

Characterization of Respiratory Exposures at a Microwave Popcorn Plant with Cases of Bronchiolitis Obliterans

Greg Kullman, Randy Boylstein, William Jones, Chris Piacitelli, Stephanie Pendergrass, and Kathleen Kreiss

National Institute for Occupational Safety and Health (NIOSH), Morgantown, West Virginia

Eight former workers from a microwave popcorn packaging plant were reported to have severe obstructive lung disease consistent with bronchiolitis obliterans. Investigations into respiratory exposures at this plant were done during August through November of 2000. Samples were collected to assess airborne particulate concentrations, particle size distributions, endotoxins, oxides of nitrogen, organic gases and vapors, and other analytes. Bulk corn and flavoring components were also analyzed for endotoxins and culturable bacteria and fungi. Workers in the microwave production areas of the plant were exposed to particulates and a range of organic vapors from flavorings. The particles were comprised largely of salt and oil/grease particles. Respirable dust concentrations (area plus personal) in the microwave mixer job category, the highest job exposure category in the plant, ranged from 0.13 milligrams per cubic meter of air (mg/m³) to a high of 0.77 mg/m³. Endotoxin concentrations were below 60 endotoxin units per cubic meter of air (EU/m³). Qualitative sampling for volatile organic compounds (VOCs) in the air detected over 100 different VOCs in the microwave area. The predominant compounds identified in the microwave mixing room included the ketones diacetyl, methyl ethyl ketone, acetoin, and 2-nonanone, and acetic acid. Diacetyl, the predominant ketone in the plant, was present in concentrations ranging from below detectable limits to 98 parts per million parts air by volume (ppm), with a mean of 8.1 ppm (standard deviation 18.5 ppm). The average ketone concentrations were highest in the microwave mixing room where the 10 area samples had a mean diacetyl concentration of 37.8 ppm (SD 27.6 ppm) and a mean acetoin concentration of 3.9 ppm (SD 4.3 ppm). These data show that workers involved in microwave popcorn packaging can be exposed to a complex mixture of VOCs from flavoring ingredients; animal studies show that diacetyl can cause airway epithelial injury, although the contributions of other specific compound(s) associated with obstructive respiratory disease in these workers is still unresolved.

Keywords artificial butter flavoring, bronchiolitis obliterans, diacetyl, ketones

In May 2000, eight former workers from a factory that packages microwave popcorn were reported to the Missouri Department of Health by an occupational medicine physician to have bronchiolitis obliterans, a severe lung disease characterized by fixed airflow obstruction. Four of these workers were placed on a lung transplant list. Clinical investigation of the 117 current plant workers (87% response) showed similar airways disease.⁽¹⁾ The current plant workers had 2.6 times the expected rates of chronic cough and shortness of breath. Overall, current plant workers had 3.3 times the rate of obstructive spirometry abnormalities, 10.8 times the national expected rate in “never smokers.” The first known case of bronchiolitis obliterans at this plant occurred in 1993, but cases only came to public health attention in May of 2000; these cases had onset of cough, shortness of breath, and wheezing 5 months to 9 years after starting work at the plant with a median employment duration of 2 years.⁽²⁾

Recognized risk factors for bronchiolitis obliterans include exposures to nitrogen dioxide and other oxides of nitrogen from agricultural settings (silo fillers lung).⁽³⁾ Bronchiolitis has also been reported from exposures to other strongly irritating substances such as ammonia, chlorine, hydrogen fluoride, hydrogen sulfide, phosgene, and sulfur dioxide.^(3,4) Many of these reports associate this respiratory disease with acute exposure incidents or spills involving strongly irritating inorganic vapors or gases. One report describes a case of bronchiolitis obliterans associated with exposures to overheated vegetable cooking oil.⁽⁵⁾ McConnell and Hartle report severe fixed airways obstruction, consistent with bronchiolitis obliterans, among employees in a mixing room that produced flavorings for the baking industry.⁽⁶⁾ The workers at this microwave popcorn plant were involved in the mixing of flavoring ingredients for microwave popcorn, in work on the microwave popcorn filling lines, or in quality control operations. On the basis of the initial case reports, we studied the respiratory exposures at this plant. In conjunction with medical studies, environmental surveys were conducted at the plant between August and November

Address correspondence to: Greg Kullman, NIOSH, 1095 Willowdale Rd., Morgantown, WV 26505; e-mail: gkj1@cdc.gov.

of 2000. Exposure control recommendations and respiratory protection program assistance were initially provided and continued as the longitudinal respiratory health study progressed at this plant.

BACKGROUND

The plant in this study has been in operation since 1983 and employs approximately 135 workers who package popcorn for both national and international distribution under private label. The plant produces packaged popcorn kernels and since 1986, microwave popcorn. Background discussions describe the plant in November of 2000 and do not reflect current exposure control changes. Whole kernel corn is obtained largely from Missouri and Nebraska, and three to four hybrid varieties are processed. The popcorn arrives by truck and is unloaded by gravity. An organophosphate insecticide is applied, and the corn is transferred by conveyor to plant silos. The corn is typically stored in the silos for 2 months or less prior to processing. From the silo, the corn is screened and then air-cleaned on a gravity table. One worker (outside processing job category) oversees this operation. Following this processing,

the popcorn is sent to either the microwave packaging area or the polyethylene packaging area.

