NIOSH HEALTH HAZARD EVALUATION REPORT

HETA #2006-0195-3044
Yatsko's Popcorn
Sand Coulee, Montana

April 2007

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

National Institute for Occupational Safety and Health

PREFACE

The Respiratory Disease Hazard Evaluations and Technical Assistance Program (RDHETAP) of the National Institute for Occupational Safety and Health (NIOSH) conducts field investigations of possible health hazards in the workplace. These investigations are conducted under the authority of Section 20(a)(6) of the Occupational Safety and Health (OSH) Act of 1970, 29 U.S.C. 669(a)(6), or Section 501(a)(11) of the Federal Mine Safety and Health Act of 1977, 30 U.S.C. 951(a)(11), which authorizes the Secretary of Health and Human Services, following a written request from any employers or authorized representative of employees, to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found.

RDHETAP also provides, upon request, technical and consultative assistance to federal, state, and local agencies; labor; industry; and other groups or individuals to control occupational health hazards and to prevent related trauma and disease. Mention of company names or products does not constitute endorsement by NIOSH.

ACKNOWLEDGMENTS AND AVAILABILITY OF REPORT

This report was prepared by Greg Kullman, PhD, CIH, and Nancy Sahakian, MD, MPH, of the RDHETAP, Division of Respiratory Disease Studies (DRDS). The industrial hygiene field survey was done by Greg Kullman, PhD, CIH, and Thomas Jefferson. Analytical support was provided by the NIOSH Division of Applied Research and Technology, NIOSH Health Effects Laboratory Division, and Clayton Group Services, Inc. Graphical support was provided by Nicole Edwards. Desktop publishing was performed by Richard Farley.

For the purpose of informing affected employees, copies of this report shall be posted by the employer in a prominent place accessible to the employees for a period of 30 calendar days.

Highlights of the NIOSH Health Hazard Evaluation of Yatsko's Popcorn

After NIOSH identified a risk for lung disease in workers exposed to airborne butter flavoring chemicals at microwave popcorn plants, the owners of a small popcorn popping plant were concerned about the possibility of similar risks associated with the use of artificial flavorings at their plant.

What NIOSH Did

- We measured the air concentrations of flavoring chemicals at this popcorn popping plant.
- We analyzed bulk flavoring materials for the types of chemicals released on heating.
- We obtained and reviewed medical records for the three workers (two former and one current) at this plant and interviewed two of those same workers and the spouse of the third worker.

What NIOSH Found

- Diacetyl (a butter flavoring chemical known to cause injury to airways in animal studies) was present in work area air samples at levels too low to measure, less than 0.01 parts per million parts of air (ppm). A peak concentration of 0.14 ppm was measured in the air directly above a heated container of butter-flavored oil.
- Aldehydes were the predominant class of volatile organic compounds identified in plant air.
- Some of the airborne dust from powdered flavorings was small enough that it could be inhaled into the lung. Dust exposures were higher during popcorn bagging activities than during other activities; and on the day when powdered flavorings were used than on the day when powdered flavorings were not used.
- Three workers developed respiratory disease while working at the plant.
  - One worker had airways obstruction with clinical characteristics of asthma and possible bronchiolitis obliterans.
  - One worker had symptoms suggestive of asthma and radiographic evidence suggestive of bronchiolitis obliterans.
  - One worker had symptoms of asthma and a clinical test result suggestive of asthma.

What Managers Can Do

This plant closed its popcorn production operations in May 2006. If the plant reopens, we suggest the following:

- Use engineering controls to decrease exposures to flavoring chemicals.
- Provide closed containers for the handling and storage of flavoring chemicals and assure that good housekeeping procedures are followed.
- Train workers on the potential health risks from exposures to flavorings and on the best ways to minimize exposures.
- Until the production processes are engineered to reduce exposures, assure that workers wear NIOSH-approved respirators for dust and organic vapors as part of a formal respiratory protection program.
- Perform regularly scheduled spirometry tests for all workers, beginning at hire and repeated at least every 6 months.

What Employees Can Do

- Know how to properly wear and maintain your respirator and use it during all popcorn production operations.
- Keep all containers of flavorings tightly closed when not in use.
- Be aware of health risks from exposure to flavorings and ways to minimize exposure.
- Participate in spirometry tests offered by your employer.
- Promptly report any persistent, recurrent, or severe shortness of breath or cough, or problems with your eyes, nose, throat, or skin to your supervisor and your doctor and show them a copy of this page.

What To Do For More Information:

We encourage you to read the full report. If you would like a copy, either ask your health and safety representative to make you a copy or call 1-800-232-2114 and ask for HETA Report # 2006-0195-3044

NIOSH

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SUMMARY

In March 2006, NIOSH received a request for a Health Hazard Evaluation (HHE) from owners of Yatsko's Popcorn, a small popcorn popping plant, located in Sand Coulee, Montana. The company had originally operated out of a smaller building from 1979 to 1999, when the operation was moved to the current location. The occupational exposure concerns cited in this request included flavoring chemicals from popcorn production activities; reported health concerns included breathing problems, shortness of breath, wheezing, tightness in the chest, and skin disorders. This request was based on health concerns following NIOSH investigations of fixed obstructive lung disease consistent with bronchiolitis obliterans in microwave popcorn plant workers associated with exposure to butter flavorings.

We conducted an industrial hygiene survey at the popcorn popping plant on April 12 and 13, 2006. Air samples were collected for total and respirable particles, particle size distributions, volatile organic compounds, total hydrocarbons, ketones (diacetyl, acetoin, and 2-nonanone), inorganic acids, and acetaldehyde. Bulk samples of flavoring ingredients were collected and analyzed for the emission of volatile organic compounds (VOCs) on heating. We reviewed medical records for two former workers and one current worker and we interviewed two workers and the spouse of the other worker. In May 2006, subsequent to our survey, the plant closed its operation. The main findings from this HHE include:

- At this plant, popcorn was popped and bagged; powdered cheese and jalapeno pepper flavorings were manually applied to some of the popped popcorn. Popping and bagging operations were done approximately twice a week for 2 to 4 hours per day depending on orders.
- Popping was done in a small building with a wall exhaust fan; the worker wore a disposable dust mask during popping; however, this was not a NIOSH-approved respirator.
- Diacetyl was detected by gas chromatography with mass spectroscopy (GCMS) in vapors released from a bulk sample of flavored oil heated to 50°C in an analytical laboratory, although it was not a predominant volatile organic compound released from the oil.
- Diacetyl was also detected by GCMS in two- and four-hour area air samples. Concentrations were too low to be detected (less than approximately 0.01 parts per million (ppm) in four-hour personal and area air samples by NIOSH method 2257). Using a direct-reading instrument, a peak diacetyl concentration of 0.14 ppm was measured in the air directly above a heated container of butter-flavored oil.
- Aldehydes were the predominant type of VOC identified in area air samples. However, acetaldehyde concentrations were less than the detectable (0.09 ppm) or quantifiable (0.15 ppm) concentrations.
- Average area particle concentrations in air using gravimetric analysis were 2.72 milligrams per cubic meter of air (mg/m^3) for total particles and 0.89 mg/m^3 for respirable particles. Particle concentrations were higher during popcorn bagging activities than during other activities; particle concentrations were also higher on the day that powdered flavorings were applied to the popcorn than on the day when powdered flavorings were not used.

- Airborne exposures of this popcorn popping operation included lower diacetyl concentrations and more aldehyde compounds than was observed in microwave popcorn production.
- All three workers who worked at the company developed respiratory disease while working there. One former worker, who had only worked at the original smaller plant and who eventually died as a result of his respiratory disease, had airways obstruction that improved with a bronchodilator, which is consistent with asthma. Two other workers who had worked at both the original smaller plant and the current plant had symptoms of asthma; one of these had pulmonary function test results that improved significantly with a bronchodilator, which also is consistent with asthma. Some evidence suggests possible bronchiolitis obliterans in the worker who died and in one of the other two workers. While employed at the plant, all three workers experienced worsening of their respiratory symptoms the days they worked.

NIOSH investigators found that aldehydes were the predominant type of volatile organic compound identified in air samples at the plant. Diacetyl was present in the air of the plant with a concentration too low to be quantified. Average area particle concentrations in air using gravimetric analysis were 2.72 mg/m^3 for total particles and 0.89 mg/m^3 for respirable particles. All three workers who worked at the plant developed respiratory symptoms while working there and had worsening of respiratory symptoms on days worked. Evidence from medical records and radiographs of these three individuals was consistent with asthma in all three workers and suggestive of possible bronchiolitis obliterans in two of the workers.

Keywords: NAICS 311911 [Other Snack Food Manufacturing], popcorn, flavorings, respiratory health, bronchiolitis obliterans, asthma, and diacetyl.

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INTRODUCTION

In March 2006, the National Institute for Occupational Safety and Health (NIOSH) received a request for a Health Hazard Evaluation (HHE) from the owners of Yatsko's Popcorn, a small popcorn popping company, in Sand Coulee, Montana. The exposure concerns cited in this request included diacetyl and other butter flavorings from popcorn popping operations. The reported health concerns included breathing and respiratory problems, shortness of breath, wheezing, chest tightness, and skin disorders. NIOSH investigators conducted an industrial hygiene survey at the popcorn popping plant on April 12 and 13, 2006. In addition, medical records of all three workers who had been employed at the company—two former workers and one current worker—were obtained for review and two of these three workers and the spouse of the third (deceased) worker were interviewed. In May 2006, the plant was closed by decision of the owners. This HHE report presents findings and recommendations of the NIOSH investigators.

BACKGROUND

In August 2000, NIOSH learned that eight former workers of a microwave popcorn production plant in Missouri had moderate to severe fixed obstructive airways lung disease consistent with bronchiolitis obliterans, an uncommon illness. A NIOSH investigation at this plant revealed an excess prevalence of airways obstruction on spirometry testing among current workers. Increasing cumulative exposure to diacetyl, the predominant butter flavoring chemical present in the air of the plant, was associated with an increased prevalence of abnormal lung function.[1,2,3] In animal experiments conducted by NIOSH, rats exposed to vapors from a butter flavoring used at this plant, or to diacetyl alone, developed severe injury to their airways.[4,5] After investigating several other plants and finding further evidence that workers who are occupationally exposed to flavorings are at risk for fixed obstructive airways diseases NIOSH disseminated an ALERT to raise awareness of the inhalation risk posed by flavorings chemicals and to provide preventive recommendations.[3] The request for the current HHE was made after the owners of the company contacted NIOSH to report several cases of obstructive lung disease among workers at the plant.

Description of the Production Processes and Exposure Controls of the Popcorn Popping Plant

Popcorn production at this plant was typically done by one worker per work shift; occasionally, the work would be done by two workers on the same shift. A normal work shift lasted only 2 to 4 hours, and occurred only 1 to 2 days per week depending on the number of popcorn orders received. If necessary, an additional shift would be worked to produce whatever additional popcorn was needed to fill orders in any given week.

This popcorn popping plant consisted of a one-room building approximately 20 by 32 feet with a 10-foot ceiling (Figure 1). The corn was popped using poppers heated by an open propane flame; two poppers were operated concurrently throughout the work shift. A scoop (30 milliliter) of a butter-flavored salt (Flavacol™) was first added to one quart of popcorn and this corn / salt mixture was dumped into a popper pre-heated to approximately 177 degrees Celsius (°C) (i.e., 350 degrees Fahrenheit (°F)). Once the corn began popping, one cup of butter-flavored canola oil (Gregg's Ultrapop™) was added to the popper by hand from a glass measuring cup. This flavored oil was kept at a temperature of approximately 49°C (120°F) in a heated beverage dispenser without a lid (labeled "Oil" in Figure 1). After popping was completed, the worker would screen the popcorn to remove unpopped kernels and then pour the popped corn into a large paper bag. The worker would usually be standing to the side of the labeled "Seat" in Figure 1. For flavored popcorn, powdered flavorings were added to the popcorn as it was screened. At the time of our visit, three different flavorings were used, including cheddar cheese, white cheddar cheese, and jalapeno flavorings (Corn Treats™ brand). The flavorings were dispensed by hand onto the popcorn while it was still hot—approximately 127°C (260°F)—using a container with holes in the lid. After allowing 10-15 seconds for the popped corn to cool, the worker would move to the other side of the table and transfer the popped corn from the paper bag into 2 plastic bags which were then closed with ties. Visible clouds of airborne dust were observed both during the application of powdered flavorings and during the bagging operation. It would take approximately 5 minutes or less to pop and package one batch of popcorn. The bags of popcorn were then placed on a floor pallet located in the room and stored until delivery to regional customers. Popcorn production generally involved the production of popcorn using butter-flavored salt and butter-flavored oil early in the shift, then popcorn flavored with powdered cheese flavorings, and then popcorn flavored with powdered jalapeno flavoring at the very end of the shift.

An axial wall fan (Figure 1) was located on the wall next to the poppers and operated to exhaust air from the building continuously during popping operations. The three windows furthest away from the poppers were opened to provide outside makeup air. The worker wore a disposable dust mask during the production process. This was not a NIOSH-approved respirator and had no substrate to collect organic vapors generated by the popcorn popping processes.

The current building was used for popcorn production and packaging from 1999 until May 2006 when the operation was closed. From 1979 until 1999, the corn popping processes had been done in a smaller building (approximately 8 feet wide, 15 feet long, and 7 feet high). Openings to this former building included a front door and a rear window; a floor fan was generally used to exhaust air out the front door with the rear window open. The former building also had a small ceiling exhaust fan, approximately 9 inches in diameter, positioned over the poppers.

