of bertrandite ore feedstock material from two mine pits (referred to as the Blue Chalk pit and the Monitor pit) were each pulverized with a tungsten carbide shatterbox mill (SPEX CertiPrep, Metuchen, NJ) and characterized as described later.

### Collection of Process-Sampled Particles

Process-sampled particles were collected from the local exhaust ventilation ductwork of each process using an isokinetic sample probe (model 280N, Graseby-Andersen, Smyrna, GA) connected to a 5-stage aerosol cyclone (model 285, Graseby-Andersen) followed by an electrostatic precipitator (ESP) with a backup thimble filter operated at 28 L/min (Stefaniak et al., 2003, 2004). The $D_{50}$ values for process-specific sampling conditions (gas temperature, flow rate) were >5.6, 2.3, 1.4, 0.7, 0.4, and <0.4 μm (beryl ore crushing, beryl ore grinding); >6.7, 3, 2, 0.9, 0.5, and <0.5 μm (melting); >8.3, 4.0, 3.1, 1.2, 0.6, and <0.6 μm (heat treating); and >5.4, 2.2, 1.3, 0.6, 0.4, and <0.4 μm (product drumming) for stages 1 to 5 and the backup ESP, respectively.

### Determination of Physical Characteristics

Morphology of aerodynamically size-separated particles was determined using transmission electron microscopy (TEM, model CM30 electron microscope, Philips Electron Optics, Eindhoven, the Netherlands). All samples were prepared on 300-mesh gold electron microscopy grids coated with a lacey carbon substrate (Ted Pella, Inc., Redding, CA).

Particle Brunauer, Emmett, and Teller (BET) nitrogen surface area was determined in accordance with ASTM B922-02: Standard Test Method for Metal Powder Specific Surface Area by Physical Adsorption (ASTM, 2002). With the exception of the powder from the beryllium hydroxide product drumming operation, samples were vacuum degassed (P ~0.015 torr) prior to surface area measurement for a minimum of 4 h at 200°C (Flovac degasser, product number 05076, Quantachrome) to remove physisorbed material, e.g., water. At temperatures above ~200°C, beryllium hydroxide decomposes to form beryllium oxide and beryllium oxyhydroxide (Kiiko et al., 1985; Pletnev et al., 2005). To avoid altering morphology, chemical composition, and crystalline structure of the beryllium hydroxide material, this powder was vacuum degassed (P ~0.015 torr) overnight without heating to remove physisorbed material. Surface area (NOVA 2000e surface area analyzer, Quantachrome) was estimated from full isotherms (minimum of 20 adsorption points from relative pressures, $P/P_0=0.01$ to 0.95; 15 desorption points from $P/P_0=0.95$ to 0.3) of each sample using at least 5 adsorption points in the range $P/P_0=0.05$ to 0.35; a value of 16.2 $Å^2$ was assumed for the cross-sectional area of a nitrogen molecule. Beryl ore is not considered to be a highly porous material and the surface area of these samples was estimated by measuring a seven-point adsorption isotherm (from $P/P_0=0.05$ to 0.35) using ultra high purity nitrogen. Surface area measurements ($m^2$) were normalized by dry powder mass (determined gravimetrically) to obtain specific surface area (SSA) with units of square meters per gram. A titanium dioxide powder (SRM 2001, Quantachrome) with certified SSA of $8.46 \pm 0.9$ $m^2/g$ was used as a reference standard and analyzed in parallel with powder samples periodically throughout the study. The average measured SSA for this control sample, $8.44 \pm 0.41$ $m^2/g$, was within 1% of the certified value.

Density ($g/cm^3$) was measured by gas displacement using a multipynometer (product number 03035, Quantachrome) with ultra-high-purity helium gas. Density was determined as the arithmetic mean of triplicate measurements. A tungsten oxide ($WO_3$) sample with well-characterized density of 7.20 $g/cm^3$ was used as a reference standard and was measured before and after measurement of the size-separated samples.

The measured average density of the $WO_3$ reference standard was 7.22 ± 0.01 $g/cm^3$, which was within 1% of the known value.

### Determination of Chemical Composition

Crystalline chemical composition of bulk bertrandite powders and process-sampled particles was determined using powder x-ray diffraction (XRD, Siemens model D500 powder diffractometer, Bruker AXS, Inc., Madison, WI) with Cu k-alpha radiation. XRD samples were mounted in a shallow titanium metal cavity or as a smear on an off-axis-cut quartz plate and run from 2 to 140° 2θ overnight to ensure adequate counting statistics for beryllium. The identity of constituents was determined by comparing diffraction patterns to reference patterns in the Inorganic Crystal Structure Database (ICSD, Fachinformationszentrum [FIZ] Karlsruhe, http://icsdweb.fiz-karlsruhe.de/index.php). Relative abundances of crystalline phases were obtained from Rietveld and full-pattern fitting methods (Bish & Howard, 1988; Chipera & Bish, 2002).

Elemental chemical composition of process-sampled particles was evaluated using TEM–energy-dispersive x-ray spectrometry (TEM-EDS). The TEM-EDS system, a germanium detector (Princeton Gamma-Tech, Princeton, NJ) connected to a Power Macintosh running the Desktop Spectrum Analyzer software (National Institute of Standards and Technology, Gaithersburg, MD), can collect and display chemical information for elements with atomic number greater than 6 (carbon). Thus, elemental beryllium (atomic number 4) could not be detected using EDS. The crystalline chemical composition of process-sampled particles was also evaluated using TEM-selected area electron diffraction (TEM-SAD). Electron diffraction patterns generated were compared to published reference patterns (Pearson et al., 1991) to identify crystalline constituents. Chemical analyses were performed using the same grid samples prepared for TEM morphology analyses.