In the polyethylene area, the corn is mechanically packaged in polyethylene bags with no flavorings or food additives. Typically, three workers (packers and stackers) operate the polyethylene line with one supervisor present. There is one polyethylene packaging line at this plant and it is typically operated daily. After packaging, the bags are boxed, stacked, wrapped in plastic, and transported to the warehouse by forklift.

A majority of the corn processed at this plant is packaged in the microwave packaging area, which encompasses a mixing room and packaging lines to produce microwave bags containing popcorn and flavorings. The flavoring ingredients include soybean oil, salt, butter flavorings, and coloring agents. The flavoring agents are batch mixed in the mixing room (Figure 1), which opens onto a large room with seven packaging lines (Figure 2). The mixing room has a salt dump station that augers salt into a heated tank of soybean oil (approximately 135 to 140°F) to which other flavorings are added by raising the lid. Typically, one worker, a mixer, operates the mixing room. Following mixing, the flavorings mixture is piped as a liquid to holding tanks above the microwave popcorn packaging lines.



FIGURE 1. Microwave mixing room



FIGURE 2. Microwave packaging lines

These tanks are maintained at a temperature above 108°F to keep the flavorings mixture from solidifying. On the line operations, the popcorn and flavorings are automatically added to the popcorn bags by a Bartelt machine; one worker on each line, the machine operator, oversees this process. After the popcorn and flavorings have been added on each line, the bags of popcorn are sealed, labeled, and automatically enclosed in a plastic wrap on the packaging line. The bags of popcorn are next placed into boxes for distribution to market. Two different packaging stations are operated on each line, and small boxes are placed in larger boxes. Approximately three workers per line complete the packaging operations. Following packaging, the boxes of microwave popcorn are stacked on pallets and enclosed in a cold plastic wrap. One worker is typically involved in stacking operations for one or two of the seven lines. The microwave area typically operates three shifts per day and 5 days or more per week depending on the season.

After the boxes of popcorn are stack-wrapped on pallets, they are transported to a large warehouse by workers operating forklifts. These workers also load the product onto trucks from the warehouse loading dock. The plant has quality control operations for both the microwave popcorn and polyethylene products. Maintenance personnel keep the lines operating. Management and clerical workers are located in an office physically removed from the microwave packaging area.

METHODS

Industrial hygiene sampling was done to measure contaminants generated by the production of popcorn and microwave popcorn with both full-shift, personal and area samples, and for some gases, partial shift and grab samples. We collected samples and made process observations during three separate visits: a preliminary walkthrough survey, a qualitative environmental survey, and a cross-sectional industrial hygiene survey.

The walkthrough survey (August 2000) provided the opportunity to become familiar with the plant processes and materials and to assess potential process contaminants for later evaluation. During the subsequent environmental survey (September 2000), we conducted area sampling for airborne total dusts, total endotoxins, and organic vapors. We collected bulk samples of corn and soybean oil for microbiological analysis. The sampling results from this survey helped to refine the potential analytes for the subsequent quantitative industrial hygiene survey conducted in November of 2000. The cross-sectional industrial hygiene survey included personal sampling for respirable dusts and qualitative organic vapors in air. We conducted area air sampling for a number of analytes including total and respirable dusts (both high and low volume sampling), particle size distributions, endotoxins, volatile

organic compounds (VOCs) in air, ketones (diacetyl, acetoin, 2-nonanone, and methyl ethyl ketone), acetaldehyde, acetic acid, and inorganic gases. Culturable fungi and bacteria were measured in several bulk materials and we measured air temperature and relative humidity. Special emphasis was placed on quantifying exposures generated by or unique to the microwave production areas, consistent with patterns of fixed airways obstruction observed among plant workers. The industrial hygiene sampling methods are presented in Table I.^(7–14)

RESULTS

Particulate Matter

Total dust concentrations (full-shift, time-weighted averages [TWAs]) from the 55 area samples ranged from below detectable concentrations ($<0.007 \text{ mg/m}^3$) to a high of 1.0 mg/m^3 , with a mean concentration of 0.24 mg/m^3 (SD 0.19 mg/m^3) as seen in Table II. Total dust concentrations were highest in the

microwave mixing area as contrasted to other plant locations or jobs (Figure 3). Scanning electron microscopic evaluation of airborne samples, collected when the lid of a holding tank was lifted, suggested the presence of salt and oil particles in plant air (Figures 4a and 4b). The noncombustible fraction of five high-volume airborne total dust samples ranged from approximately 15 to 30% by weight (average 21%). Microscopic examination of the noncombustible fraction showed generally higher salt content in the mixing room samples. Scanning electron micrographs of the salt used in the microwave popcorn flavoring mixture suggest that much of the salt has a physical diameter below 10 micrometers and, consequently, would contain a substantial respirable fraction (Figure 4a). The 140 TWA respirable dust samples had a mean of 0.13 mg/m^3 with a SD 0.11 mg/m^3 . Respirable dust samples included both personal and area measures; although these groups (personal and area) had similar means and standard deviations (Table II). The average total and respirable dust concentrations were highest in the