The flavorings used by this company have changed some since the company first began operation in 1979. In 1979, a solid butter-flavored coconut oil (Vo-Pop™) was used. Sometime prior to 1985, this was substituted with another solid butter-flavored coconut oil (Gregg's Popcorn Oil™); and in 1998, this was changed to a liquid butter-flavored canola oil (Gregg's Ultrapop™). Intermittently from 2004 to 2006, another liquid butter-flavored canola oil (Act II™) was used when the distributor for Gregg's Ultrapop™ was out of stock. Flavacol™ was used from 1979 to 2006; cheddar cheese powdered flavoring from 1988 to 2006; jalapeno powdered flavoring from 1991 to 2006; and white cheddar cheese powdered flavoring from 2003 to 2006. No accidental flavoring spills resulting in excessive exposures were known to have occurred.

METHODS

Industrial Hygiene

On April 12 and 13, 2006, we conducted industrial hygiene sampling to measure contaminants generated during corn popping, bagging, and flavoring operations at this plant. Time-weighted average (TWA) area air samples were collected for total and respirable particles, particle size distributions, volatile organic compounds, ketones (diacetyl, acetoin, and 2-nonanone), inorganic acids, and acetaldehyde. TWA personal air samples were also collected for diacetyl, acetoin, and 2-nonanone. (Note: These samples were collected over the full work shift, which was approximately 2 hours, or over two such full work shifts.)

Real-time diacetyl measurements were also taken using a fourier transform infrared (FTIR) gas analyzer [Gasmet DX-4010, Temet Instruments Oy, Helsinki, Finland]. A ppbRAE real-time volatile organic compound monitor was used to quantify real-time volatile organic compounds in air (RAE Systems, Inc., Sunnyvale, CA). Real-time respirable particle measurements were taken using a PersonalDataRAM, model pDR-1000An/1200 (Thermo Electron Corporation, Franklin, MA).

The area samples were collected at two different sampling locations as illustrated in Figure 1. Details on the industrial hygiene sampling methods used during this survey are provided in Table 1. Sampling results that were below detectable limits were assigned a value of one-half of the minimum detectable concentration in air for statistical analyses.

Bulk samples of flavoring ingredients collected at the plant were refrigerated until analyzed. In the laboratory, they were heated and the released vapors were analyzed for volatile organic compounds (VOCs). Approximately 25 to 50 mg of each liquid or powder sample was placed in a quartz tube and secured at both ends with glass wool. Each bulk sample was rapidly heated to 50°C or 180°C and held for 10 minutes in a thermal desorption system (Model 400 automatic thermal desorption system; PerkinElmer, Inc., Boston, Mass.). The thermal unit was interfaced directly to a gas chromatograph (GC, Model 6890A gas chromatograph; Agilent Technologies, Inc., Palo Alto, CA), with a mass selective detector (Model 5973 mass selective detector; Agilent Technologies, Inc.,) that was operated under normal electron impact conditions. A 30-meter, DB-1 fused silica capillary column was used in the GC to separate components. Compounds were then identified by mass spectrometry by matching fragmentation patterns of the individual peaks to library spectra (Wiley 275 mass spectral library software). The chromatograms resulting from the analyses recorded the relative (not absolute) abundance of each chemical detected vs. retention time.

A bulk sample of Flavacol™ was analyzed using a derivatization technique.[6] Diacetyl is a di-carbonyl compound (i.e., each molecule of diacetyl has two oxygen atoms that are double-bonded to carbon atoms). The derivitization technique utilized in this analysis converts carbonyl groups to oxime groups (i.e., nitrogen double-bonded to carbon). The oximes that are formed are more stable than underivatized diacetyl, and more easily analyzed by gas chromatography with mass spectroscopy. Three samples were prepared and analyzed: 1) Flavacol™ dissolved in water with derivatization agent; 2) Flavacol™ partially dissolved in acetonitrile with derivatization agent; and 3) Flavacol™ partially dissolved in methanol with derivatization agent.

Medical Interviews and Review of Medical Records

All 3 of the employees who had worked for this company developed work-related symptoms within 10 to 15 years of beginning to work for the company.

We obtained and reviewed medical records of these three workers, including two former employees (Employees A and B) and one current employee (Employee C). We also interviewed Employees B and C and the surviving spouse of Employee A. Medical records for Employee A consisted of Veterans Administration records and hospital records that included emergency department notes, hospital discharge summaries, and laboratory, radiology, and pulmonary test results. Medical records for Employees B and C consisted of relevant doctor's notes, consultative reports, and radiology and pulmonary test results.

We extracted from the medical records results for spirometry, plethysmography, diffusing capacity of the lungs for carbon monoxide (DLCO), arterial blood gases, and radiographic imaging of the chest. The digital images of the high resolution computed tomography (CT) of the chest had been destroyed for Employee A but were available for Employees B and C. We obtained copies of the CT images for Employees B and C and had them reviewed by a pulmonary radiologist. (Appendix A presents a general description of clinical tests done on these patients and general approaches to their interpretation.)

RESULTS

Industrial Hygiene

Emissions of Volatile Organic Compounds (VOCs) from Bulk Flavorings

Figures 2-A, 2-B, and 2-C provide semi-quantitative analysis of the VOCs released from bulk flavoring components heated to 50°C and/or 180°C. (Note: A temperature 180°C was used to approximate the temperature of the corn in the poppers prior to the addition of the preheated canola oil; a temperature of 50°C was used to approximate the temperature of the preheated canola oil from the dispenser).

VOCs released from the heated butter-flavored salt (Flavacol™) are shown in Figure 2-A. Predominant VOCs identified when this sample was heated to 50°C, ordered by predominance, included diethylphthalate, hexamethylcyclotrisiloxane, and dimethylphthalate. Predominant VOCs released from this sample heated to 180°C, ordered by predominance, included diethylphthalate, hexanal, 2-ethylhexanol, di-tert-butyl phenol, nonanal, and delta-decalactone. VOCs released from the heated butter-flavored corn popping oil (Gregg's Ultrapop™) had a more complex spectrum (Figure 2-B). Predominant VOCs identified when this sample was heated to 50°C, ordered by predominance, included propylene glycol, cyclohexane, nonanal, methyl propyl ketone, hexamethylcyclotrisiloxane, diethylphthalate, and styrene. Predominant VOCs identified in this sample heated to 180°C, ordered by predominance, included propylene glycol, tert-butyl hydroquinone, 2-tert-butylquinone, triacetin, diethylphthalate, delta-dodecalactone, and delta-decalactone.

Diacetyl was detected when the butter-flavored oil sample was heated to 50°C, although it was not one of the predominant VOCs released. Diacetyl was not detected in the butter-flavored oil sample heated to 180°C. Of the three powdered flavorings, heated jalapeno flavoring had greater emissions of VOCs than either cheddar or white cheddar cheese flavorings (Figure 2-C). The predominant VOCs released from the jalapeno powdered flavoring when heated to 50°C, ordered by predominance, included myristicin, cis-3-hexenyl isovalerate, propylene glycol, diethylphthalate, ethyl caprylate (octanote), ethyl caprate (decanoate), and sesquiterpene ($C_{15}H_{24}$).

Derivatization Analysis of Bulk Flavacol™ Sample

Using the derivatization technique, no diacetyl was identified in the bulk sample of butter-flavored salt (Flavacol™) dissolved or partially dissolved in water, acetonitrile, or methanol.

Volatile Organic Compounds (VOCs) in Air

Figures 3-A and 3-B provide semi-quantitative analysis of VOCs from two of the three area air samples collected during two days of sampling. Figure 3-A is the chromatogram for an area air sample collected on April 12, 2006, when no powdered flavorings were used. Figure 3-B is the chromatogram for an area air sample collected over two days of air sampling (April 12-13, 2006) including one day (April 13th) when powdered flavorings were used. (It should be noted that butter-flavored oil and butter-flavored salt were used on all sampling days.) The predominant VOCs identified in all three air samples are listed in Table 2 and include many different aldehydes: valeraldehyde, furfural, dimethylfurfural, hexanal, 2-heptenal, methyl furfural, octanal, nonanal, 2-decenal, and 5-(hydroxymethyl) furfural. Other predominant VOCs identified in air during popping operations included: seven-carbon (C-7) aliphatic hydrocarbons including heptane, propylene glycol, toluene, furfuryl alcohol, limonene, decamethylcyclopentasiloxane, t-butylcresol, alpha-terpineol, triacetin (glycerol triacetate), levoglusan, and diethylphthalate. Furfuryl alcohol and 5-(hydroxymethyl) furfural were identified only in the air samples which were collected both days, including the second day of production when the powdered flavorings were used. Diacetyl was detected in all three of these air samples, but it was a very small component of each sample.

Concentrations of total VOCs in air are presented in Table 3. Concentrations from the six samples ranged from 0.47 milligrams per cubic meter of air (mg/m^3) at sampling location #1 on the first day of sampling (when no powdered flavorings were used) to a high of 8.14 mg/m^3 at sampling location #2 on the second day of sampling (when powdered flavorings were used). The two-day VOC concentration from sampling location #2 (1.30 mg/m^3) seems unusually low by comparison to the concentrations from other samples in this same location, but no reason was identified to consider any of these samples invalid. VOC concentrations were approximately 60-165% higher on the second day of sampling compared to the first day of sampling. Figures 4-A and 4-B show real-time concentrations of VOCs collected from location #2 and reported in parts per billion parts of air units (ppb units). (Note: Since air samples contain many different VOCs, this is not a true ppb concentration but a general measure of total VOCs determined from calibration using an isobutylene standard.) Figure 4-A shows the concentrations of VOCs on April 12 (when powdered flavorings were not used), which ranged from a low of 46 ppb units to a high of 274 ppb units, with a mean concentration of 194 ppb units. Figure 4-B shows the concentrations of VOCs on April 13 (when powdered flavorings were used) were higher, ranging from a low of 158 ppb units to a high of 373 ppb units. The mean total VOC concentration for this second day was 243 ppb units, approximately 25% higher than for the first day of sampling.

Ketone Concentrations in Air

All ketone samples, including two personal and twelve area samples for diacetyl, acetoin, and 2-nonanone, were below detectable limits. For diacetyl and 2-nonanone, the minimum detectable concentration in air was approximately 0.02 parts per million parts of air by volume (ppm) for the 2-hour samples and approximately 0.01 ppm for the 4-hour (2-day) samples. For acetoin, the minimum detectable concentration in air was approximately 0.03 ppm for the 2-hour (1-day) samples and approximately 0.01 ppm for the 4-hour (2-day) samples.

The real-time measurements of diacetyl in workplace air by FTIR were also below detectable limits on both days of sampling. This included both area and personal breathing zone measurements during corn popping operations and during the application of powdered flavorings. A measurement taken directly above the heated, butter-flavored popping oil in the dispenser had a detectable diacetyl concentration of approximately 0.14 ppm measured over a one-minute time period.

Acetaldehyde Concentrations in Air

Seven of the eight acetaldehyde samples were below the minimum detectable concentration in air, approximately 0.09 ppm for the 2-hour samples and approximately 0.04 ppm for the 4-hour (2-day) samples. One (2-day) sample had a detectable concentration of acetaldehyde, but this concentration was below the minimum quantifiable concentration in air (approximately 0.15 ppm).

Inorganic Acid Concentrations in Air

Concentrations of hydrobromic acid, nitric acid, phosphoric acid, and sulfuric acid were all below detectable or quantifiable limits in air (less than approximately 0.05 ppm) in the six samples collected for each analyte. Hydrochloric acid was present at a concentration of 0.08 ppm in one sample and was below detectable or quantifiable limits in five other samples; hydrofluoric acid was present at 0.06 ppm in one sample and was below detectable or quantifiable limits in five other samples.

Particulate Concentrations in Air

Total and respirable Area concentrations of total and respirable particles in air are presented in Table 4 as time-weighted averages from gravimetric analyses. When inhaled, respirable particles (particles with an aerodynamic diameter of less than approximately 10 micrometers) can deposit in the gas exchange regions of the lung—the alveoli and respiratory bronchioles; in contrast, nonrespirable particles are deposited in the upper airways, including the nasal passages, and never reach the gas exchange regions.[7] Total particle concentrations ranged from 1.19 mg/m^3 to 4.52 mg/m^3. The mean total particle concentration was 2.72 mg/m^3 with a standard deviation of 1.24. Total particle concentrations were higher on the second day of sampling (when powdered flavorings were used). Respirable particle concentrations ranged from 0.56 mg/m^3 to a high of 1.11 mg/m^3. The mean respirable particle concentration was 0.89 mg/m^3 with a standard deviation of 0.19. The two-day respirable particle concentration from sampling location #1 (0.56 mg/m^3) seems unusually low by comparison to the concentrations from other samples in this same location, but no reason was identified to consider any of these samples invalid.

Real-time concentrations of respirable particles are presented in Figures 5-A and 5-B. These concentrations are reported in units of mg/m^3 as determined by optical measures (instead of gravimetric measures as reported above); consequently, they are not always equivalent to particle concentrations determined by gravimetric analysis. Figure 5-A provides sampling results from April 12 (when no powdered flavorings were used). Respirable particle concentrations ranged from 0.12 mg/m^3 to a high of 4.78 mg/m^3, with a mean of 3.25 mg/m^3. Figure 5-B shows the real-time respirable particle sampling results for April 13 (when powdered flavorings were used). Concentrations were higher this second day, ranging from 1.3 mg/m^3 to 6.3 mg/m^3, with a mean of 4.17 mg/m^3. The repeating peak concentrations evident in these figures occurred during bagging operations when the operator dumped popped corn from the paper bag (which had been used to receive screened popcorn) into the plastic bags.