### Statistical Analyses

Total beryllium mass concentrations and dust concentrations measured using 37-mm cassette and MOUDI samplers placed side by side were compared with the PROC CORR procedure in PC-SASS version 9.1 (SAS Institute, Inc., Cary, NC). Pearson correlation coefficients and *p* values associated with the correlations were obtained.

## RESULTS

### Work Environmental Aerosols

Within many continuous-operation work areas (e.g., bertrandite ore wet grinding; beryl ore melting, heat treating, and sulfation; B-product filtration), airborne particle number concentration was relatively constant, whereas in batch-operation work areas (e.g., beryl ore crushing and fritting; product drumming), number concentration was highly variable. Figure 2 is a plot of the background-corrected number concentration of particles with diameter 0.3 to 1 μm for the beryl ore crusher that illustrates the influence of work activity on number concentration over a 4-h period. The four peaks in number concentration that are identified in the figure correspond to times when the hopper for the ore crusher was loaded using a diesel-powered front loader. Each time the ore hopper was loaded, the number concentration of 0.3- to 0.4-μm particles rapidly increased by a factor of 4 to 11, then returned to baseline. During the overnight period when there was no ore crushing activity and the front loader was off, particle number concentrations in the size range 0.3 to 1 μm were less than 500 particles/$cm^3$ (data not shown). Similar patterns of work-activity-influenced variability in particle number concentration were observed during fritting and product drumming (data not shown).

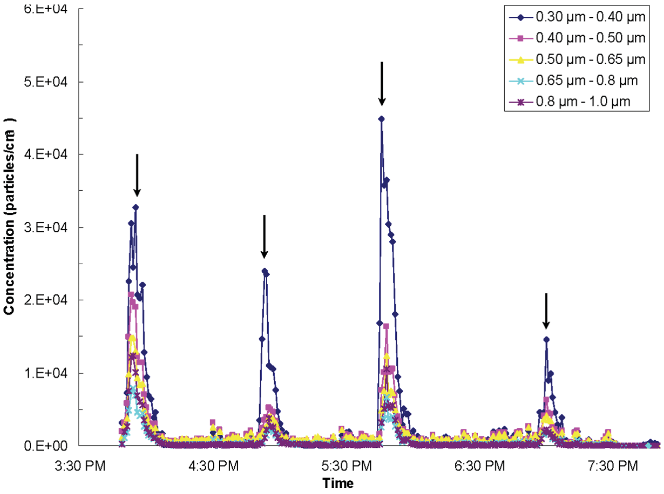

**FIG. 2.** Background-corrected number concentration of particles with diameter 0.3 to 1 μm versus time for the beryl ore crusher. The four peaks identified with arrows correspond to times when the hopper for the ore crusher was loaded using a diesel-powered front loader and illustrate the influence of work activity on number concentration; the optical particle counter could not discriminate beryllium-containing particles from other types of particles, including diesel particulate matter emissions from the front loader.

Table 1 summarizes the mass concentrations of airborne beryllium and total dust determined with 37-mm cassette and MOUDI samplers by work area. Among the 12 cassette substrates collected, the masses of total dust were below the LOD for 2 filters. For the 120 MOUDI substrates collected, the masses of beryllium and total dust were below the LODs for 6 filters (5%) and 8 filters (7%), respectively, typically in the smallest size fractions (stages 6 through the final filter). Using 37-mm cassette samplers, beryllium concentrations ranged from 0.001 $\mu g/m^3$ (beryl grinding) to 2.1 $\mu g/m^3$ (beryl crusher) and dust concentrations ranged from <4 $\mu g/m^3$ (beryl heat treating, beryl grinding) to 257 $\mu g/m^3$ (bertrandite ore crusher). Using MOUDI samplers, beryllium concentrations ranged from 0.02 $\mu g/m^3$ (A-product filtration, B-hydrolysis) to 1.7 $\mu g/m^3$

**TABLE 1**

Concentrations of beryllium and total dust by work area measured using 37-mm cassette and micro-orifice uniform deposit impactor (MOUDI) samplers ($n$ = 1 matched pair of samplers per work area)

| | 37-mm Cassette | | | MOUDI | | |
|---|---|---|---|---|---|---|
| Work area | Beryllium (μg/m$^3$) | Dust (μg/m$^3$) | Be/dust (%) | Beryllium (μg/m$^3$) | Dust (μg/m$^3$) | Be/dust[a] (%) |
| Bertrandite line | | | | | | |
| Crushing | 0.9 | 257 | 0.4 | 1.5 | 260 | 0.5 (0.01–0.8) |
| Wet Grinding | 1.1 | 213 | 0.5 | 1.2 | 320 | 0.5 (0.1–0.7) |
| Beryl line | | | | | | |
| Crushing | 2.1 | 146 | 1.5 | 1.7 | 100 | 1.2 (0.1–2.2) |
| Melting | 0.3 | 63 | 0.4 | 0.3 | 71 | 1.4 (0.1–5.8) |
| Fritting | 0.2 | 45 | 0.5 | 0.2 | 49 | 1.3 (0.1–6.4) |
| Heat treating | 0.3 | < 4 | —[b] | 0.4 | 20 | 1.8 (0.3–6.6) |
| Grinding | 0.001 | < 4 | — | 0.1 | 8 | 1.3 (0.2–2.8) |
| Sulfation | 0.3 | 33 | 0.9 | 0.4 | 52 | 1.3 (0.1–4.4) |
| Solvent extraction line | | | | | | |
| A-Product filtration | 0.02 | 19 | 0.1 | 0.02 | 11 | 0.1 (0.01–0.3) |
| B-Hydrolysis | 0.02 | 10 | 0.3 | 0.02 | 16 | 0.2 (0.01–0.8) |
| B-Product filtration | 0.02 | 10 | 0.2 | 0.06 | 22 | 0.6 (0.01–1.6) |
| Product drumming | 0.04 | 15 | 0.3 | 0.03 | 15 | 0.3 (0.01–0.8) |

[a] Values of the beryllium/dust ratio for the eight-stage MOUDI are average (range) for all substrate in sample; ratio was not calculated for stages with beryllium or dust value below analytical limits of detection.