TABLE I. Industrial Hygiene Sampling Methods

Analytes	Media/Sampler	Flow (L/min)	Analytical Methods
Total dust in air	37-mm PVC filter, open face filter cassette	3.0	Gravimetric analysis by <i>NIOSH Manual of Analytical Methods</i> (NMAM), Method 0500 (NIOSH, 2003) ⁽⁷⁾
Respirable dust in air	37-mm PVC filter, BGI [®] Cyclone	4.2	Gravimetric analysis by NMAM Method 0600 (NIOSH, 2003) ⁽⁷⁾
High volume total dust	37-mm PVC filter, open face filter cassette	28.2	Filter ashing and gravimetric analysis (NIOSH, 2003) ⁽⁷⁾
Total endotoxin in air	37-mm PVC filter, open face filter cassette	3.0	Kinetic <i>Limulus</i> amebocyte lysate test (BioWhittaker: Kinetic-QCL, <i>Limulus Amebocyte Lysate 192 Test Kit</i> , 2000) ⁽⁸⁾
Particle size distributions in air	Six-stage cascade impactor	2.0	Gravimetric analysis (NIOSH, 2003; Hinds, 1982) ^(7,9)
Airborne particles	37-mm polycarbonate filter, open face or glass slide	2.0	Analysis by light and scanning electron microscopy ^(10,11)
VOCs in air	Thermal desorption tube	0.03 to 0.05	Gas chromatography/mass spectrometry by NMAM Method 2549 (NIOSH, 2003) ⁽⁷⁾
	Photoionization meter	—	Direct-reading instrument (ACGIH, 1995) ⁽¹²⁾
Ketone compounds in air	Anasorb [®] CMS tube	0.03	Gas chromatography by NMAM Methods 2557, 2558, and 2553 (NIOSH, 2003) ⁽⁷⁾
Acetaldehyde in air	Sorbent tube (silica gel treated with 2,4 dinitrophenylhydrazine)	0.025	High performance liquid chromatography by NMAM method 2016 (NIOSH, 2003) ⁽⁷⁾
Acetic acid in air	Long-term diffusion tubes	—	Direct-reading results by colorimetric methods (ACGIH, 1995; Lechnitz, 1989) ^(12,13)
Inorganic gases in air	Short-term indicator tube	—	Direct-reading results by colorimetric methods (ACGIH, 1995; Lechnitz, 1989) ^(12,13)
Culturable fungi and bacteria in corn and soybean oil	Nutrient agar	—	Enumeration of bacteria and fungi by dilution plating (ACGIH, 1999) ⁽¹⁴⁾
Air temperature and percent relative humidity	Psychrometer	—	Direct-reading meter (ACGIH, 1995) ⁽¹²⁾

TABLE II. Total and Respirable Dust Concentrations in Air

Analyte	No. Samples	Mean (mg/m ³)	SD	GM (mg/m ³)	GSD	Min (mg/m ³)	Max (mg/m ³)
Total dust (area samples)	55	0.24	0.19	0.18	2.40	ND	1.0
Respirable dust (personal and area samples)	140	0.13	0.11	0.10	2.23	ND	0.76
Personal samples	84	0.13	0.10	0.11	1.80	ND	0.78

Notes: SD = standard deviation; GM = geometric mean; GSD = geometric standard deviation; ND = below the minimum detectable concentration in air, approximately 0.007 mg/m³.

microwave areas (Figure 3), with the highest mean concentration in the mixing room. In mixing, the mean respirable dust concentration of seven personal samples was 0.38 mg/m³ (SD 0.22 mg/m³).

Particle size distributions from cascade impactors in the microwave mixing room were predominantly unimodal, with mass median aerodynamic diameters (MMADs) ranging from 2.3 to 5 μ m. The nine particle size distributions from the locations, including microwave machine operators, packers, and stackers, had a MMAD of 2.5 or less; most of the samples appeared unimodal (Figure 5). The polyethylene packaging lines and the warehouse had larger particle size distributions with MMADs ranging from 5 to 8.5 μ m.

The endotoxin concentration from the microwave mixing room air was 56 EU/m³. The concentration from the Line 1 machine operator location was 58 EU/m³ and from the Line 1 packaging area, 26 EU/m³. Fungi and bacteria were below detectable limits (<2 CFU/mL) in the bulk sample of soybean oil; fungi and bacteria were also below detectable limits (<7 CFU/gram) in the bulk samples of popcorn obtained from line operations following air cleaning processes. While some spores were detected by light and scanning microscopy

analysis of plant air samples, they were not common. Review of company sampling records for aflatoxin in bulk corn (year 2000) indicated that the samples were all below detectable limits when analyzed by thin layer chromatography.

Ketones and Other Organic Compounds

Qualitative sampling for VOCs in the air indicated that over 100 different compounds were present in the microwave processing area (Figure 6); the predominant compounds identified in the microwave mixing room included the ketones diacetyl, methyl ethyl ketone (MEK), acetoin, and 2-nonanone, and acetic acid. The 53 area samples for diacetyl ranged from below detectable limits (approximately 0.01 ppm) to 98 ppm, with a mean of 8.1 ppm (SD 18.5 ppm) as seen in Table III. Acetoin concentrations were lower with a mean of 0.92 ppm (SD 2.33 ppm). Only 3 of the 53 2-nonanone samples had quantifiable levels with the highest concentration being 0.06 ppm. The two samples analyzed for MEK had concentrations of 3.1 and 4.7 ppm. The average ketone concentrations were highest in the microwave mixing room (Figure 7), where the 10 area samples had a mean diacetyl concentration of 37.8 ppm (SD 27.6 ppm) and a mean acetoin concentration of 3.9 ppm