<u>Particle size distributions</u> Figure 6 presents the aerodynamic size distribution of airborne particles by sampling date during corn popping operations. On April 12 (when no powdered flavorings were used), approximately 90% of the airborne particle mass was less than 10 micrometers in aerodynamic diameter (a size range that would be considered respirable) and approximately 75% of the airborne particle mass was less than 3.5 micrometers in aerodynamic diameter. On April 13 (when powdered flavorings were used), approximately 50% of the particles were less than 10 micrometers in aerodynamic diameter and approximately 30% was less than 3.5 micrometers in aerodynamic diameter. The two samples that were run concurrently both days had an intermediate distribution, with approximately 65% of airborne particulate mass less than 10 micrometers in aerodynamic diameter and 45% below 3.5 micrometers in aerodynamic diameter.

Air Temperature and Percent Relative Humidity

Room air temperatures ranged from 72°F (22°C) to 96°F (35°C) during the two days of sampling. The lowest temperature was measured at the start of production before the room had warmed. The highest temperature was measured at sampling location #2 near the poppers towards the end of the shift. Measured room temperatures were approximately 80°F (27°C) during most of the production shift. Relative humidity ranged from 19% to 35%.

Exposure Controls

An axial wall fan (twelve inches in diameter) was operated during popcorn production (Figure 1). This exhaust fan was located next to the corn poppers and operated at a flow rate of approximately 3,720 cubic feet per minute (CFM). The two windows across the room from the fan were opened during production while the window next to the fan was kept closed. A disposable dust mask was also used by the worker during popping; this was not a NIOSH-approved respirator.

<u>Medical Findings</u>

Employee A

Employee A was a lifetime nonsmoker who had a long history of atopic dermatitis (documented in medical records at least from 1956 to 1965), a father who had emphysema, and an uncle who had asthma. As a teenager, he worked part-time (four hours weekly during the winter months) for 3 years in a small family-owned coal mine. After serving in the Army for 2 years, he worked for 6 months as a construction helper, then for 2-3 years as a lineman assistant for the utility company, then for 5-6 years as a bottler in a brewery; and then for 5-6 years as a truck driver behind a grader on a county road crew that maintained unpaved roads. From 1963 to 1998, he worked part-time (7 hours weekly) in a bar. From 1979 to 1994, he worked part-time in the popcorn popping operation in the original smaller facility. In 1994, he retired from the popcorn popping operation due to respiratory problems.

In 1990, Employee A developed symptoms of intermittent shortness of breath, a loose non-productive cough, and wheeze which were worse when popping popcorn (symptoms persisted the remainder of the day after the work shift). He was treated for respiratory problems in the emergency department 23 times from 1991 to 1998 (11 times from 1991-1994 and 12 times from 1995-1998); 21 visits indicated wheeze on physical examination and 19 visits indicated treatment with an intravenous steroid and/or the initiation or increased dosage of oral prednisone. Metered-dose inhalers (short-acting beta-agonist and steroid) were begun in 1991; oral theophylline was added in 1993; a nebulized beta-agonist was added in 1995; metered-dose anti-inflammatory (nedocromil) and long-acting beta-agonist inhalers were added in 1996; theophylline and nedocromil were stopped and prophylactic antibiotic (trimethoprim/sulfamethoxazole) was begun in 1997; and a diuretic (furosemide) was begun in October 1998 for pre-tibial edema. He was hospitalized with admitting diagnoses of: asthma with exacerbation in May 1992; chronic obstructive pulmonary disease (COPD) with asthmatic bronchitis in April and September 1994; status asthmaticus in July 1995; exacerbation of COPD in October 1998; and status asthmaticus with acute respiratory failure in November 1998. During that November 1998 hospitalization, he died (in December 1998) at the age of 65; the hospital discharge summary listed "status asthmaticus with acute cardiopulmonary arrest" as the primary diagnosis. No autopsy was done.

Employee A's other medical problems included coronary artery disease for which coronary artery bypass surgery was done in August 1991. A coronary angiogram in June 1991 demonstrated a subtotal proximal occlusion of the left anterior descending coronary artery, and a thallium stress test in October 1991 demonstrated inferior ischemia. Symptoms during his June 1991 hospitalization included left upper chest and back pain that worsened with exertion and was relieved with rest. There were no clinical signs of heart failure, such as rales, pedal edema, cardiac murmur, or enlargement of the heart. During his August 1991 hospitalization his pre-operative chest x-ray was interpreted as having a slightly enlarged heart. However, an echocardiogram during his terminal hospitalization was reported as showing normal left and right ventricular size and function, and a normal ejection fraction (55-60%).

Spirometry results demonstrated a mixed pattern of airways obstruction and restriction. The airways obstruction was responsive to bronchodilator. However, the forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) levels did not normalize completely after the administration of bronchodilator, indicating the possibility that some of his airways obstruction was fixed (i.e. irreversible) (Table 5).

Lung volumes measured by plethysmography are available at two points in time, 1995 and 1998. In December 1995, when the results of a spirometry test were interpreted as obstruction with significant reversibility after bronchodilator, the total lung capacity (TLC) and residual volume (RV) were normal (TLC was 91% of predicted, RV was 118% of predicted) and the RV/TLC ratio was 43% (higher than the calculated predicted value of 33%). In June 1998, during pulmonary rehabilitation, the TLC was 76% of predicted (below the lower limit of normal), the RV was normal at 97% of predicted, the RV/TLV ratio was 42% (higher than the predicted value of 34%) (Table 6). The pulmonary function report interpreted the results of the spirometry and lung volumes as moderate obstructive airways disease with a marked bronchodilator response and also indicated that there was a restrictive process. Diffusing capacity for carbon monoxide (DLCO) corrected for hemoglobin, carboxyhemoglobin, and altitude was low at 67% of predicted (Table 7).

As early as May 1992, arterial blood gases while breathing room air indicated low oxygen content (hypoxemia) and low oxygen saturation of hemoglobin, despite slight hyperventilation indicated by a low partial pressure of carbon dioxide. Several blood gases in subsequent years also indicated hypoxemia.

Chest radiographs obtained from March 1991 and January 1994 were reported to show accentuation or borderline prominence of bronchovascular markings in the right lung. Chest radiographs obtained in September 1994, July 1995, and February 1997 were reported to show atelectasis or probable atelectasis in the right lung. A chest radiograph in December 1997 was reported to show a left lower lobe infiltrate. High resolution computed tomography of the chest without expiratory images in June 1998 were reported to show no evidence of interstitial lung disease; however, there was air trapping within the periphery of both segments of the middle lobe and the anterior segment of the upper lobe of the right lung (mosaic pattern) and bronchial wall thickening involving the bronchi of the right lung in both segments of the middle lobe and the superior segment of the lower lobe.

Employee B

Employee B is a former employee and lifetime nonsmoker who had a history of seasonal allergies and a family history of asthma. She worked at the original smaller popcorn popping building from 1985 to 1999 (14 years) and at the current building from 1999 to 2004 (5 years). Other employment included work as a hairdresser from 1977 to 2006. In 1994, she developed mild respiratory symptoms of chest heaviness and cough on days worked popping popcorn; symptoms progressively worsened until leaving this employment in 2004. Shortness of breath and chest tightness began from within one hour of the beginning of the shift to one hour after the end of the shift; and persisted for about 6-8 hours to 24 hours after the end of the shift. Respiratory symptoms were not noted to be associated with any specific chemical exposures in the plant. On July 7, 2004, her primary care physician documented expiratory wheeze on physical examination. While working in this operation, she also developed an itchy rash on the hands; there was no burning of the skin on contact with any specific chemical exposure in the plant. When working specifically with the powdered flavorings, she experienced dry, itchy eyes. This employee also reported mucus production during the work shift consistent with sinus drainage but did not report any throat or nasal irritation or excessive headaches during employment. After leaving this employment in September 2004, her respiratory symptoms improved despite continuing hairdressing work. Current symptoms include daily coughing, and wheezing with exposure to cold air; the skin rash resolved after one year of leaving popcorn popping employment.

Spirometry, phlethysmography, and DLCO were completed in August 2004. The pulmonologist's note at the time of these studies indicated that the patient noted some problems with the use of aerosol products in hairdressing. Spirometry revealed: FVC, 104% of predicted; FEV_1, 96% of predicted; FEF_{25-75}, 75% of predicted; and a FEV_1/FVC ratio of 76%. FVC, FEV_1, and FEV_1/FVC ratio were all above the lower limits of normal. FEV_1 improved by 6% and 170 milliliters and FEF_{25-75} increased by 19% following the administration of a bronchodilator. Plethysmography values were: TLC, 103% of predicted; RV, 98% of predicted; airways resistance, 322% of predicted; and a RV/TLV ratio of 33% (compared to a predicted value of 34%). The DLCO was 91% of predicted. Body mass index was 36.9. No methacholine challenge test was performed. These pulmonary functions were interpreted by the pulmonologist as showing some mild airways obstruction with improvement post-bronchodilator and thought to show an underlying component of mild airways hyper responsiveness secondary to asthma. In September 2004, the primary care physician prescribed albuterol for reactive airway symptoms, which helped lessen her respiratory symptoms. Albuterol was last prescribed in March 2006 and asthma medications are currently not being used.

High resolution computed tomography of the chest with inspiratory and expiratory images in June 2006 was interpreted as showing no evidence of lung disease. NIOSH investigators had the computed tomography reviewed by a pulmonary radiologist who identified moderate bronchial wall thickening, probable air trapping in the left lower lobe, and a mosaic pattern in the same lobe which was consistent with but not diagnostic of bronchiolitis obliterans. Other possible diagnoses would include asthma.

Employee C

Employee C is a lifetime nonsmoker who was working at the facility during the time of our survey. From 1972 until 1988, he had worked in a bakery. From 1972 until approximately 1980, he directly handled flour and was involved in mixing dough. During this time period, Employee C experienced symptoms such as itchy skin, sneezing, red eyes, coughing, and shortness of breath (which began during the evening hours on days worked). In 1980, this employee was evaluated for flour allergy and had a positive skin test for flour. When moved to the bread slicing section of the operation, all listed symptoms resolved.

Employee C worked at the original smaller popcorn popping facility from 1990 to 1999 (9 years) and at the current facility from 1999 to May 2006 (7 years) when the facility was closed. In 2000, he began experiencing mild chest tightness on days worked at the popcorn popping plant. Symptoms progressively worsened. By 2004, he was experiencing symptoms of chest tightness, coughing, wheezing, and shortness of breath on days worked; symptoms generally persisted for 1 to 2 days after working a shift. By 2006, symptoms were persisting 3 to 4 days after popping popcorn. Exposure to jalapeno powdered flavoring resulted in eye irritation, sneezing, and a running nose. Employee C developed an itchy rash on the thumb during the last year of employment at the popcorn popping plant. Three months after leaving this employment, his respiratory symptoms have improved, although he continues to have occasional chest tightness and wheezing; the skin rash has also persisted.

Spirometry, plethysmography, and DLCO were completed in March 2006. Spirometry revealed: FVC, 104% predicted; FEV_1, 96% of predicted; FEF_{25-75}, 85% of predicted; and a FEV_1/FVC ratio of 74%. FVC, FEV_1, and FEV_1/FVC ratio were all above the lower limits of normal. FEV_1 improved by 11% and 480 milliliters and FEF_{25-75} increased by 21% following the administration of a bronchodilator. Plethysmography values were: RV, 150% of predicted; TLC, 127% of predicted; airways resistance, 133% of predicted; and a RV/TLC ratio of 35% (compared to a predicted value of 30%). The DLCO was 100% of predicted. Body mass index was 26.6. These pulmonary function tests were interpreted by the pulmonologist as showing mild asthma and a significant response to bronchodilator. High resolution computed tomography of the chest with inspiratory and expiratory images in June 2006 was interpreted as not showing any evidence of lung disease. NIOSH investigators had the computed tomography reviewed by a pulmonary radiologist who identified mild bronchial wall thickening and expiratory air trapping consistent with asthma.

DISCUSSION

<u>Occupational Diseases Associated with Exposure to Flavoring Chemicals</u>

In 2000, a highly unusual cluster of moderate to severe fixed obstructive airways lung disease at a microwave popcorn production plant in Missouri came to the attention of NIOSH. The affected workers shared clinical characteristics consistent with bronchiolitis obliterans. A NIOSH investigation at that plant concluded that the disease was caused by exposures to flavoring chemicals at the plant. The investigation found an excess prevalence of airways obstruction on spirometry testing among current workers and also that increased prevalence of abnormal lung function among these workers was associated with increasing cumulative exposure to diacetyl, the predominant butter flavoring chemical present in the air of the plant.[1,2,3] In animal experiments conducted by NIOSH toxicologists, rats exposed to vapors from a butter flavoring used at this plant, or to diacetyl alone, developed severe injury to their airways.[4,5] Some workers with severe flavoring-related disease have been placed on lung transplant waiting lists.[3,8]

Bronchiolitis obliterans is characterized by inflammation and eventual scarring within the smallest airways (bronchioles) of the lung; it can lead to severe and permanent obstruction to airflow through these airways.[9] The distinctive pathology of bronchiolitis obliterans is only diagnosed on the basis of examination of lung tissue. Because obtaining such tissue involves a degree of risk and because of the difficulty of finding this distinctive pathology within tissue specimens (due to the patchy nature of the disease and the degree of experience and diligence required by the pathologist), clinicians often infer the presence of bronchiolitis obliterans on the basis of other clinical findings. This has given rise to the term 'bronchiolitis obliterans syndrome', which encompasses cases for which tissue specimens are not available or not diagnostic, but for which the clinical picture is otherwise consistent with bronchiolitis obliterans. The main respiratory symptoms associated with bronchiolitis obliterans include cough and shortness of breath on exertion. Usually these have a gradual onset and progression, but severe symptoms can occur suddenly. Even when bronchiolitis obliterans is caused by occupational exposure, the symptoms typically do not improve when the worker goes home at the end of the workday or on weekends or vacations. In clear-cut cases, lung function testing with spirometry reveals airways obstruction that does not improve with bronchodilator (i.e., fixed airways obstruction), and medical treatment does little to reverse the condition.