[b] Dust value was below the analytical limit of detection (20 μg/filter), precluding calculation of the Be/dust ratio.

(beryl crusher) and dust concentrations ranged from 8 μg/m$^3$ (beryl grinding) to 319 μg/m$^3$ (bertrandite wet grinding). Among all samples, beryllium concentrations were significantly correlated ($r$ = .94, $p$ < 0.0001) between side-by-side 37-mm cassette and MOUDI samplers; concentrations of dust were also markedly correlated ($r$ = .94, $p$ < 0.0001). The mass fraction of beryllium in airborne dust measured with 37-mm cassette samplers ranged from 0.1 (A-product filtration) to 1.5% (beryl ore crushing). The beryllium content of airborne dust measured with MOUDI samplers indicated size-dependent differences in particle beryllium fraction, with a maximum value of 6.6% (heat treating).

Table 2 summarizes the size distributions and respirable mass fractions of beryllium-containing particles and dust calculated from MOUDI sample results by work area. Beryllium particle MMAD ranged from <0.18 (heat treating) to 13.8 μm (B-hydrolysis), whereas dust particle MMAD values ranged from 0.7 (beryl ore grinding) to 10.5 μm (bertrandite ore crushing). Beryllium particle MMAD were smallest in the beryl melting, fritting, heat treating, grinding, and sulfation work areas and largest in the in the bertrandite ore crushing, beryl ore crushing, B-hydrolysis, and product drumming work areas. Dust particle MMAD values were largest in the bertrandite ore crushing and wet grinding work areas and the beryl ore crushing work area. The respirable mass fraction of beryllium-containing particles was 80 to 90% in the beryl melting, fritting, heat treating, grinding, and sulfation work areas and less than 50% in all other work areas.

## Process-Sampled Particles

### *Physical Characteristics*

Figure 3 shows TEM micrographs of particles collected during beryl ore crushing and beryllium hydroxide product drumming. Particles collected from the beryl ore crushing operation had variable morphology, either large flakes with submicrometer-sized smooth, spherical particles attached to the larger flakes (Figure 3a), or clusters of smooth, spherical primary particles (Figure 3b). Particles collected in the beryllium hydroxide product drumming work area were stacks of plate-like primary particles with long straight edges (Figure 3c). Particles from the beryllium hydroxide product drumming operation were beam sensitive; two images taken of the same particle at the same magnification about a minute apart and after focusing the TEM beam (300 kV) on the particle for a few seconds resulted in the particles shrinking and the primary particle structure changing from plates to smaller, more equiaxial but less distinct grains (data not shown).

Table 3 summarizes measured densities for process-sampled particles by work area. Process-generated aerosol particles (beryl ore crusher, melting, grinding work areas) had

**TABLE 2**

Mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) and respirable mass fraction of airborne beryllium-containing particles and dust by work area measured using micro-orifice uniform deposit impactor (MOUDI) samplers

| | Beryllium | | | Dust | | |
|---|---|---|---|---|---|---|
| Work area | MMAD (µm) | GSD | Resp. mass (%)[a] | MMAD (µm) | GSD | Resp. mass (%) |
| Bertrandite line | | | | | | |
| Crushing | 9.8 | 2.2 | 16 | 10.5 | 2.1 | 15 |
| Wet grinding | 4.7 | 3.0 | 48 | 8.5 | 1.9 | 28 |
| Beryl line | | | | | | |
| Crushing | 11.2 | 2.6 | 15 | 9.2 | 3.2 | 22 |
| Melting | 0.2 | 29.2 | 83 | 6.6 | 4.2 | 37 |
| Fritting | 0.2 | 12.4 | 85 | 4.0 | 2.8 | 45 |
| Heat treating | < 0.18[b] | — | 90 | 2.1 | 5.2 | 62 |
| Grinding | 0.2 | 11.4 | 89 | 0.7 | 11.2 | 75 |
| Sulfation | 0.2 | 11.6 | 88 | 1.8 | 3.4 | 78 |
| Solvent extraction line | | | | | | |
| A-Product filtration | 7.8 | 2.9 | 28 | 1.1 | 5.4 | 78 |
| B-Hydrolysis | 13.8 | 3.4 | 19 | 2.2 | 4.4 | 64 |
| B-Product filtration | 6.1 | 2.9 | 36 | 0.8 | 6.0 | 80 |
| Product drumming | 10.6 | 2.7 | 17 | 3.2 | 10.6 | 54 |

[a] Resp. mass is the respirable mass fraction of particles calculated for each sample by summing the average respirable fraction per impactor stage using the International Organization for Standardization (ISO) respirable dust criteria (Lippman, 1999).

[b] Greater than 50% of the measured mass of analyte was on the final filter of the impactor (i.e., less than 0.18 µm aerodynamic diameter), precluding calculation of an exact value for the mass median aerodynamic diameter.