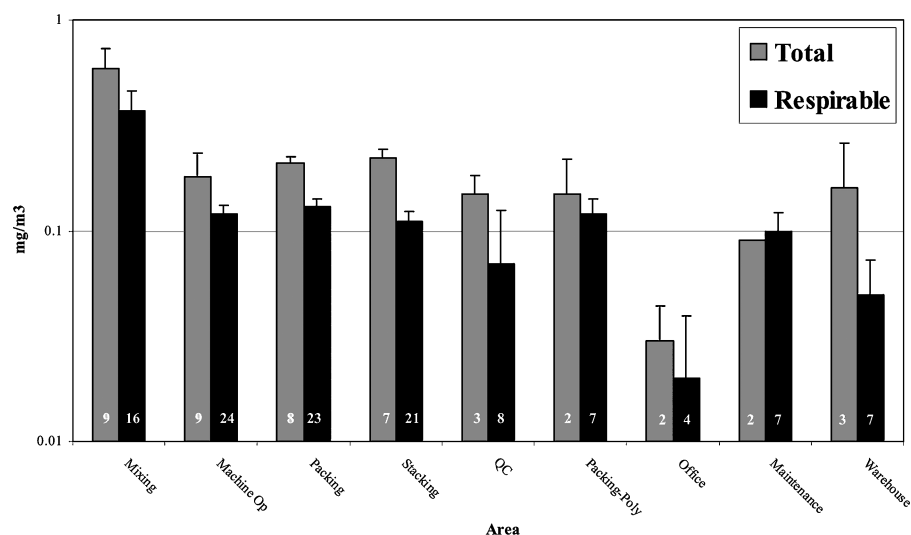
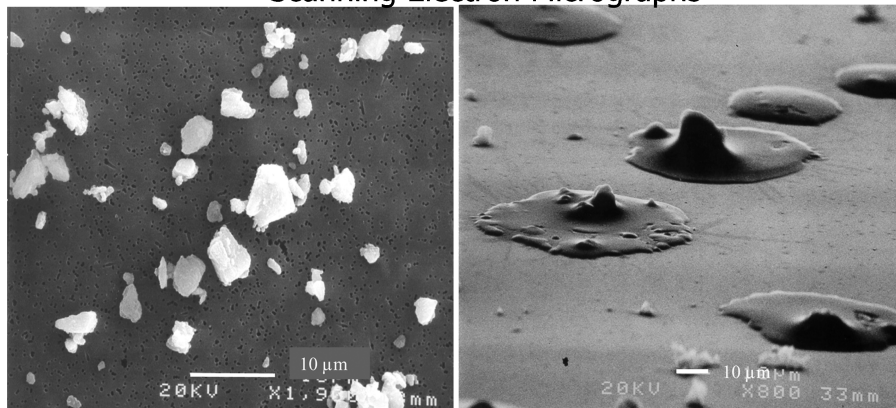


FIGURE 3. Total and respirable dust concentrations by area. Error bars provide the 95% confidence interval

Scanning Electron Micrographs



a) Salt Particles

b) Salt & Oil Particles

FIGURE 4. Microscopy of airborne particles

(SD 4.3 ppm). Diacetyl was also detected in areas outside of microwave production, including the polyethylene line area, warehouse, and office areas; however, most of the samples from these locations were below quantifiable levels (Table IV). Analysis of total organic vapors using a direct reading photoionization meter showed that mixing operations with flavorings were the primary point source for the release of volatile

organic gases and vapors into plant air. The microwave bag filling operations were not considered a significant point source for organic vapors including diacetyl; photoionization meter readings taken next to the bag filling injection ports for the butter flavoring and oil mixtures were no different from background levels measured throughout the packaging area.