Bronchiolitis obliterans has several known causes, including inhalation of certain chemicals, certain infections, reactions to certain medications, and organ transplantation. Long-known causes of bronchiolitis obliterans due to occupational exposures include gases such as nitrogen oxides (e.g., silo gas), sulfur dioxide, chlorine, ammonia, and phosgene.[9] Recent reports concerning the microwave popcorn industry and other work settings have raised concern that workers are at risk of bronchiolitis obliterans from exposures to flavorings chemicals in the manufacture of other food products besides microwave popcorn and in the manufacture of flavorings themselves.[10,11] In 2004, the Flavoring and Extract Manufacturers Association (FEMA) distributed to its members a priority list of chemicals thought to have sufficient volatility and chemical reactivity to pose a risk of respiratory injury.[12] Exposure to acetaldehyde has been implicated as causing fixed obstructive airways disease among flavoring manufacturing workers[11]; bronchiolitis obliterans with organizing pneumonia has been reported in a spice process technician who dumped seasonings (including salt, pepper, onion, garlic, paprika, and others) into a hopper.[13] A case of constrictive bronchiolitis obliterans has been reported in an individual exposed to overheated cooking oil fumes without smoke.[14]

Bronchiolitis obliterans is not the only disease that can cause generalized obstruction of airflow through the airways of the lung. Asthma, which can involve bronchioles and the larger airways, is also characterized by generalized airflow obstruction. In contrast to the essentially irreversible (i.e., fixed) obstruction that characterizes bronchiolitis obliterans, asthma is typified by variable airways obstruction (though in some cases of severe asthma, an irreversible component airways obstruction may result after years of disease.) Occupational asthma is defined as variable airways obstruction or airways hyper-responsiveness due to occupational exposures. In typical occupational asthma, the airways obstruction temporarily improves following use of a bronchodilator drug and temporarily worsens following exposure to the causative occupational agent or a test drug (e.g., methacholine).

The Association of Occupational and Environmental Clinics has listed well over 300 substances that can cause occupational asthma.[15] Occupational exposures that cause asthma include sensitizing agents (resulting in immunologically-based asthma) or non-specific irritants (resulting in asthma that is not immunologically-based). A single, intense inhalational exposure to a respiratory irritant can cause asthma, as can repeated lower level exposures to respiratory irritants over months to years.[16] Irritants that can cause asthma include such substances as smoke, chlorine, ammonia, and acids, some of which are also known causes of bronchiolitis obliterans. Thus, it follows that irritant exposures can cause a spectrum of airways disease, including both bronchiolitis obliterans and asthma. In fact, in some of the microwave popcorn facilities investigated by NIOSH, statistically significant elevated rates of self-reported physician-diagnosed asthma have been found.[1,17] NIOSH researchers interpreted this finding as likely to be due in part to the misdiagnosis of bronchiolitis obliterans as asthma. An investigator of bronchiolitis obliterans in flavoring manufacturing workers concluded that some workers at one plant did have occupational asthma.[3]

The specific agent(s) responsible for causing asthma in microwave popcorn workers exposed to flavoring chemicals have not been identified. Identifying specific chemical compound(s) responsible for occupational asthma among workers is difficult. There are about 100,000 known chemical compounds that workers are exposed to and only a small proportion of these chemicals have been investigated for their ability to cause asthma. In addition, workers who develop occupational asthma are often exposed to a number of different chemicals at the same time, making it difficult to determine which chemical is responsible. To provide risk assessment guidance in the absence of other documentation that a particular chemical can cause asthma, researchers are studying chemical structure-activity relationships to identify certain chemical structures that are more likely to cause asthma. One report identifies chemicals with the following components as having a high potential for causing asthma: nitrogen, sulfur, two or more atoms of oxygen, two or more double bonds, ethene derivative, ethanolamine backbone, beta-lactam ring, benzyl, acrylate derivative, amine, anhydride, carboxylic acid, and two or more carbonyl groups.[18]

In addition to airways problems, eye irritation has commonly been reported by workers exposed to butter flavoring vapors, and some exposed workers have required medical treatment for chemical burns to their eyes.[3] Workers exposed to butter flavoring vapors have also reported skin irritation, and one worker at a microwave popcorn plant developed a disabling skin allergy to butter flavorings.[3,8] Aldehydes and capsaicin, which are components of some flavorings, are known eye and skin irritants.[19,20]

Exposures at this Popcorn Popping Plant

Given the recent implication by NIOSH investigators of diacetyl as one likely cause of the severe airways disease among microwave popcorn workers, it is reasonable to first turn attention to diacetyl exposure in this popcorn popping plant. At the time of our survey, workers' exposures to air concentrations of diacetyl were below 0.01 ppm. This contrasts with much higher mean diacetyl levels found in the air of microwave popcorn plants where cases of bronchiolitis obliterans syndrome have occurred—0.02 ppm to 37.8 ppm in mixing rooms and 0.3 ppm to 1.9 ppm in packaging areas.[1,2,3,21] Nevertheless, no safe level for exposure to diacetyl has been established, and diacetyl was detected by GCMS in all thermal desorption tube air samples from this plant and reached quantifiable levels in the air above a heated container of butter-flavored oil in this plant (0.14 ppm).

The only apparent source of diacetyl in this facility at the time of our survey was butter-flavored oil (Gregg's Ultrapop[TM]), as organic compounds released from this oil when heated in the laboratory did include diacetyl. What remain unknowable are the past levels of diacetyl in this plant (and its smaller predecessor plant). While the processes and levels of production have been similar through the history of these plants, we are unable to reconstruct historical diacetyl exposures when other brands of flavored oils were used. Our analysis of the current formulation of the butter-flavored salt (Flavacol[TM]) used in this plant at the time of our survey found that it contained no diacetyl. However, we cannot conclude on this analysis alone that this brand never contained diacetyl.

We identified other potential causative agents for lung disease in the air of this popcorn popping plant. These other agents include valeraldehyde and furfural, which were predominant chemicals in the air in this plant and which are listed by FEMA as having potential to cause respiratory injury.[12] Of the 17 predominant VOCs that we measured at this plant and that have known structural formulas, 12 have at least one chemical component[18] in sufficient quantity to confer a potential risk for asthma. These VOCs included propylene glycol, toluene, furfural, furfuryl alcohol, 2-heptenal, methyl furfural, dimethylfurfural, limonene, 5-(hydroxymethyl) furfural, t-butylcresol, 2-decanal, and triacetin (glycerol triacetate) (Table 2).

Furfuryl alcohol, one of the predominant VOCs identified in air in the popcorn popping plant on the day that powdered flavorings were used, is also identified as an asthmagen by the Association of Occupational and Environmental Clinics.[22] Furfuryl alcohol is implicated in a case of occupational asthma in a foundry mold maker who developed severe asthma several weeks after beginning work with a furan binder; his work required him to mix sand with a resin that contained furfuryl alcohol, paraformaldehyde, and xylene with a catalyst containing sulfuric acid, phosphoric acid, and butyl alcohol. When challenged with furfuryl alcohol mixed with either sulfuric acid or butyl alcohol, the worker had an asthmatic response; when he avoided further exposure to the furan binder, his symptoms resolved.[23] Asthma was attributed to a volatile reaction product of furfuryl alcohol.

Formaldehyde, also present in air of the popcorn popping plant (though at relatively low levels compared to other identified volatile organic compounds), has been shown to be associated with asthma in studies among healthcare workers and other workers.[24-26]

One of the flavorings used at this popcorn popping plant was powdered jalapeno flavoring. The predominant component of hot pepper spice is capsaicin (8-methyl-*N*-vanillyl-6-nonenamide). Exposure to capsaicin may cause temporary respiratory symptoms (such as cough, shortness of breath, phlegm production, runny nose, nasal irritation, and hoarseness), and short-lasting bronchoconstriction.[19,27] Capsaicin stimulates sensory nerve endings within the surface of the airways, causing airways constriction and cough through vagal and cough reflexes. Stimulation of these nerves also releases mediators that cause inflammation of the airways, resulting in mucus secretion and airways constriction.[28] The cough response to capsaicin is more pronounced in individuals with asthma compared to healthy individuals.[29] Although spirometry test results of 22 chili production workers exposed to capsaicinoids did not differ from those of a group of office workers in one study,[30] and although researchers in another study were not able to demonstrate cross-shift changes in FEV_1 among chili grinders[31] or changes in FEV_1 after inhalation of capsaicin,[32] airways resistance (a more sensitive measure of airways obstruction) has been shown to transiently increase in asthmatic and non-asthmatic individuals exposed to capsaicin.[27] Also, immunoglobulin E antibodies specific to paprika (dry powder of *Capsicum annuum*) were identified in a butcher who developed asthma one year after beginning to use paprika when making sausages.[33]

Air concentrations of total and respirable particles measured at the plant during our survey were well below the Occupational Safety and Health Administration (OSHA) permissible exposure limits (PELs) for particulates not otherwise regulated (PNOR). These PELs are 15 mg/m^3 and 5 mg/m^3 (as 8-hour time-weighted averages) for total and respirable particles, respectively. However, the PNOR PELs are intended for particulates that have little biological activity and low toxicity,[34] and may not be protective for some of the particles generated during corn popping and the application of powdered flavorings.

Diseases and their Work-Relatedness among Workers at the Plant

All three of the workers at this popcorn popping plant developed symptoms of airways disease while employed at the plant. All three were lifelong non-smokers whose symptoms were consistent with asthma (i.e., episodic wheeze, shortness of breath, and cough; diffuse expiratory wheezes on examination) which were reported to be work-related (i.e., symptom exacerbations were temporally related to working at the plant). The two workers with less severe disease (Employees B and C) both had improvement in asthma symptoms after their employment at the plant ceased. Employee B was treated with bronchodilators which improved her symptoms. Employee C never was prescribed bronchodilators. Pulmonary function testing of these two workers, who were currently employed at the plant at the time of testing, did not show any major impairments on the day of testing, but did reveal evidence suggestive of airways obstruction (i.e., post-bronchodilator FEV_1 increase in Employee C and increased airways resistance in Employee B). Computerized tomography images of the chest in these two workers were interpreted as normal by the local radiologist, but showed evidence of airways disease when reviewed for NIOSH by a pulmonary radiologist.

The worker who died of respiratory disease (Employee A) had clear evidence of asthma (e.g., several pulmonary function tests that showed significant airways obstruction with substantial post-bronchodilator improvement) corresponding to improvement in symptoms and wheezing following intensive asthma treatments. His surviving spouse reported that his symptoms varied in severity, worsening the days he worked at the popcorn plant, suggesting an occupational cause of his airways disease. Some clinical evidence in this worker suggested possible bronchiolitis obliterans in addition to asthma. Employee A's radiographic abnormalities (i.e., mosaic pattern of attenuation on computed tomography) may be more indicative of bronchiolitis obliterans than of asthma, though distinguishing severe asthma from bronchiolitis obliterans can be difficult in some cases.[35] Regardless of Employee A's exact pathology, because of the known respiratory hazards of flavorings chemicals and the fact that all three workers at this plant were affected by apparent occupational airways disease, it seems reasonable to conclude that exposures at the popcorn popping plant may have contributed to his respiratory disease.

Employee C reported the jalapeno pepper flavoring to be irritating to the eyes and nasal passages, which is not surprising given that capsaicin is a component of that particular flavoring. Employees B and C both developed skin rash during employment, which may also have been due to flavoring exposures.[8]

CONCLUSIONS

All three workers at this plant were exposed to many different volatile organic compounds (including aldehydes) and complex particles associated with popcorn popping and with the use of flavorings. Some of these flavoring chemicals are known irritants that could possibly cause airways diseases (including occupational asthma and bronchiolitis obliterans) and eye and skin irritation. Respiratory health outcomes occurred among all three workers despite exposure over a reduced work-week (less than 40 hours per week). These workers all had clinical presentations consistent with asthma associated with occupational exposures at this popcorn popping company. Based on evidence presented in this report, there is reason to suspect that a component of airways disease in workers at this plant (in particular Employees A and B) may have been bronchiolitis obliterans, a condition known from previous studies to affect popcorn workers exposed to flavorings.

This investigation emphasizes that many flavoring chemicals, not solely diacetyl, may be responsible for respiratory disease among workers exposed to flavoring chemicals. It also emphasizes that, in addition to causing bronchiolitis obliterans, flavoring chemicals can cause occupational asthma. Further, it suggests that these two airways diseases, not surprisingly, may occur together in the same affected worker. The increasing body of evidence implicating flavoring chemicals as causes of occupational respiratory disease should motivate a systematic approach to identify the spectrum of occupational respiratory disease among workers in industries where flavorings are used or manufactured, to measure flavoring chemical exposures other than diacetyl in these industries, and to conduct animal toxicology studies to document potential respiratory risks of occupational exposure to specific flavoring chemicals.