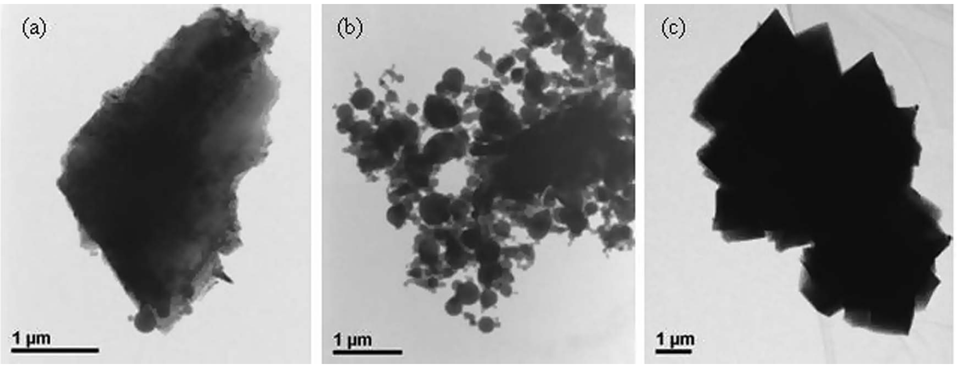

**FIG. 3.** Transmission electron micrographs of particles collected from the beryl ore crushing unit operation and the beryllium hydroxide product drumming unit operation. The morphology of particles collected from the beryl ore crushing operation was highly variable and included (a) large flakes with submicrometer-sized round smooth spherical particles attached to the surface and (b) clusters of round smooth spherical primary particles. The morphology of particles collected from the beryllium hydroxide product drumming operation (c) was stacks of plate-like primary particles.

density that ranged from 2.2 to 2.5 g/cm$^3$. Table 4 summarizes particle SSA for process-sampled particles by work area. Particle SSA varied by a factor of 80 among all particle sizes and work areas and generally decreased with material processing from ore to final product.

### *Chemical Composition*

The bertrandite ore materials from the Blue Chalk and Monitor pits were mainly comprised of smectite, quartz, and feldspar, with minor amounts of calcite, dolomite, fluorite, and mica, but no actual beryllium-bearing phases were identified using XRD.

**TABLE 3**
Density (g/cm$^3$) of process-sampled particles by work area

| | Density (g/cm$^3$) | | | | |
|---|---|---|---|---|---|
| Stage[a] | Crushing (beryl) | Melting | Heat treating | Grinding (beryl) | Product drumming |
| 1 | 2.49 ± 0.03 | —[b] | — | 2.43 ± 0.01 | 1.91 ± 0.01[c] |
| 2 | — | — | — | 2.46 ± 0.02 | 1.91 ± 0.01 |
| 3 | — | — | — | 2.47 ± 0.00 | — |
| 4 | — | — | — | 2.44 ± 0.01 | — |
| 5 | — | 2.21 ± 0.00 | — | 2.47 ± 0.02 | — |
| ESP | — | 2.23 ± 0.01 | — | 2.43 ± 0.01 | — |

[a] ESP, electrostatic precipitator.

[b] Insufficient mass of material collected in this size fraction of the aerosol cyclone for density analysis using helium pycnometry.

[c] Theoretical density value of beryllium hydroxide is 1.92 g/cm$^3$.

**TABLE 4**
Specific surface area (m$^2$/g) of process-sampled particles by work area

| | SSA (m$^2$/g)[a] | | | | |
|---|---|---|---|---|---|
| Stage[b] | Crushing (beryl) | Melting | Heat treating | Grinding (beryl) | Product drumming |
| 1 | 7.03 ± 0.47 | 10.51 ± 0.52 | 8.94 ± 0.59 | 4.32 ± 0.01 | 0.34 ± 0.03 |
| 2 | 25.87 ± 2.50 | —[c] | — | 4.69 ± 0.04 | 0.40 ± 0.05 |
| 3 | — | 7.14 ± 0.15 | — | 4.99 ± 0.03 | — |
| 4 | 17.78 ± 0.62 | 8.66 ± 0.39 | — | 5.65 ± 0.06 | — |
| 5 | 13.21 ± 0.70 | 10.59 ± 0.33 | — | 6.41 ± 0.12 | — |
| ESP | — | 13.39 ± 0.98 | — | 5.17 ± 0.10 | — |

[a] SSA, specific surface area; values are average ± standard deviation of triplicate samples.

[b] The $D_{50}$ for the process-sampled particles using the aerosol cyclone were: >5.6, 2.3, 1.4, 0.7, 0.4, and <0.4 µm (beryl ore crushing, beryl ore grinding); >6.7, 3.0, 2.0, 0.9, 0.5, and <0.5 µm (melting); >8.3, 4.0, 3.1, 1.2, 0.6, and <0.6 µm (heat treating); and >5.4, 2.2, 1.3, 0.6, 0.4, and <0.4 µm (product drumming) for stages 1 to 5 and the backup electrostatic precipitator (ESP), respectively.

[c] Insufficient mass of material collected in this size fraction of the aerosol cyclone for surface area analysis using nitrogen gas adsorption.

Additional analyses of the Blue Chalk and Monitor pit ore powders using inductively coupled plasma (ICP)–mass spectroscopy determined that beryllium was present at 0.2% by weight. The crystalline chemical composition of process-sampled particles differed within and among work areas. During beryl ore crushing (Figure 4) and melting (data not shown), particles collected in stage 1 of the aerosol cyclone contained crystalline beryllium in the form of beryl; however, particles collected in stage 3, stage 5, and the ESP were amorphous as illustrated by the smooth curves for these materials. Note that titanium peaks visible in the plot for the ESP fraction of the ore crusher particles are from the titanium sample mount. Heat treating particles (sufficient mass of powder for XRD analysis of stage 1 material only; data not shown) and grinding particles (Figure 5) contained minor amounts of crystalline beryllium in the form of poorly crystalline beryllium oxide (BeO). Again, titanium peaks visible in the plot for the fine particle sizes are from the sample mount. Process-sampled particles collected during product drumming (Figure 6) were pure beryllium hydroxide.