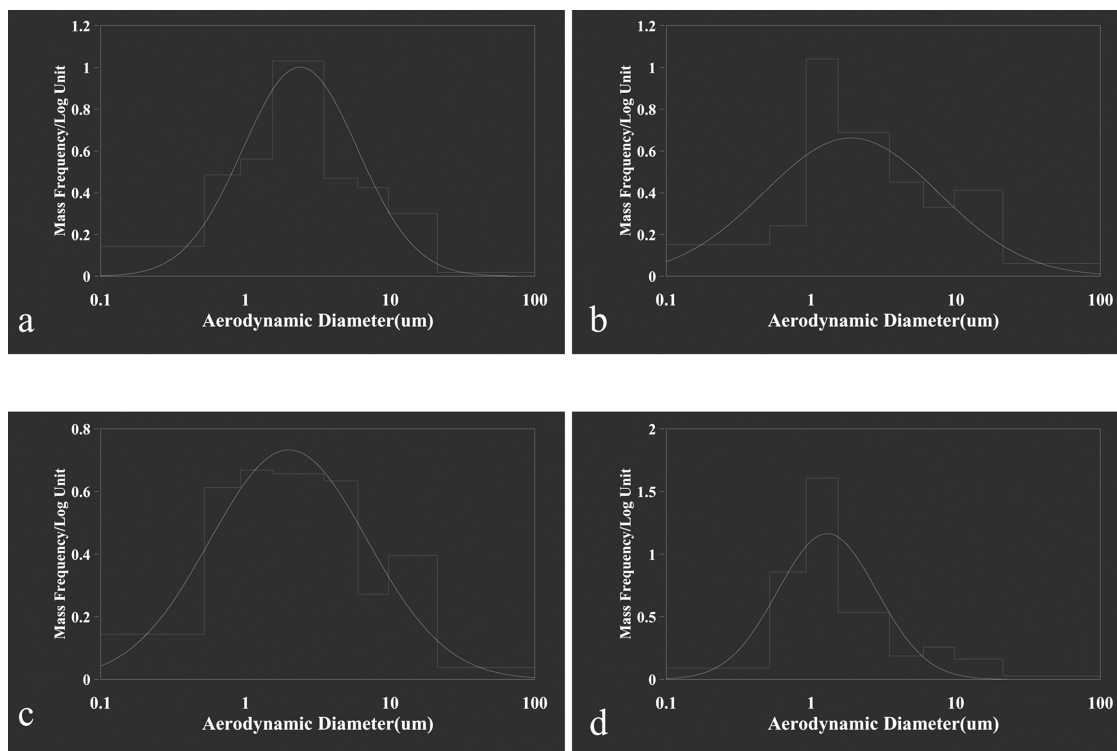


FIGURE 5. Particle size distributions from (a) microwave mixing, (b) microwave machine operators, (c) microwave packaging, and (d) microwave stacking

TABLE III. Ketone Area Concentrations in Air

Analyte	No. Samples	Mean (ppm)	SD	GM (ppm)	GSD	Min (ppm)	Max (ppm)
Diacetyl	53	8.1	18.5	0.71	14.4	ND	98
Acetoin	53	0.92	2.33	0.10	7.93	ND	12
2-Nonanone	53	Only three samples with quantifiable levels; the high concentration was 0.06 ppm.					
Methyl ethyl ketone	2	3.87	1.12	3.79	1.34	3.08	4.66

Notes: SD = standard deviation; GM = geometric mean; GSD = geometric standard deviation; ND = below the minimum detectable concentration in air, approximately 0.01 ppm for diacetyl and 0.02 ppm for acetoin.

Acetic acid was detected in air samples from the microwave mixing, packaging, maintenance, and quality control areas. The airborne TWA acetic acid concentrations from 49 samples (all area samples) ranged from below detectable limits (<0.04 ppm) to a high of 12.4 ppm, with a mean concentration of 1.4 ppm (SD 2.3 ppm). The highest acetic acid concentrations were measured in the mixing area, with a mean of 5.5 ppm (SD 3.2 ppm) from eight samples. In the microwave packaging area, 24 samples had a mean of 2.7 ppm (SD 2.7). Acetaldehyde concentrations were low, ranging from below detectable limits (approximately 0.007 ppm) to 0.1 ppm.

Inorganic Gases

Short-term indicator tube samples were taken to measure airborne concentrations of several inorganic gases including ammonia (0.25 to 3.0 ppm), formaldehyde (0.2 to 2.5 ppm), hydrochloric acid (1.0 to 10 ppm), nitrogen dioxide (0.5 to 10 ppm), oxides of nitrogen (0.5 to 10 ppm), and nitric acid (1.0 to 15 ppm). Three to seven samples were collected for each gas from the mixing room, upper deck holding tank area, and machine operators' workstation. All samples for these gases were below detectable limits as noted by the measurement ranges in parentheses following each gas.

Ventilation

The seven microwave packaging lines were located in an open, two-story room approximately 80 ft × 150 ft. The general dilution ventilation for this area included three large axial exhaust fans located on the south wall of the microwave packaging area. These fans were not routinely operated during the winter or when ambient temperatures were low. In the summer of 1999, a local exhaust ventilation system was added to the microwave mixing room to control dust emissions from salt dumping operations and this system was operated during salt dumping (less than approximately 30 min per shift). At this same time, roof air intake systems were also added to the microwave packaging area; however, like the wall exhaust fans, these outside air intakes were not operated during the winter. In consequence, the microwave packaging areas and mixing room had no mechanical ventilation during winter operating conditions in November of 2000.

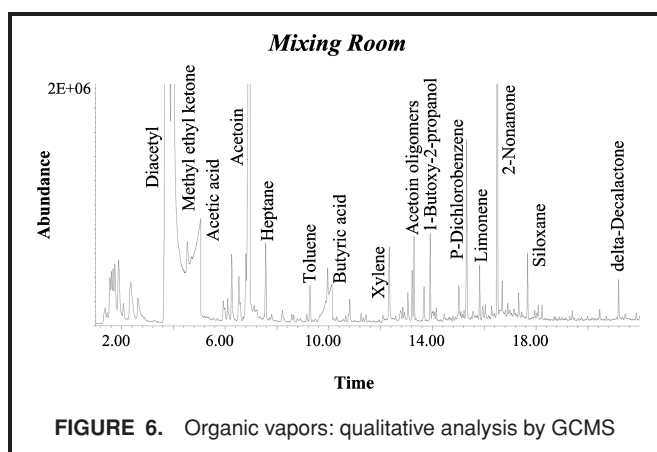
DISCUSSION

Current and former workers from this microwave popcorn packaging plant were found to have severe obstructive lung disease consistent with bronchiolitis obliterans.⁽¹⁾ Industrial

TABLE IV. Diacetyl Area Concentrations in Air

Area	N	Mean (ppm)	SD	GM (ppm)	GSD	Min (ppm)	Max (ppm)
Mixing	10	37.8	27.6	26.0	3.03	2.3	98.0
Machine op (micro)	9	1.68	1.61	1.15	2.589	0.26	5.53
Packing (micro)	6	2.05	1.69	1.59	2.22	0.44	5.32
Stacking (micro)	7	1.98	2.24	1.322	2.46	0.54	6.8
QC	3	0.54	0.30	0.49	1.69	0.33	0.89
Bag printing	1	ND	—	ND	—	ND	ND
Poly line packing	2	0.04	0.05	0.03	4.18	ND	0.07
Warehouse	3	0.09	0.14	0.04	5.35	ND	0.25
Maintenance	2	0.60	0.27	0.57	1.6	0.41	0.79
Office	2	0.02	0.011	0.02	1.952	ND	0.03
Outside processing	3	ND	—	ND	1	ND	ND

Notes: SD = standard deviation; GM = geometric mean; GSD = geometric standard deviation; ND = below the minimum detectable concentration in air, approximately 0.01 ppm for diacetyl.