RECOMMENDATIONS

We make the following recommendations (with the understanding that this popcorn popping plant has closed) so that this guidance will be available to other popcorn popping operations, and this plant, should it be reopened.

Engineering Controls:

- Obtain engineering consultation to identify and implement process changes or modifications to the existing ventilation system that would better control the emission of particles and VOCs. This could include better exhaust hood design with more enclosure of the heated oil, and popping, bagging, and powdered flavor application operations.

- Regularly check and maintain all exhaust ventilation systems and other engineering controls, to ensure efficient operation and minimize the possibility of a malfunction.

Work Practices:

- Always keep containers of flavorings tightly sealed when not in use. Empty flavoring containers that still contain residual flavorings also need to be tightly sealed. If these containers are to be washed, the worker doing this should wear a NIOSH-approved respirator and gloves.

- Minimize particle dispersion by using high efficiency particulate air (HEPA) vacuums when cleaning floors. Do not dry sweep, which increases particle dispersion. Avoid spills and promptly clean up when spills occur. Wear appropriate respiratory, eye, and skin protection when cleaning up spills.

Respiratory Protection:

- Until the production process is reengineered to control exposures to popping and flavoring chemicals, require mandatory respirator use for all workers involved in popcorn popping, bagging, and flavoring application. A formal respiratory protection program that adheres to the requirements of the OSHA Respiratory Protection Standard (29 CFR 1910.134) is required. This program requires a written program, training of workers, fit testing of respirators, and a program administrator. The program administrator that you select for the program must have adequate training and experience to run it and regularly evaluate its effectiveness. Details on the Respiratory Protection Standard and on how a company can set up a respiratory protection program are available on the OSHA website (www.osha.gov).

- Assure that workers understand how and when to wear a respirator, the nature of the respiratory hazards associated with exposure to flavoring chemicals, and that a respirator must be used 100% of the time during the production of popcorn.

- A NIOSH-certified half-facepiece negative-pressure respirator with organic vapor cartridges and particulate filters is the minimum level of respiratory protection recommended; these respirators should be used in conjunction with goggles or safety glasses with side-shields. A full-facepiece respirator would provide eye protection as well. A loose-fitting powered air-purifying respirator (PAPR) with a particulate filter and organic vapor cartridge is an option to consider for increased worker comfort and, unlike tight-fitting respirators, these respirators do not require fit testing.

Medical Surveillance:

- Perform a baseline spirometry test on all new workers. Have a physician evaluate new workers who have pre-existing lung disease or abnormal spirometry on pre-placement testing to determine the risk of progression of their lung disease from work exposures. It is important that the spirometry test be performed by a health care provider who can assure high quality tests in order to compare results over time to determine whether lung function is remaining stable. This health care provider should provide documentation that the spirometry technician has attended a NIOSH-certified spirometry course, that routine calibrations of the spirometer are performed as recommended by the American Thoracic Society, and that the spirometry administered meets quality assurance standards.

- Perform spirometry tests at least every 6 months on all production workers. Use results to identify any workers with falling lung function who should receive more intense surveillance and education on health effects of exposures, and who should be removed from further exposure.

- Encourage workers to report persistent or recurrent respiratory symptoms to plant management and their personal physician. Workers who report such symptoms should provide a copy of this report to their physician.

- Refer any symptomatic workers and those with abnormal or declining spirometry results for further medical evaluation. This evaluation should establish the likelihood of compensable work-related lung disease and identify measures to prevent further injury or progression, including respiratory protection and relocation or exposure restriction.

Continued Communication with NIOSH:

- Contact NIOSH if the popcorn popping plant is reopened so that we can update you on medical and industrial hygiene surveillance recommendations or provide assistance in the implementation of these recommendations.

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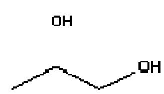
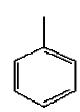
TABLES AND FIGURES

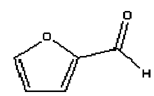
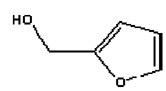
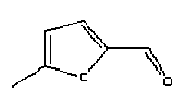
Table 1. Industrial hygiene sampling methods

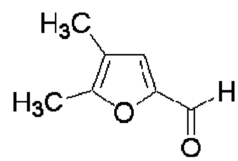
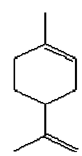
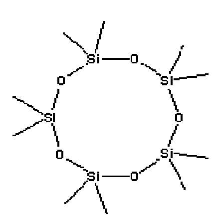
Analytes	Media/sampler	Flow rate (lpm*)	Analytical methods
Total particles in air	37-mm PVC filter, open-face filter cassette	3.0	Gravimetric analysis by NIOSH Manual of Analytical Methods (NMAM) Method 0500[36]
Respirable particles in air	37-mm PVC filter, BGI® Cyclone	4.2	Gravimetric analysis by NMAM Method 0600[36]
Real-time respirable particles in air	Photometric meter, PersonalDataRAM pDR-1000AN/1200	--	Direct-reading instrument[37] (Thermo Electron Corporation, Franklin, MA)
Particle size distributions in air	Eight stage cascade impactor; PVC filter media for all stages	2.0	Gravimetric analysis[36,37]
Volatile organic compounds (VOCs) in air (screening for identification)	Thermal desorption tube	0.03 to 0.05	Gas chromatography / mass spectrometry by NMAM Method 2549[36]
Real-time VOCs in air	Photoionization meter, ppbRAE	--	Direct-reading instrument[37] (Rae Systems, Inc., Sunnyvale, CA)
Total VOCs in air (quantitative for total mass)	Coconut shell charcoal (CSC) tubes	0.05	Gas chromatography by NMAM Method 1550[36]
Ketone compounds in air (diacetyl, acetoin, and 2-nonanone)	Anasorb® tube	0.03 to 0.15	Gas chromatography by NMAM Methods 2557 and 2558[36]
Real-time diacetyl, acetoin, and nonanone concentrations in air	Fourier transform infrared (FTIR) gas analyzer	--	Direct-reading instrument[37] (Gasmet DX-4010,™ Temet Instruments Oy, Helsinki, Finland)
Acetaldehyde in air	Sorbent tube (silica gel treated with 2,4 dinitrophenylhydrazine)	0.03	High performance liquid chromatography (HPLC) by NMAM Method 2016[36]
Inorganic acids in air	Sorbent tube (silica gel)	0.5	Ion chromatography by NMAM Method 7903[36]
Air temperature and % relative humidity	Psychrometer	--	Direct-reading meter[37]

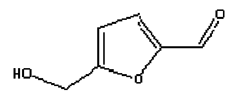
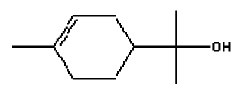
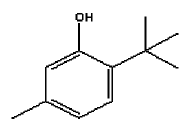
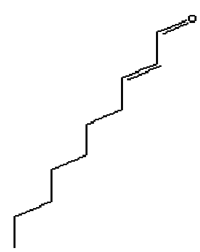
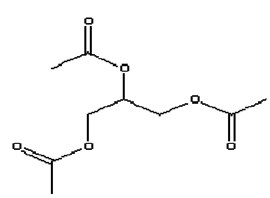
*lpm, liters per minute

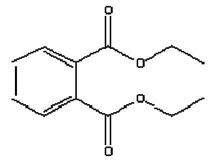
Table 2. Molecular weight, structural formula, and asthmagenic groups of predominant volatile organic compounds in air

Compound	ID[1]	Structural Formula	Molecular Weight	Asthmagenic groups[2]
C-7 Aliphatic hydrocarbons	20	Various	Various	—
Valeraldehyde	21		86.1	One carbonyl group One atom of oxygen
Heptane	22		100.2	—
Propylene glycol	23		76.1	*Two oxygen atoms*
Toluene	24		92.1	*One benzyl group*

Hexanal*	26		100.2	One carbonyl group
Furfural	28		96.1	One carbonyl group *Three double bonds* *Two oxygen atoms*
Furfuryl alcohol	30		98.1	*Two double bonds* *Two oxygen atoms*
2-Heptenal (trans-2-heptenal shown in structural formula)	35		112.2	One carbonyl group *Two double bonds*
Methyl furfural (5-methyl furfural shown in structural formula)	36		110.1	One carbonyl group *Three double bonds* *Two oxygen atoms*

Octanal	39		128.2	One carbonyl group
Dimethylfurfural	41		124.1	One carbonyl group *Three double bonds* *Two oxygen atoms*
Limonene	42		136.2	*Two double bonds*
Nonanal	47*		142.2	One carbonyl group
Decamethylcyclopentasiloxane*	50A		370.8	*Five oxygen atoms*

5-(hydroxymethyl) Furfural	52		126.1	One carbonyl group *Three oxygen atoms* *Three double bonds*
Alpha-terpineol	53		154.2	One oxygen atom One double bond
t-Butylcresol (6-t-butyl-m-cresol shown in structural formula)	54		164.3	*One benzyl group* One oxygen atom
2-Decenal	56		154.2	One carbonyl group *Two double bonds*
Triacetin (glycerol triacetate)	58		218.2	*Three carbonyl groups* *Three double bonds* *Six oxygen atoms*
Levoglusan	64	No structural diagram available	unavailable	---

Diethylphthalate*	67		222.2	*One benzyl group* *Two carbonyl groups* *Four oxygen atoms*

[1] ID – Thermal desorption tube sample peak identification code.
[2] Chemical functional groups / structures reported to be asthmagens among low molecular compounds (molecular weight less than 1000).[18] Italics is used to denote chemical groups of the appropriate type and sufficient number to confer increased risk of asthma.[18]
*Compounds that were also found on some blanks.

Table 3. Total volatile organic compound concentrations from area air samples

Location[1]	Date Collected	Minutes	Volume (m^3)	Concentration[2] (mg/m^3)
#1	April 12	135	0.014	0.47
	April 13	120	0.012	1.25
	April 12 & 13	261	0.026	1.11
#2	April 12	137	0.014	5.04
	April 13	118	0.012	8.14
	April 12 & 13	254	0.025	1.30
#1 and #2	Average: 2.90 mg/m^3 (Standard deviation: 3.05)			

[1] Locations are identified on Figure 1.
[2] Concentrations in milligrams per cubic meter of air (mg/m^3).

Table 4. Total and respirable particle concentrations in air from area samples

Sample Type	Location[1]	Date Collected	Minutes	Volume (m^3)	Concentration[2] (mg/m^3)
Total Particles	#1	April 12	135	0.405	1.58
		April 13	120	0.360	3.61
		April 12 & 13	261	0.783	2.68
	#2	April 12	137	0.411	1.19
		April 13	118	0.354	4.52
		April 12 & 13	254	0.762	2.76
	#1 and #2				Mean: 2.72 mg/m^3 (Standard deviation: 1.24)
Respirable Particles	#1	April 12	135	0.567	1.11
		April 13	120	0.504	1.05
		April 12 & 13	261	1.10	0.56
	#2	April 12	137	0.575	0.87
		April 13	118	0.496	0.85
		April 12 & 13	254	1.07	0.89
	#1 and #2				Mean: 0.89 mg/m^3 (Standard deviation: 0.19)

[1] Locations identified in Figure 1.
[2] Particle concentrations in milligrams per cubic meter of air (mg/m^3).

Table 5. Spirometry test results for Employee A, using NHANES prediction equations[38] for percent of predicted and lower limit of normal values

Date	BD	FEV_1 (L [% pred.])	FVC (L [% pred.])	FEV_1/FVC (%)	FEV_1 increase post-BD (% [ml])	FVC increase post-BD (% [ml])	Interpretation in medical record	Comments
3/??/90	Pre	?	?	?	?	?	Suggestive of reversible bronchospasm.	Report not in records reviewed by NIOSH§; interpretation is from physician's note in medical chart dated 4/10/90.
	Post	?	?	?				
5/26/92	Pre	2.15 [59]*	3.57 [74]*	60*	4 [90]	3 [120]	Moderate obstructive pulmonary impairment. Restrictive pulmonary impairment cannot be excluded by spirometry alone. After bronchodilator, improved FEF_{25-75}.	Hospitalization for COPD with bronchospasm [BMI=29.1]
	Post	2.24 [61]*	3.69 [76]*	83				
3/10/94	Pre	2.13 [60)]*	2.58 [54]*	61*	—	—	—	Outpatient test for Black Lung Examination; report not in records reviewed by NIOSH§
	Post	—	—	—				
7/6/95	Pre	1.76 [49]*	2.53 [53]*	70	27 [?]	26 [?]	—	Hospitalization for status asthmaticus; report not in records reviewed by NIOSH§; values are from discharge summary.
	Post	? [?]	? [?]	? [?]				
12/15/95	Pre	2.33 [66]*	3.45 [73]*	68	23 [540]	11 [370]	Respiratory obstruction with significant reversibility after bronchodilator	Outpatient§
	Post	2.87 [81]	3.82 [81]	75				
6/11/98	Pre	1.97 [57]*	3.08 [66]*	64*	15 [300]	7 [230]	Moderate obstructive airways disease with a marked bronchodilator response. There is also a restrictive process indicating that this is a combined obstructive-restrictive process.	Outpatient [BMI=34.4]
	Post	2.27 [65]*	3.31 [71]*	69				

Not shown are results of a screening spirometry test done 3/13/90, which involved only two blows for which FVC varied by more than 10%.
BD, bronchodilator; L, liter; ml, milliliter; pred, predicted; —, not done; ?, data not in records obtained by NIOSH
*Below lower limit of normal
§ No flow-volume or volume-time curves in records obtained by NIOSH.