## DISCUSSION

### Work Environmental Aerosols

*Particle Number Concentrations*

The OPC used to characterize particle number concentration demonstrated considerable variability in exposure levels in

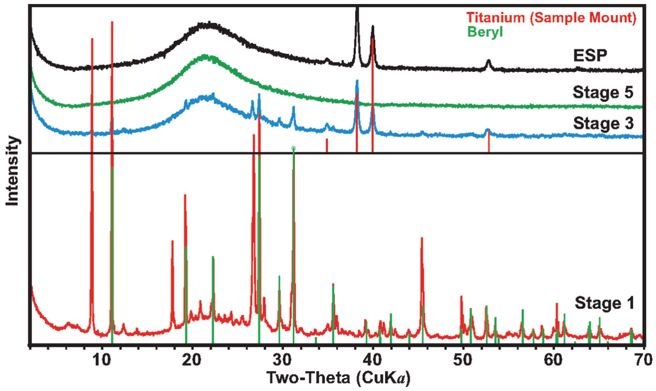

**FIG. 4.** X-ray diffractograms of process-sampled particles collected from the beryl ore crusher that illustrate particle size-dependent differences in crystalline composition: Particles collected in stage 1 of the aerosol cyclone contained beryllium in the form of beryl (red plot); in contrast, particles collected in stage 3 (blue plot) and stage 5 (green plot) of the aerosol cyclone and the backup ESP collector (black plot) were mainly amorphous (the prominent peaks visible in the plot for the stage 3 and ESP fraction are for titanium from the titanium metal sample mount).

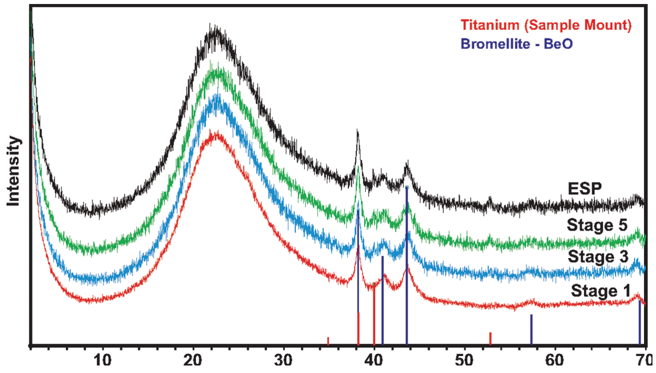

**FIG. 5.** X-ray diffractograms of process-sampled particles collected during grinding that illustrate process-dependent differences in the crystalline form of beryllium: Particles collected in stage 1 (red plot), stage 3 (blue plot), stage 5 (green plot), and ESP (black plot) of the aerosol cyclone contained a minor amount of beryllium in the form of poorly crystalline beryllium oxide (the peaks visible in the plot for the fine particle sizes are from the titanium metal sample mount). In contrast, the crystalline form of beryllium identified in the preceding beryl ore crushing and melting operations was beryl.

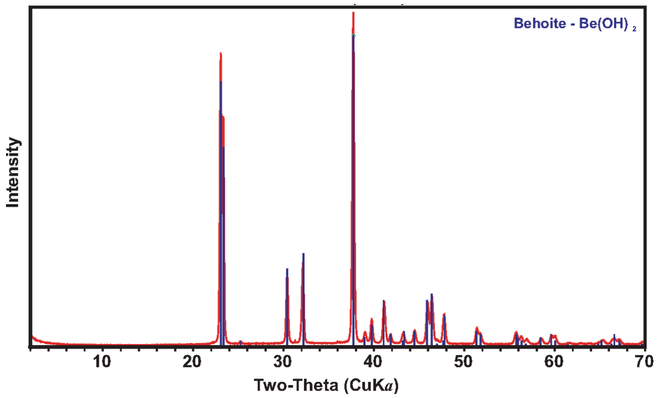

**FIG. 6.** X-ray diffractograms of process-sampled particles collected in stage 1 (red plot) of the aerosol cyclone during product drumming that illustrate process-dependent differences in the crystalline form of beryllium: Particles were pure beryllium hydroxide. In contrast, the crystalline form of beryllium identified in the preceding beryl milling operations was beryl (ore crushing, melting) and beryllium oxide (heat treating, grinding); the chemical form of aerosols generated during solvent extraction operations is unknown.

batch operation work areas such as ore crushing; however, this instrument could not discriminate beryllium-containing particles from any other particles in the air. Thus, despite airborne particle concentration during the four peak events being higher than during the overnight period, the chemical nature of particles and contributions of individual events such as diesel emissions from the engine of the front loader, re-entrainment of settled dust during operation of the front loader, dust generated by dumping beryl ore into the hopper, and dust generated during ore crushing cannot be elucidated. McCawley et al. (2001) used a scanning mobility particle sizer (SMPS) to estimate number concentration in the range 0.01 to 0.4 μm during primary production of beryllium. Like the OPC, the SMPS was unable to discriminate the chemical forms of airborne particles. For the smallest channel of the OPC that overlaps with the SMPS, 0.3 to 0.4 μm, particle number concentrations in all work areas at this mill were greater than $10^3$ particles/cm$^3$, which McCawley et al. (2001) also reported for the high-CBD-risk reduction furnace (metal powder production line) and arc furnace (copper–beryllium alloy production) work areas. However, particle number concentrations at this mill were at least a factor of 30 lower than $10^7$ particles/cm$^3$ reported for the high-CBD-risk fluoride furnace work area (metal powder production line). To better understand beryllium particle number concentration exposures, it would be desirable to have real-time methods capable of measuring beryllium-specific particle number concentration, in addition to total particle number concentration.