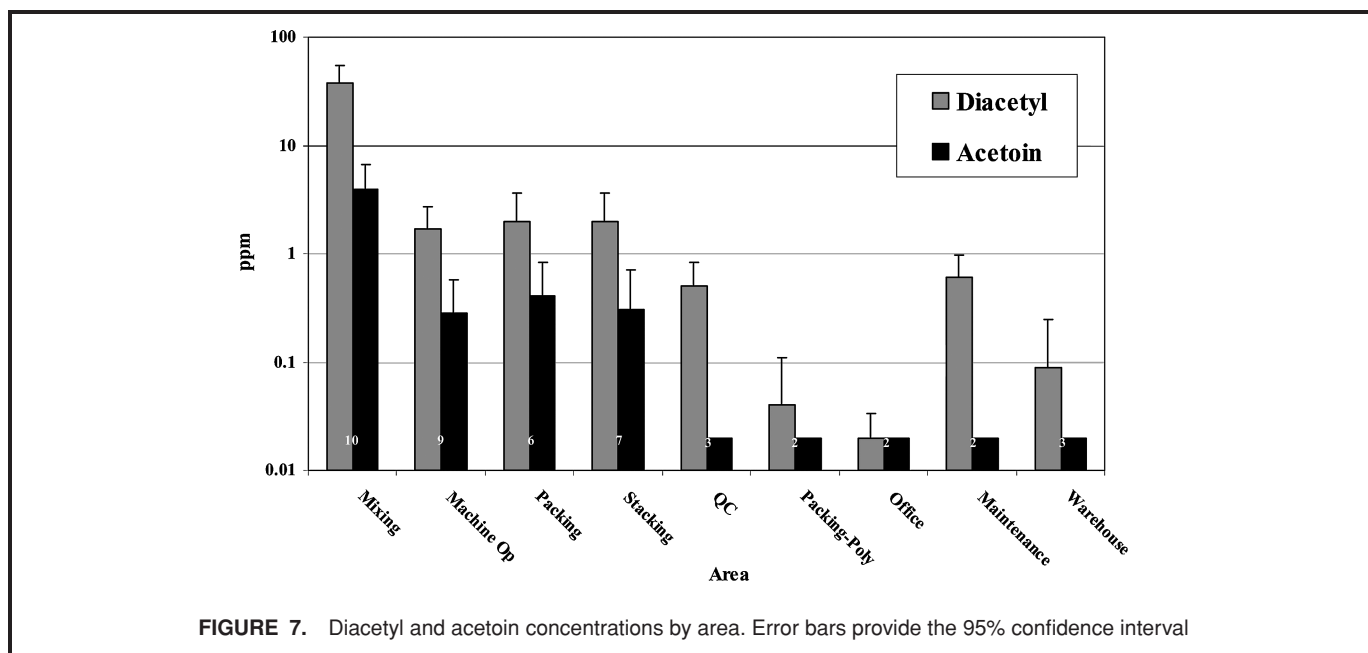


hygiene characterization of this plant suggests no obvious over-exposures, by current occupational exposure guidelines or standards, as a likely etiology. Grain dusts, associated bio-aerosols, and organophosphate insecticides are recognized exposure hazards for workers handling grain products such as popcorn; however, these agents are not recognized as risk factors for bronchiolitis obliterans.^(3,15) The mean respirable and total dust concentrations by job category at this plant were all below 0.6 mg/m³ and comprised predominantly of salt and oil/grease particles in microwave popcorn areas. Exposures to oxides of nitrogen or other strongly irritating compounds previously associated with bronchiolitis obliterans were not detected at this popcorn plant. Acute worker exposures to spills of strongly irritating compounds were also not reported by workers. Other recognized causes of bronchiolitis obliterans include sulfur dioxide, ammonia, chlorine, trichloroethylene, phosgene, chloropicrin, ozone, cadmium oxide, hydrogen fluoride, zinc powder, asbestos, and sheet silicates; however,

these were not significant exposures for microwave popcorn workers/mixers at this plant. Prior to this study, there were no reports of bronchiolitis obliterans or fixed airways obstruction among workers involved in microwave popcorn production.⁽¹⁾

A significant finding from this survey was the complex spectra of VOCs associated with the microwave areas and, specifically, flavor mixing operations. These organic compounds were largely generated by heated artificial butter flavorings. The primary popcorn flavoring ingredients (soybean oil, salt, butter flavorings, and coloring agents) were heated to temperatures up to approximately 135°F during mixing operations. Hand mixing, open transfer of materials, heating, and spillage provided the opportunity for volatilization of organic compounds from flavoring agents into plant air and subsequent worker exposures. The flavor mixing and holding tanks lacked exhaust ventilation and airtight lids. Work processes often required workers to lift the lid to add ingredients or check tank contents. Through these activities, mixing in the microwave mixing room was the primary point source for the release of VOCs into plant air, as contrasted to the line bag filling/packaging operations. Mixing operations from the oil/flavor holding tanks on the mezzanine level (above the packaging lines) were also exposure point sources for microwave popcorn workers at this plant. Additionally, during winter operating conditions, the plant had almost no ventilation to dilute or remove these air contaminants, thereby increasing the potential for worker exposures.