Table 6. Lung volumes results (by body plethysmography) for Employee A

Date	RV (L [% predicted])	TLC (L [% predicted])	RV/TLC (% [% predicted])	Interpretation from report
12/15/95	2.23 [118]	6.21 [91]	43 [129]	Normal… with perhaps slight…hyperinflation.
6/11/98	2.26 [97]	5.34 [76]*	42 [124]	Restrictive process

Percent of predicted and lower limit of normal values obtained from the medical reports
*Below the lower limit of normal per report

Table 7. Diffusing capacity (DLCO) results for Employee A

Date	DLCO (ml/min/mmHg [% predicted])	DLCO corrected for hemoglobin, carboxyhemoglobin, and altitude (ml/min/mmHg [% predicted])	DLCO corrected for lung volume (ml/min/mmHg/L [% predicted])	Interpretation from report
12/15/95	24.3 [?]	—	5.32 [107]	DLCO slightly decreased but completely normalized when corrected for lung volume. No evidence of diffusing abnormality.
6/11/98	23.9 [71]*	22.5 [67]*	5.43 [111]	Diffusing capacity is moderately reduced.

Percent of predicted and lower limit of normal values obtained from the medical reports
*Below the lower limit of normal per report

Figure 1. Diagram of popcorn popping room, approximate size 20 feet by 32 feet. with a 10-foot ceiling height

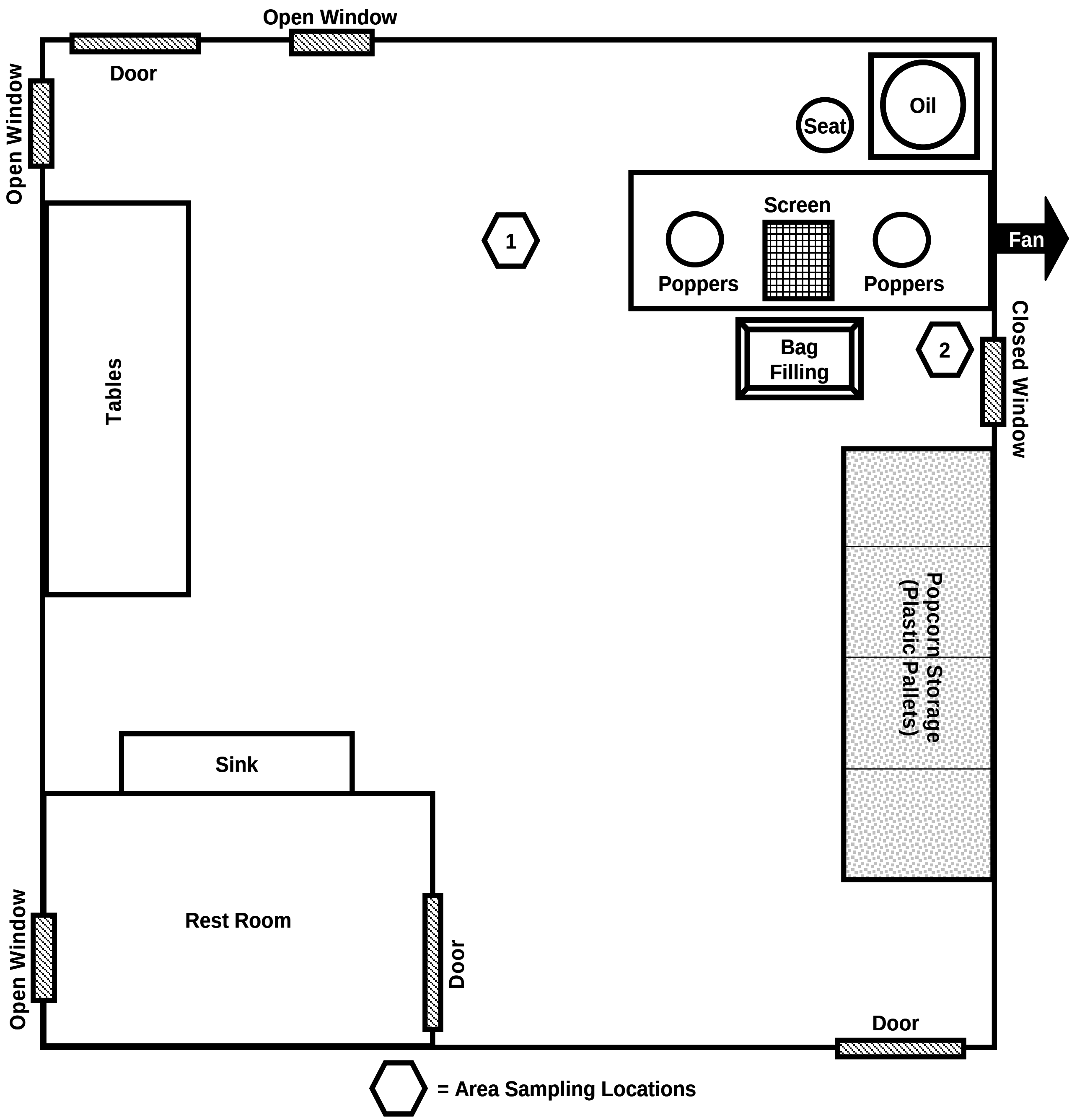
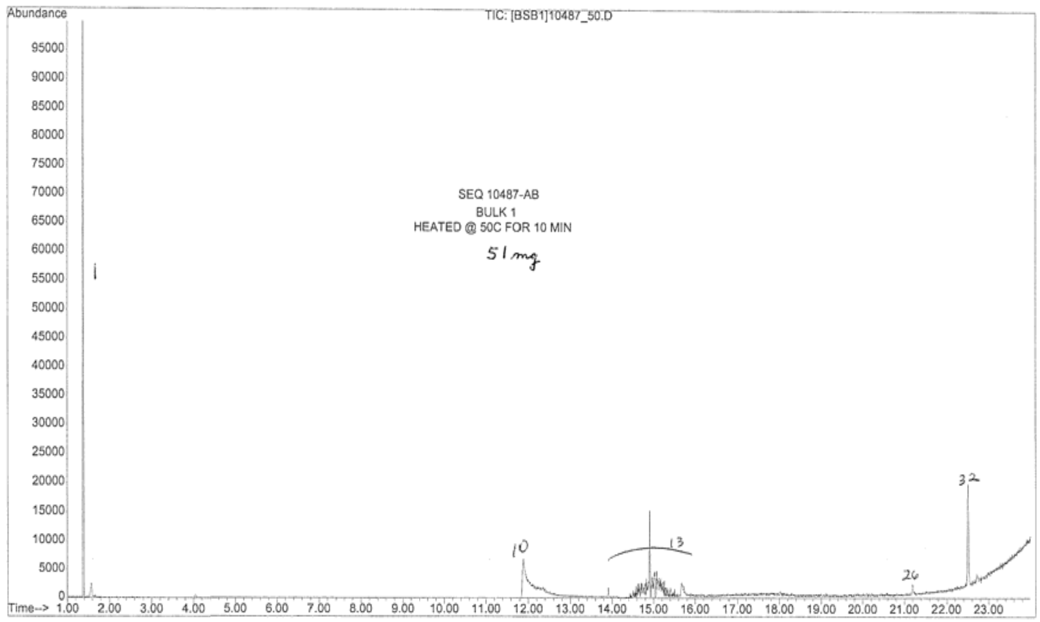
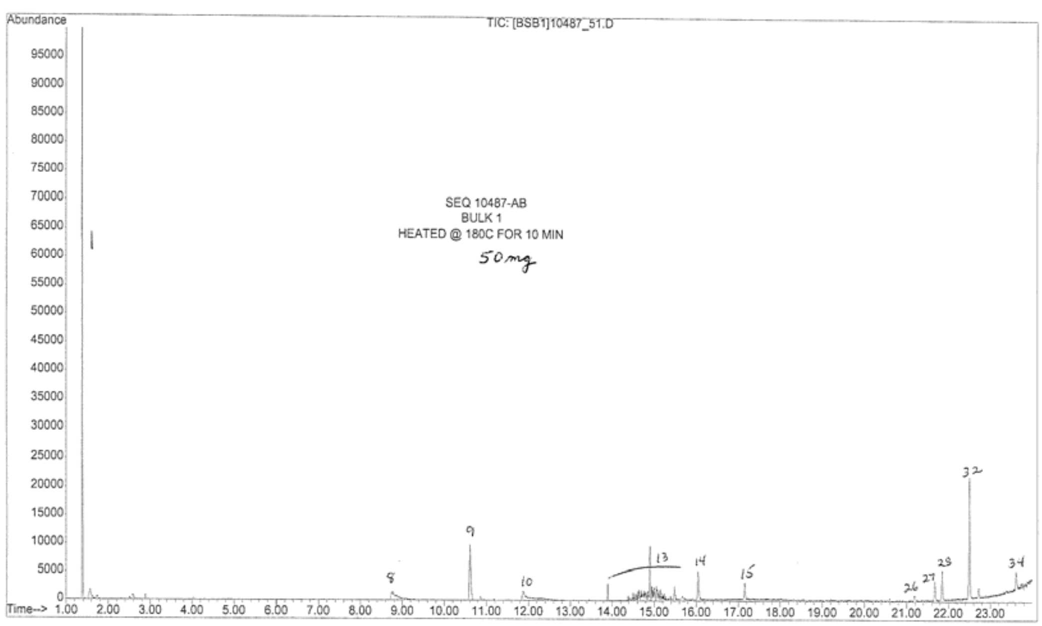


Figure 2-A. Volatile organic compounds released from a heated bulk sample of butter-flavored salt

Heated to 50^oC



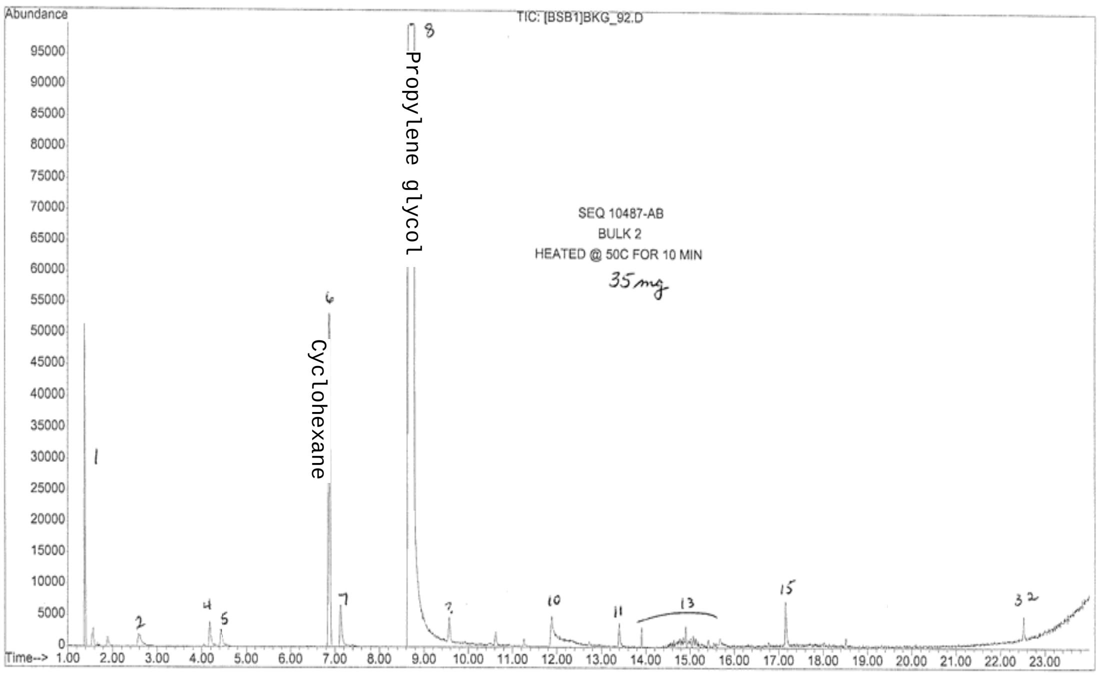
Heated to 180^oC



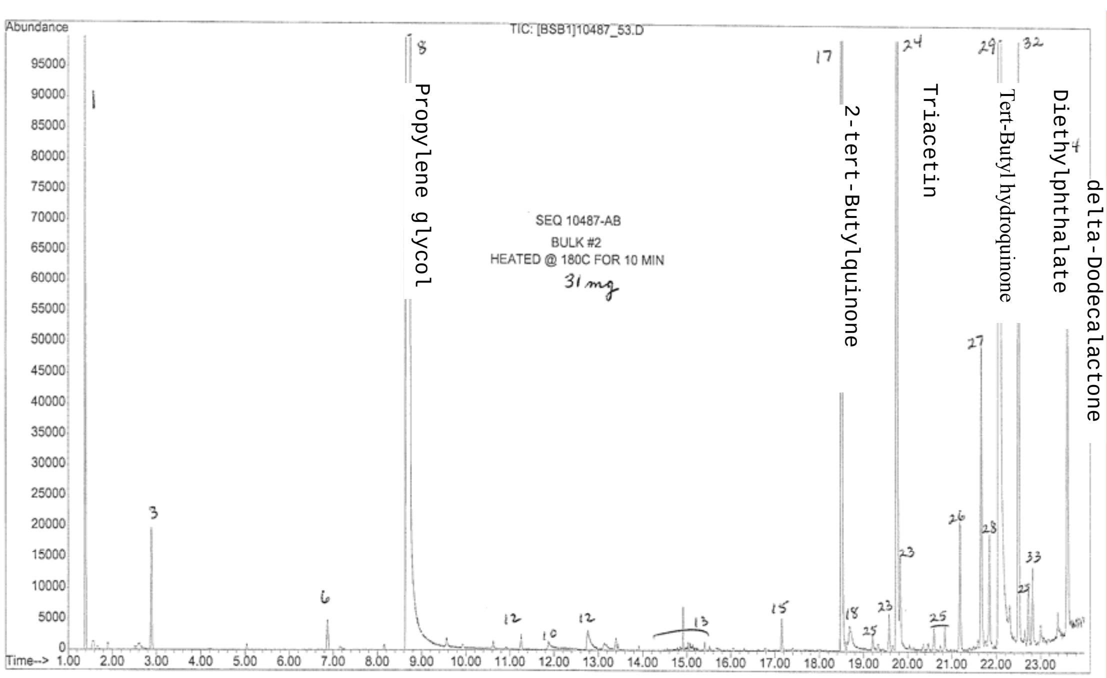
See list that follows for identification codes