### *Particle Mass Concentrations*

Estimates of total airborne beryllium mass concentration were generally low, with the exception of the bertrandite ore crushing and wet grinding work areas and the beryl crushing work area. Total airborne beryllium concentrations were at least 2- to 10-fold lower than airborne concentrations reported during beryllium ore extraction and hydroxide filtration (Thorat et al., 2003) and for gemstone cutters working with aquamarines (Wegner et al., 2000), but within the range of exposures previously reported at this mill and in primary production (Deubner et al., 2001). The observed differences in mass concentrations among our study and those by Thorat et al. (2003) and Wegner et al. (2000) may be due to the type of sample (area versus personal), sampler placement (height for area samples, lapel for personal samples), worker distance relative to the exposure source (potentially close for detailed work such as cutting gemstones), and differences in the beryllium content of the mineral materials being handled. In our study, the airborne beryllium concentration in the bertrandite wet grinding work area was 1.1 to 1.2 $\mu g/m^3$ compared to an annual median beryllium concentration reported by Deubner et al. (2001) of 0.4 $\mu g/m^3$ (maximum = 75 $\mu g/m^3$). Our estimates of airborne beryllium concentration in the beryl plant were consistent with a median 0.2 $\mu g/m^3$ reported by Deubner et al. (2001), but our estimates of airborne beryllium concentration in the solvent extraction and hydrolysis work areas were lower by a factor of 10. This 10-fold difference in mass concentrations may be due to a variety of factors, including type of sample (area versus personal), sampling conditions (close-faced cassette configuration in our study versus open-faced sampler in Deubner et al., 2001), sampler placement (height and proximity to exposure sources), and production rates.

### *Particle Beryllium Mass Fractions*

The final product beryllium hydroxide contains 21% beryllium by weight, which is 65-fold higher than the bertrandite ore feedstock and 5-fold higher than the beryl ore feedstock. Fractions of beryllium in dust (see Table 1) determined from 37-mm cassette samples in the bertrandite line were consistent with beryllium mass fractions of bertrandite ore feedstock material (0.32%). The beryllium particle content in dust determined using MOUDI samplers indicated size-dependent differences of up to twofold higher than in the bulk ore. Fractions of beryllium determined from 37-mm cassette and MOUDI samples in the beryl line were generally less than or equal to the beryllium mass fraction in feedstock ore material (4.18%). Beryllium content in some size fractions of the MOUDI samples in the melting, fritting, and heat treating work areas exceeded that of the beryl ore feedstock, suggesting enrichment due to processing or size-dependent differences in particle beryllium content. Beryllium content in dust was up to several hundred times lower in the solvent extraction line relative to the beryllium mass fraction in the beryllium hydroxide final product. Among work areas, the mass fraction of beryllium in dust varied by a factor of 15. The fraction of beryllium in airborne dust was generally higher in the beryl ore extraction line relative to the bertrandite ore extraction line, possibly due to the higher beryllium content of beryl feedstock. Interestingly, the fraction of beryllium in airborne dust was higher in the beryl ore extraction line compared to the solvent extraction line, despite enrichment of beryllium during processing in the solvent extraction plant. One possible explanation for this observation is that beryl ore processing involves potentially dusty processes such as crushing and milling, whereas the solvent extraction line involves wet processes such as filtering. Further analysis of MOUDI samples revealed that the fraction of beryllium in dust was approximately independent of particle size in the bertrandite wet grinding and beryl melting work areas. For example, in the wet grinding work area the fractions were 0.51, 0.07, 0.57, 0.60, 0.67, 0.70, 0.59, 0.42, 0.24, and 0.34% for the inlet, stages 1 to 8, and the final filter of the MOUDI sampler, respectively. The fraction of beryllium in dust was approximately proportional to particle size in the bertrandite ore crushing, beryl ore crushing, A-product filtration, B-hydrolysis, B-product filtration, and product drumming work areas. In the beryl ore crushing work area, the fractions were 2, 2.2, 1.7, 1.5, 1.4, 1.3, 1.3, 0.2, 0.1, and 0.1% for the inlet through final filter of the MOUDI sampler, respectively. In contrast, the fraction of beryllium in dust was approximately inversely proportional to particle size in fritting, heat treating, beryl grinding, and sulfation. For example, in the beryl fritting work area the fractions were 0.3, 0.2, 0.1, 0.1, 0.1, 0.2, 0.6, 1.2, 3.8, and 6.4% for the inlet through final filter of the MOUDI sampler, respectively. The beryllium content of aerosol particles observed at this mill facility were fourfold lower than previously reported for aerosols generated during primary production of beryllium metal powder, oxide powder, and copper beryllium alloy ingots. Stefaniak et al. (2004) collected aerosol particles from 5 different work areas in a primary production facility that were associated with high risk of CBD and reported that beryllium content of particles ranged from 1.5 (beryllium metal production) to 30.5% (beryllium oxide production).