Ketones (including diacetyl and acetoin) were predominant among the VOCs generated from flavor mixing operations at this plant. Diacetyl is a common synthetic flavoring agent and adjuvant used in the food industry. It is extremely irritating to skin, eyes, mucous membranes, and the respiratory tract.^(16,17) Diacetyl concentrations (all area samples) ranged



from below detectable concentrations (approximately 0.01 ppm) to a high of 98 ppm. The highest ketone concentrations were found in the microwave mixing room where the mean diacetyl concentration was 37.8 ppm (SD 27.6 ppm). Workers with obstructive respiratory disease were seen in several job categories besides mixers, such as machine operators and packer/stacker job categories, where mean diacetyl exposures averaged approximately 1.7 to 2.0 ppm. Currently there are no National Institute for Occupational Safety and Health (NIOSH), Occupational Safety and Health Administration (OSHA), or American Conference of Governmental Industrial Hygienists (ACGIH[®]) occupational exposure standards or guidelines for diacetyl, acetoin, or nonanone.^(18–20) The MEK concentrations in plant air (mean 3.8 ppm, SD 1.1 ppm) were well below the existing OSHA permissible exposure limit (PEL) for MEK, 200 ppm. Acetic acid concentrations in plant air had a mean of 1.4 ppm (SD 2.3 ppm). One of the 49 acetic acid samples exceeded the OSHA PEL, NIOSH recommended exposure limit, and the ACGIH threshold limit values (TLVs[®]), all 10 ppm as a TWA; this sample was from the microwave mixing room. Acetaldehyde was also present in plant air but concentrations were all below 0.1 ppm and less than the OSHA PEL of 200 ppm as a TWA or the ACGIH TLV, 25 ppm as a short-term exposure limit.^(18–20) Other compounds were detected in mixing room air including heptane, butyric acid, toluene, p-dichlorobenzene, limonene, delta-decalactone, and others; however, these compounds were not quantified in our initial cross-sectional survey at this plant.

While there have been no previously reported cases of bronchiolitis obliterans associated with the production of microwave popcorn, McConnell and Hartle report severe fixed airways obstruction, consistent with bronchiolitis obliterans, among two nonsmoking, previously healthy employees in a mixing room that produced flavorings for the baking industry.⁽⁶⁾ These workers mixed batches of liquid and powdered flavoring ingredients to produce a variety of baking flavors including a Cinna Butter product. Acetic acid, diacetyl, and ethyl acetate were among ingredients used at this plant; however, the specific etiology was not identified. Recent animal exposure studies conducted at NIOSH further show that diacetyl, and other VOCs from butter flavorings, are etiologic agents for the fixed airways disease in these microwave popcorn workers.^(21,22) Rats exposed to vapors liberated from heated butter flavoring for 6 hours by inhalation, and necropsied 1 day after exposure, were found to have necrosis of the nasal, bronchial, and bronchiolar epithelium.⁽²¹⁾ Subsequent exposure of Sprague-Dawley rats for 6 hours to diacetyl alone (concentrations of approximately 198 ppm or higher) produced significant necrosis of the nasal and tracheal epithelium with associated neutrophilic inflammation.⁽²²⁾ Diacetyl was a predominant organic constituent in the flavorings used at this popcorn facility and exposures to the air concentrations identified in this paper likely put workers in the microwave popcorn production areas at risk for the development of fixed obstructive airways disease.

CONCLUSIONS

Severe obstructive lung disease consistent with bronchiolitis obliterans was seen in both former and current workers involved in the packaging of microwave popcorn. Plant workers were not exposed to any previously recognized risk factors for bronchiolitis obliterans. Worker exposures included a complex mix of VOCs. The predominant compounds identified included the ketones diacetyl, acetoin, MEK, 2-nonanone, and acetic acid. The presence of these compounds in plant air was likely increased through the heating of oil and flavorings mixtures. Diacetyl was the predominant VOC identified in plant air and the average ketone concentrations were highest in the microwave mixing room, as were most other plant exposures. Collectively, these VOCs and specifically diacetyl are likely etiologic agents in the fixed airways disease seen among these workers, although the contribution of specific VOCs, other than diacetyl in disease etiology is still unresolved. Longitudinal medical and environmental follow-up study, with cooperation of plant management, is under way to provide a foundation for prevention in this industry.

Recommendations provided to reduce worker exposures to VOCs associated with the production of microwave popcorn include:

1. Use closed processes to transfer flavorings and eliminate flavor spillage.
2. Reduce mixing and holding tank temperatures for butter flavorings and mixtures. To the extent possible, work with nonheated flavorings.
3. Install local exhaust ventilation in the mixing room and on flavor holding/mixing tanks.
4. Physically isolate the mixing room (and all flavor holding tanks) from other plant operations and maintain this area on a separate ventilation system under negative pressure.
5. Provide general dilution ventilation to plant packaging areas.
6. Minimize the time workers spend in the mixing room.
7. Substitute flavorings that generate lower emissions of VOCs and diacetyl.
8. Use respiratory protection, especially for mixing operations, in accordance with a formal respiratory protection program. (Respirators should be equipped with NIOSH-approved P-100 type filters and cartridges for protection against organic vapors.)
9. Use skin and eye protection when handling volatile flavorings.
10. Educate workers regarding the hazards associated with exposure to plant operations involving exposure to flavorings.