Figure 2-B. Volatile organic compounds released from a heated bulk sample of butter-flavored canola oil

<u>Heated to 50^{o}C</u>



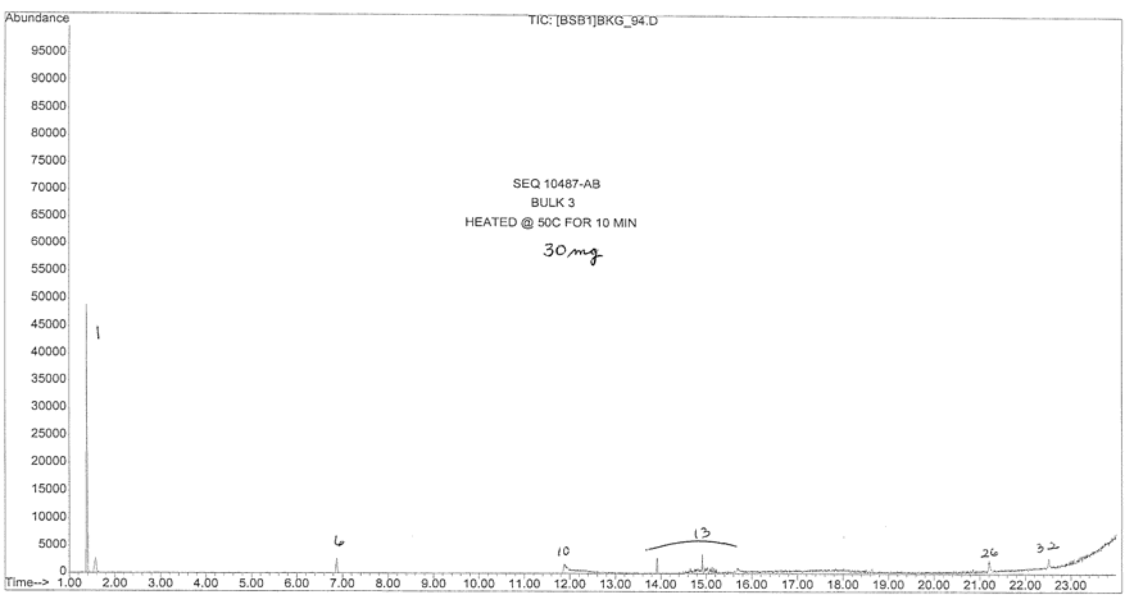
<u>Heated to 180^{o}C</u>



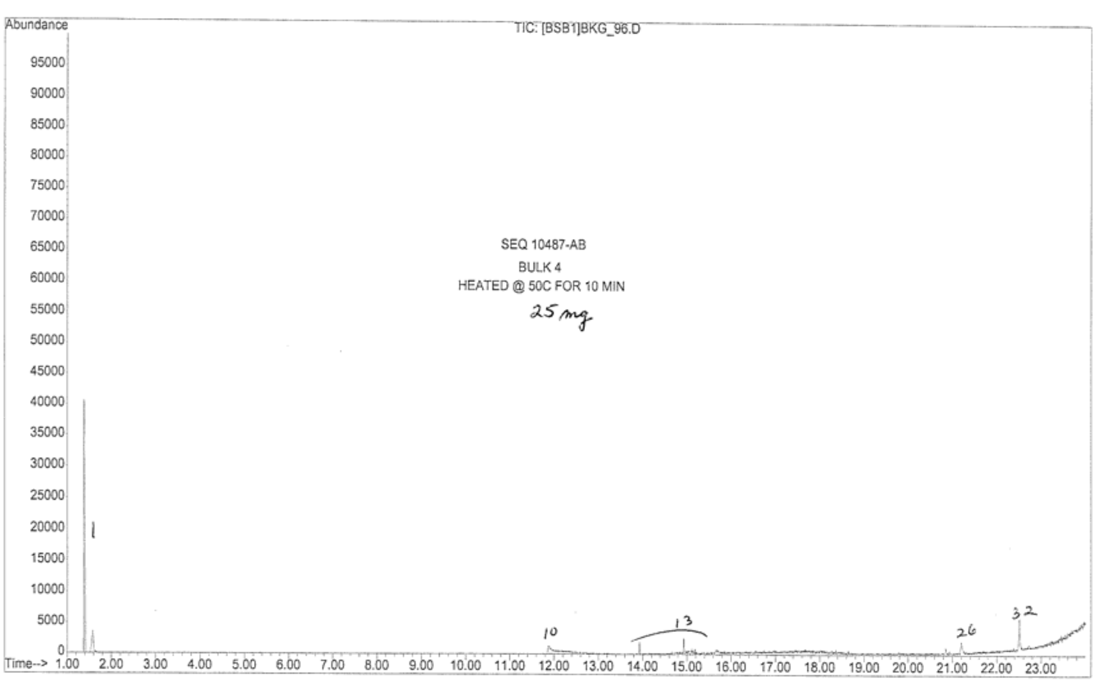
See list that follows for identification codes

Figure 2-C. Volatile organic compounds released from heated (50^{o}C) bulk samples of powdered flavorings

<u>White Cheddar Cheese Flavor</u>



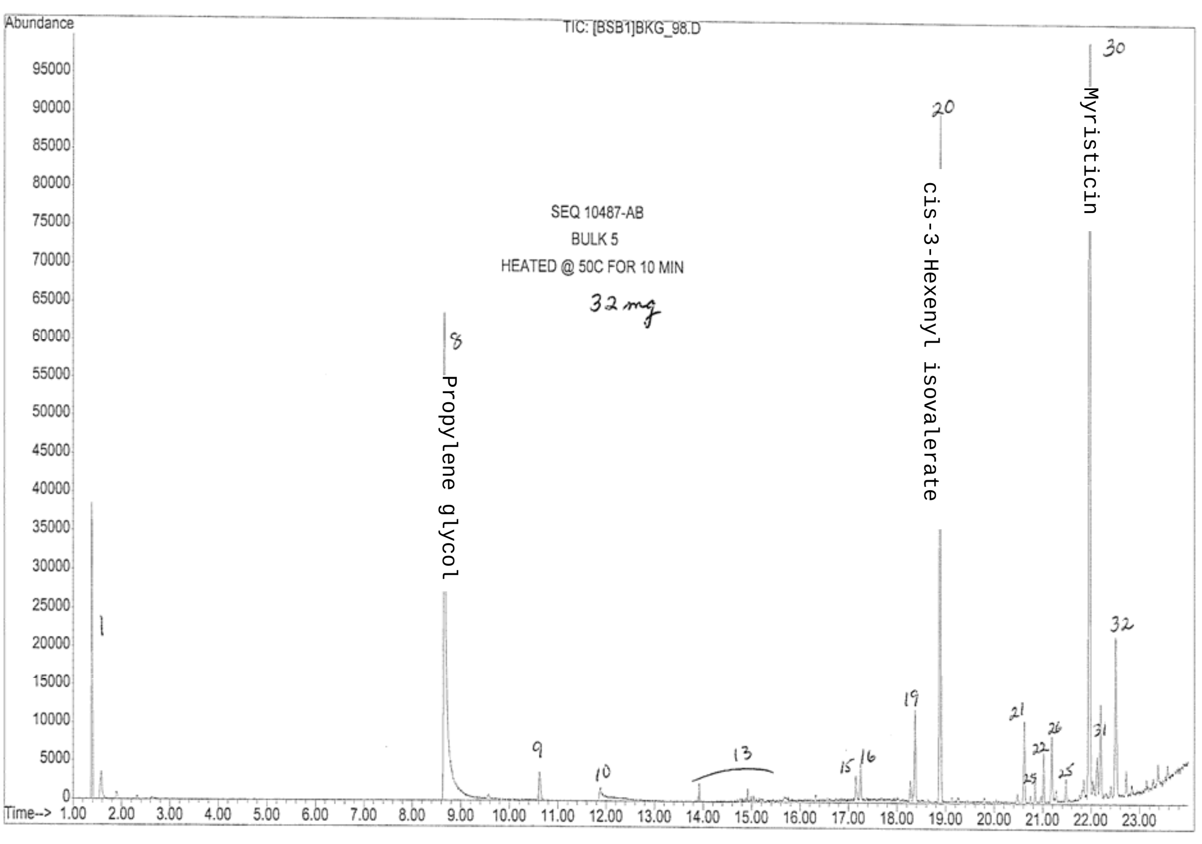
<u>Cheddar Cheese Flavor</u>



See list that follows for identification codes

Figure 2-C (Continued). Volatile organic compounds released from heated (50°C) bulk samples of powdered flavorings

Jalapeno Flavor



See list that follows for identification codes

Identification key for VOC peaks from samples of bulk flavorings shown in Figures 2-A, 2-B, and 2-C

Peak No.	Peak Identification	Peak No.	Peak Identification
1	air*/CO_2*	18	diacetin
2	acetone	19	ethyl caprylate (octanoate)
3	pentane	20	cis-3-hexenyl isovalerate
4	diacetyl	21	ethyl caprate (decanoate)
5	methyl ethyl ketone (MEK)	22	terpene derivative?
6	cyclohexane	23	decadienals
7	methyl propyl ketone (MPK)	24	triacetin
8	propylene glycol	25	aliphatic/aliphatic esters?
9	hexanal	26	dimethylphthalate*
10	hexamethylcyclotrisiloxane*	27	delta-decalactone
11	styrene	28	di-tert-butyl phenol
12	aliphatic?	29	tert-butyl hydroquinone
13	system background	30	myristicin
14	2-ethylhexanol	31	$C_{15}H_{24}$, sesquiterpene
15	nonanal	32	diethylphthalate*
16	amyl isovalerate	33	acetovanillone
17	2-tert-butylquinone	34	delta-dodecalactone

*Compounds that were also found on some blanks.

Figure 3-A. Volatile organic compounds in 2-hour air sample collected at location #1 on 4/12/2006 (no powdered flavorings used)

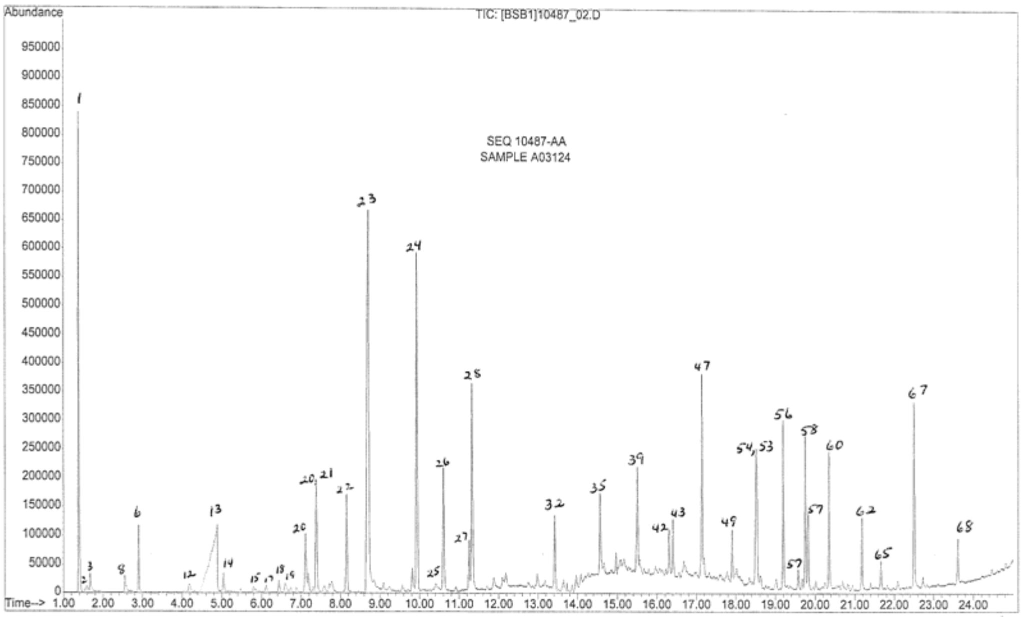
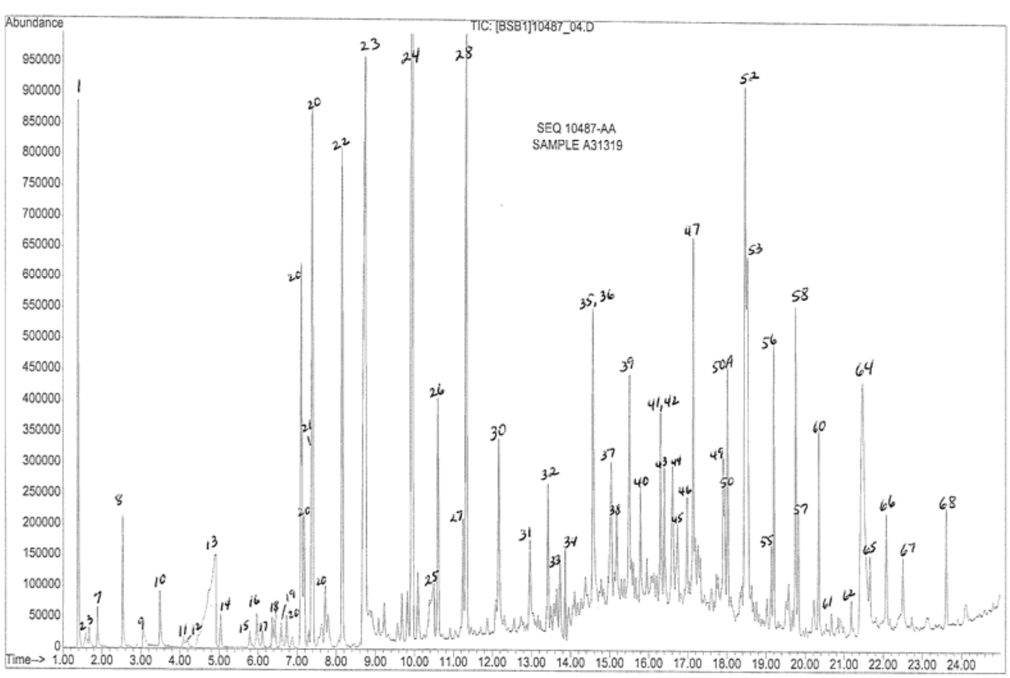