### *Particle Size*

Beryllium MMAD values were generally nonrespirable (i.e., $D_{50}$ greater than 4 μm) among work areas engaged in mechanical activities requiring low energy such as ore crushing and product drumming. Thorat et al. (2003) also observed large particle sizes (MMADs up to 9 μm) in work areas engaged in crushing of sintered ore and in product powder handling. In contrast, airborne beryllium particle MMAD values were respirable (i.e., aerodynamic diameter <10 μm with $D_{50}$ of 4 μm; Lippmann, 1999) in work areas engaged in high-energy activities such as heating and milling.

### *Health Implications*

In regard to the hazard potential of aerosols generated during milling of beryllium silicate ores, it is interesting to speculate on the role of exposure material characteristics in risk of sensitization and disease in the context of our solubility hypothesis (Stefaniak et al., 2003). Note that this hypothesis only addresses the exposure material component of exposure factors (which also include time, exposure intensity, etc.) and does not account for host factors (genetic susceptibility etc.). The exposure material component includes: (1) physical properties, e.g., aerosol particle size, which influences respiratory tract deposition; (2) chemical properties, e.g., bulk and surface chemistry, which influences chemical dissolution rate; and (3) physicochemical properties that may be a factor when both the physical and chemical properties are intertwined, which potentially influences the synergy of the physical and chemical properties. Under this solubility hypothesis, development of beryllium sensitization among workers employed exclusively at this milling facility may be influenced, at least in part, by the rate of beryllium released from inhaled particles with both a high beryllium mass fraction determined from the cassette and/or MOUDI samplers (Table 1) and respirable mass fraction calculated from the MOUDI data (Table 2) such as might be encountered in the melting, fritting, heat treating, grinding, and sulfation work areas. In addition to particle size, the chemical form of airborne beryllium generated during milling may be an important consideration for development of sensitization (e.g., silicate, oxide, salt; see later discussion). According to Wegner et al. (2000), beryllium in silicate dusts generated during grinding of beryl gemstones may become bioavailable, as evidenced by measurable levels of beryllium in urine among gem cutters. The apparently low prevalence of CBD among workers employed exclusively at this milling facility may be attributed, in part, to the dilute beryllium content and/or low respirable mass fraction of airborne particles in many work areas. Despite some work processes that generate a small respirable mass fraction capable of depositing in the alveolar region of the lung, these particles contain little beryllium relative to aerosols encountered during primary production (Stefaniak et al., 2004) and may not have the ability to dissolve at a rate sufficient to sustain inflammation over a long period of time. Those particles with a high beryllium mass fraction and high respirable mass fraction may be sufficient to provoke the beryllium immune response, but have poor capacity to sustain inflammation for a period long enough to support formation of granulomas, owing to their potentially short dissolution lifetime.

## Process-Sampled Particles

### *Physical Characteristics*

Measured particle densities were generally consistent within work areas. Additionally, beryllium hydroxide samples had a measured density of 1.91 ± 0.01 g/cm$^3$, consistent with a known density of 1.92 g/cm$^3$. With the exception of dusts sampled from the beryl ore crusher, SSA estimates were generally consistent with the expected relationship of increasing SSA with decreasing particle size (for smooth compact spherical particles, $SSA = 6/\rho D$, where $\rho$ is the particle density and $D$ the particle diameter). The SSA values of particles collected from the beryl ore crusher were independent of particle aerodynamic diameters, not unexpected given the observed highly variable particle morphologies (Figures 3a and 3b) and variable crystalline chemical compositions (described below). Among all work areas, SSA values tended to decrease as production proceeded from ore crushing to melting to heat-treating to grinding to product drumming, consistent with the progressive homogenization of particle morphology from flakes with high-SSA submicrometer-size primary particles attached to the surface to smooth plate-like particles (Figure 3).

Measured SSA values for aerosol particles generated during milling of beryl ore were less than or equal to the SSA values of particles and powders encountered in primary production work areas associated with high risk of beryllium sensitization and CBD (Stefaniak et al., 2003). Note that estimates of surface area by gas adsorption are not chemical specific; therefore, with the exception of pure beryllium hydroxide powder final product, the beryllium-specific fraction of the total particle surface area of the other aerosols is unknown but likely less than 100% based on their relatively low beryllium content. To determine whether beryllium was present on the surfaces of these particles would require chemical-specific analyses. For example, Stefaniak et al. (2006) used high-resolution x-ray photoelectron spectroscopy (XPS) to determine the chemical composition and relative percent abundance of elements on the surfaces of finished product beryllium metal powder, finished product oxide powder, and aerosol particles sampled from an arc furnace used to make copper-beryllium alloy. The surface layer of the beryllium oxide powder was exclusively oxide and the surface of the metal powder was a mixture of beryllium metal and oxide, whereas the surface of arc furnace particles was beryllium oxide and copper(II) oxide. Additional analyses using atomic spectroscopy coupled with the XPS data revealed that beryllium oxide was enriched by a factor of 2 to 3 on the surfaces of the arc furnace fume, depending on the particle size. In the context of our solubility hypothesis, the lung-compartment-specific rate of production of dissolved beryllium from particles would be limited, in part, by the chemical form of beryllium and the physical accessibility of beryllium to biologic fluids. The accessibility of beryllium to biological fluids is dictated, in part, by whether the surfaces of process-generated aerosol particles contain beryllium or whether the beryllium needs to diffuse from the particle core to the surface or by the relative dissolution rates of non-beryllium particle chemical constituents. Concomitantly, the apparently low prevalence of CBD among workers employed exclusively at this milling facility may be attributed, in part, to the presence of airborne particles that contain low levels of beryllium in poorly soluble chemical forms and/or low particle surface areas or to the presence of airborne particles that contain low levels of beryllium in highly soluble forms and/or low particle surface areas. Either exposure regime might yield a beryllium dissolution rate and lifetime profile with poor capacity to sustain inflammation for periods of time sufficient for development of inflammation and formation of granulomas.