ACKNOWLEDGMENTS

The authors acknowledge Thomas Jefferson and Ardith Grote of NIOSH for their contributions to this manuscript, and

the Missouri Department of Health plus company management and workers for supporting this study.

REFERENCES

1. **Kreiss, K., A. Goma, G. Kullman, K. Fedan, E. Simoes, and P. Enright:** Clinical bronchiolitis obliterans in workers at a microwave-popcorn plant. *New Engl. J. Med.* 347:330–338 (2002).
2. **Akpinar-Elci, M., W.D. Travis, D.A. Lynch, and K. Kreiss:** Bronchiolitis obliterans syndrome in popcorn production plant workers. *Eur. Respir. J.* 24:298–302 (2004).
3. **King, T.E.:** Bronchiolitis. In *Fishman's Pulmonary Diseases and Disorders*. A.P. Fishman, J.A. Elan, J.A. Fishman, M.A. Grippi, L.R. Kaiser, and R.M. Senior (eds.). New York: McGraw-Hill, 1998. pp. 825–847.
4. **Arora, N., and T. Aldrich:** Bronchiolitis obliterans from a burning automobile. *South. Med. J.* 73:507–510 (1980).
5. **Simpson, F.G., P.W. Belfield, and N.J. Cooke:** Chronic airflow limitation after inhalation of overheated cooking oil fumes. *Postgrad. Med. J.* 61:1001–1002 (1985).
6. **National Institute of Occupational Safety and Health (NIOSH):** *Health Hazard Evaluation and Technical Assistance Report: International Bakers Services, Inc., South Bend, Indiana* (Pub. No. 85-171-1710). Cincinnati, Ohio: DHHS (NIOSH), 1986.
7. **NIOSH:** In *Manual of Analytical Methods (NMAM)*, 4th ed., Third Supplement. P.C. Schlecht and P.F. O'Connor (eds.). Cincinnati, OH: Department of Health and Human Services, Public Health Service, Center for Disease Control and Prevention, National Institute for Occupational Safety and Health. DHHS (NIOSH) Publication No. 2003-154. (2003).
8. **BioWhittaker:** *Kinetic-QCL, Limulus Amebocyte Lysate 192 Test Kit* (Catalog No. 50-650U). Walkersville, Md.: BioWhittaker, 2000.
9. **Hinds, W.C.:** *Aerosol Technology*. New York: John Wiley & Sons, Inc., 1982. pp. 1–314.
10. **McCrone, W.C.:** Particle characterization by PLM. *Microscope* 30:185–206 (1982).
11. **Bozzola, J.J., and L.D. Russel:** *Electron Microscopy: Principles and Techniques for Biologists*. Boston: Jones and Bartlett Publishers, 1992. pp. 40–62 and 184–213.
12. **American Conference of Governmental Industrial Hygienists (ACGIH):** *Air Sampling Instruments for Evaluation of Atmospheric Contaminants*, 8th ed. Cincinnati, Ohio: ACGIH, 1995.
13. **Leichnitz, K.:** *Detector Tube Handbook*, 6th Edition. Lubeck, Germany: Draeger Werk AG, 1989. pp. 1–49.
14. **American Conference of Governmental Industrial Hygienists (ACGIH):** *Bioaerosols: Assessment and Control*. Cincinnati, Ohio: ACGIH, 1999. pp. 11–1–11–25.
15. **May, J.J., and M.B. Schenker:** Agriculture. In *Occupational and Environmental Respiratory Diseases*. P. Harber, M.B. Schenker, and J.R. Balmes (eds.). New York: Mosby, 1996. pp. 615–636.
16. **Technical Resources, Inc.:** 2,3 Butanedione (CAS No. 431-03-8). Rockville, Md.: Technical Resources, Inc., 1994.
17. **Lewis, R.J.:** 2,3 Butanedione. In *Hazardous Chemicals Desk Reference*, 3rd Edition. New York: Van Nostrand Reinhold, 1993. pp. 202–203.
18. **Occupational Safety and Health Administration (OSHA):** “Air contaminants,” *Code of Federal Regulations* Title 29, Part 1910.1000. 2002.
19. **National Institute for Occupational Safety and Health (NIOSH):** *NIOSH Recommendations for Occupational Safety and Health* (Pub. No. 92-100). Cincinnati, Ohio: DHHS (NIOSH), 1992. pp. 1–198.
20. **American Conference of Governmental Industrial Hygienists (ACGIH):** *Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices*. Cincinnati, Ohio: ACGIH, 2002. pp. 1–100.
21. **Hubbs, A.F., L.A. Battelli, W.T. Goldsmith, et al.:** Necrosis of nasal and airway epithelium in rats inhaling vapors of artificial butter flavoring. *Toxicol. Appl. Pharmacol.* 185:128–135 (2002).
22. **Hubbs, A.F., L.A. Battelli, R.R. Mercer, et al.:** Inhalation toxicity of the flavoring agent, diacetyl (2,3-Butanedione), in the upper respiratory tract of rats. *The Toxicologist* 78 (Number S-1), (March 2004).