### *Chemical Composition*

Relative to the Blue Chalk and Monitor pit ore powders, Wagner et al. (1969) reported similar non-beryllium phases for the bertrandite ore used in their animal studies, but the bertrandite content of their ore material was 3% by weight. Using ICP–mass spectroscopy, the beryllium content of the Blue Chalk and Monitor pit ore materials was 0.2% by weight, which is consistent with the average mass fraction of beryllium in bertrandite ore feedstock processed at this mill (Stonehouse, 1986). No information on the form of this beryllium (crystalline versus amorphous) could be gained from the analysis. X-ray diffraction analysis is well suited for identification of beryllium in heterogeneous samples (Stefaniak et al., 2004); however, this technique cannot detect beryllium in amorphous forms and is not well suited for identification of trace levels of beryllium in industrial samples (analytical LOD ~1% by weight). Thus, for samples characterized by XRD such as the Blue Chalk and Monitor bulk powders for which beryllium was not identified, our analyses cannot exclude the possibility that beryllium is present in an amorphous chemical form or in a crystalline chemical form at trace levels. Aerosol cyclone samples could not be collected from processes that either contained corrosive acids (e.g., beryl sulfation) or were performed wet (e.g., solvent extraction plant). As such, the chemical forms of beryllium aerosols in these work areas remain unknown.

Beryllium particle dissolution is a process that depends, in part, on the physicochemical properties of the exposure material, including SSA and bulk and surface chemistry (Stefaniak et al., 2003, 2004, 2006). Using XRD analysis, beryllium was definitively identified in three crystalline forms at this milling facility: beryl (ore crusher, melting), poorly crystalline BeO (heat treating, grinding), and beryllium hydroxide (product drumming). Beryllium may also exist in a fourth chemical form at this facility because the feedstock Blue Chalk and Monitor bulk powders ostensibly contain beryllium in the form of bertrandite; however, bertrandite contents of powders were below the analytical limit of detection for XRD. Exposure to beryllium-containing dusts generated during gemstone cutting and ore milling is associated with development of sensitization and apparently low prevalence of CBD (Wegner et al., 2000; Deubner et al., 2001). Exposure to highly crystalline BeO is associated with development of sensitization and CBD among beryllium primary production workers (Kreiss et al., 1997) and ceramics machinists (Henneberger et al., 2001). The apparently low prevalence of CBD among workers employed exclusively at this milling facility might be attributed, at least in part, to the chemical form of beryllium in aerosols, i.e., silicate-associated beryllium with dissolution rate having poor capacity to sustain inflammation over sufficiently long periods of time necessary to develop disease. Regarding the presence of BeO in this milling facility, it is known that “low-fired” BeO formed at 500°C dissolves 3 times more quickly than “high-fired” BeO formed at 1000°C (Finch et al., 1988). Thus, if the poorly crystalline BeO formed during heat treating at <1000°C dissolves at a faster rate than well-defined crystalline BeO encountered during primary production (Stefaniak et al., 2004, 2006), then the relatively shorter dissolution lifetime may not be sufficient to sustain inflammation for a long enough period of time to support formation of granulomas. The hazard potential of beryllium hydroxide for development of beryllium sensitization and CBD remains undefined. Thus, while apparently low, it needs to be emphasized that the real prevalence of CBD among workers exposed to beryllium during gemstone cutting and ore milling is unknown and may be much higher than previously reported (Wegner et al., 2000; Deubner et al., 2001) due to factors such as weakness of study design (i.e., cross-sectional), low study participation rates among workers in these studies, and unknown medical status of sensitized workers who declined follow-up clinical evaluation. Despite the uncertainty regarding disease status of these occupational cohorts, our exposure characteristics data in the context of a solubility model for sensitization and disease provide a potentially useful working hypothesis for understanding risk.

Rouleau et al. (2005) reported that identification of beryllium-containing particles by electron microscopy in heterogeneous industrial particle samples may be problematic when beryllium is present in trace levels. Similar difficulty was experienced in the analysis of process-sampled particles from many work areas at this beryllium ore mill. For example, using TEM-EDS the chemical composition of particles collected in stage 2 of the aerosol cyclone during beryl ore crushing was highly variable. The particle shown in Figure 3a was rich in Ca, Mg, O, and C with small spherical particles of amorphous silicon dioxide ($SiO_2$) attached, while the particles shown in Figure 3b were clusters of pure amorphous $SiO_2$ primary particles. Among all particles analyzed in this beryl crushing sample, only one particle, an assembly of crystalline and amorphous material, had a TEM-SAD pattern that contained crystalline lattice spacing consistent with beryl, but with a slightly enlarged unit cell (data not shown).

## CONCLUSIONS

The physical, chemical, and physicochemical components of airborne exposure material may influence risk of sensitization and CBD among beryllium-exposed workers. In the context of a solubility hypothesis, development of beryllium sensitization and CBD among workers employed exclusively at this milling facility may be influenced by physical factors (size, surface area) of airborne particles, chemical factors (form and content) of beryllium in particles, and physicochemical factors (properties that depend on the interaction of these physical and chemical properties) that influence the rate at which beryllium dissolves via chemical dissolution and becomes available to interact with the immune system. The observed complexity of beryllium-containing particle physicochemical properties encountered at this facility supports the need for detailed characterization of workplace aerosols to identify biologically relevant metrics of exposure for use in exposure assessment, toxicology, immunology, and epidemiology studies and to improve understanding of risk.

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