Figure 3-B. Volatile organic compounds in 4-hour air sample collected at location #2 over two days on 4/12-13/2006 (powdered flavorings used on second day)



See list that follows for identification codes

Identification key for VOC peaks from air samples shown in Figures 3-A and 3-B

Peak No.	Compound	Peak No.	Compound
2	formaldehyde	23	propylene glycol
3	SO_2	24	toluene
4	isopentane*	25	butyric acid
5	isopropanol*	26	hexanal*
6	pentane*	27	octane/methylpyrazine?
7	glyoxal	28	furfural
8	methyl glyoxal?	29	hexamethylcyclotrisiloxane*
9	formic acid	30	furfuryl alcohol
10	glycolaldehyde	31	butyrolactone/ethyl benzene
11	ethyl vinyl ketone	32	heptanal
12	diacetyl (dimethylglyoxal)	33	hydroxycyclopentenone?
13	acetic acid	34	nonan
14	hexane	35	2-heptenal
15	2-butenal	36	methyl furfural
16	acetol	37	hexanoic (caproic) acid
17	3-methylbutanal	38	aliphatic?
18	2-methylbutanal	39	octanal
19	benzene	40	decane
20	C7 aliphatic hydrocarbons	41	dimethylfurfural
21	valeraldehyde	42	limonene
22	heptane	43	2-octenal

Identification key for VOC peaks from air samples shown in Figures 3-A and 3-B (Continued)

Peak No.	Compound	Peak No.	Compound
44	heptanoic acid+nitrogen compound	56	2-decenal
45	dimethylhydroxyfuranone	57	decadienal
46	furfuryl alcohol derivative	58	triacetin (glycerol triacetate)
47	nonanal*	59	lauric acid
48	terpinolene	60	2-undecenal
49	2-nonenal	61	vanillin
50	octanoic (caprylic) acid	62	dimethylphthalate*
50A	decamethylcyclopentasiloxane */ aliphatic, oxy	63	2-dodecenal
51	decanal*	64	levoglusan
52	5-(hydroxymethyl)furfural	65	delta-decalactone
53	α-terpineol	66	t-butylhydroquinone
54	t-butylcresol	67	diethylphthalate*
55	nonanoic (pelargic) acid	68	delta-dodecalactone

*Compounds that were also found on some blanks.

Figure 4-A. Real-time air area sampling for total volatile organic compounds in air on 4/12/2006, when no powdered flavoring was used (concentrations in ppb units)

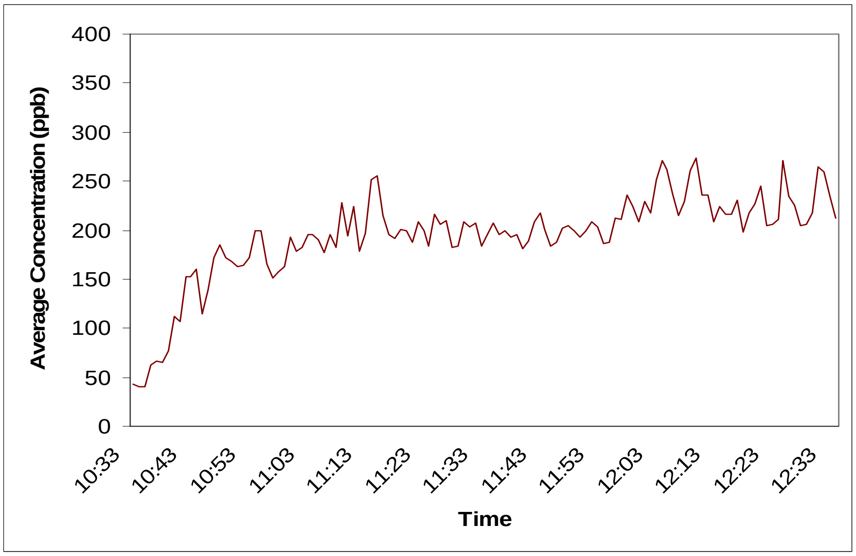


Figure 4-B. Real-time area air sampling for volatile organic compounds in air on 4/13/2006, when powdered flavoring was used (concentrations in ppb units)

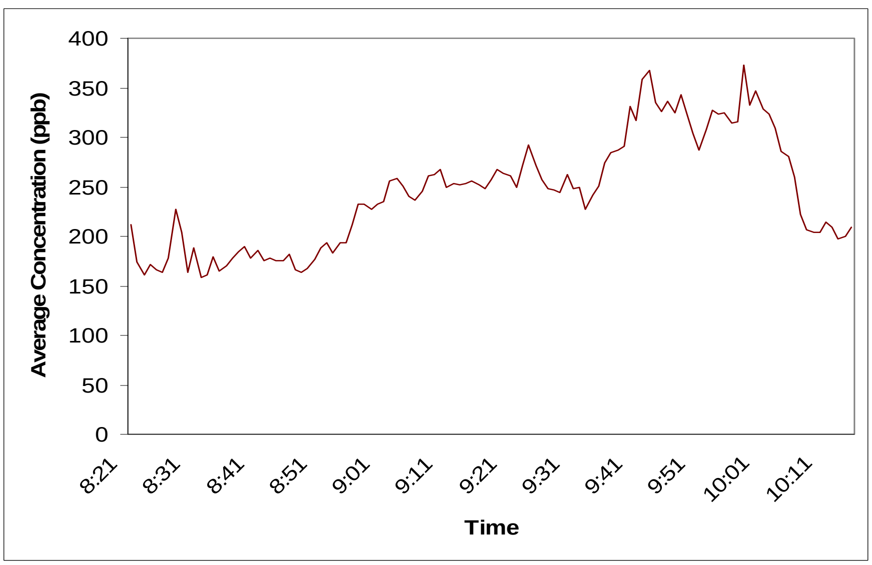
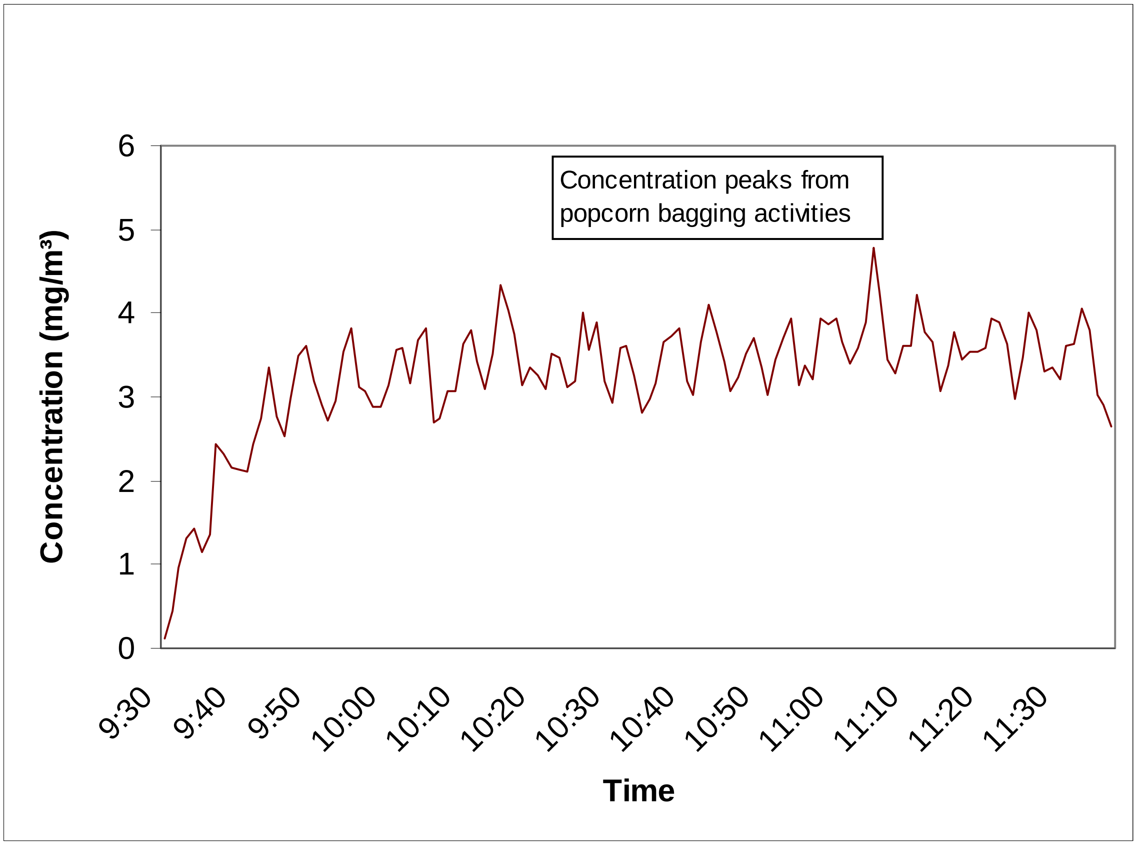
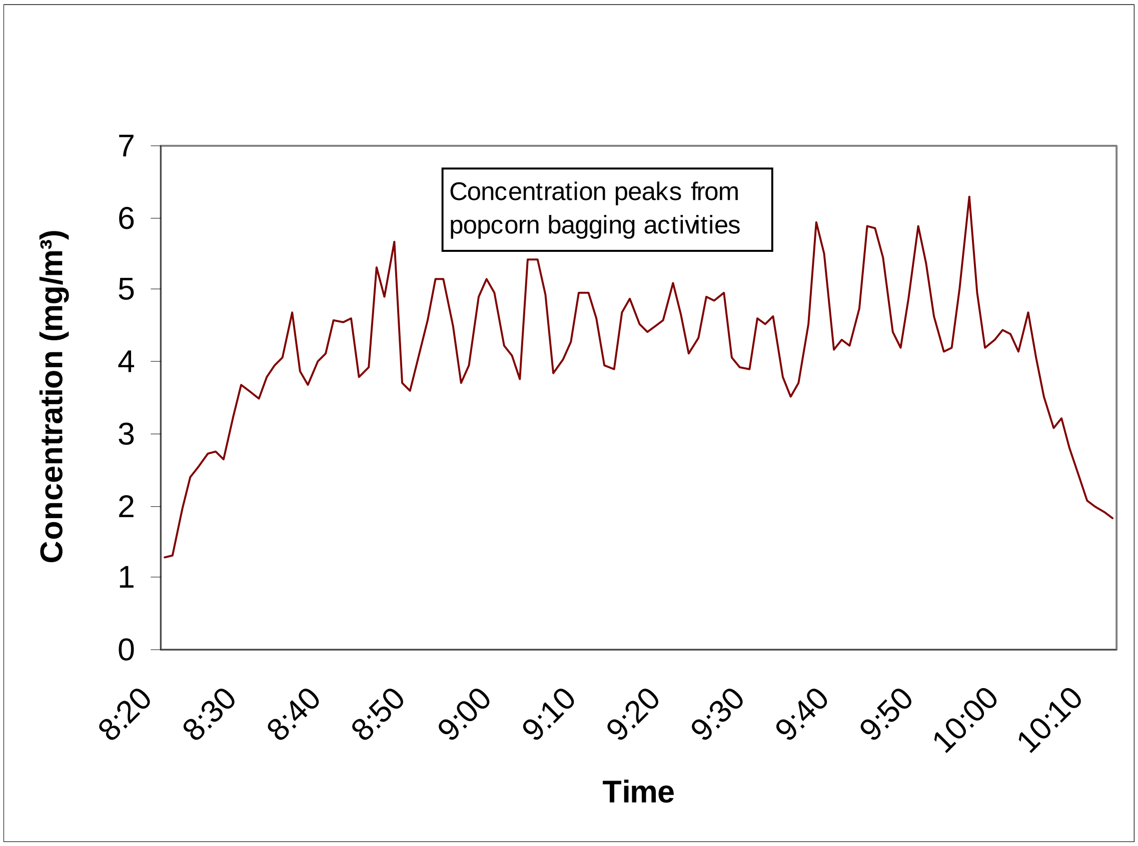


Figure 5-A. Real-time air sampling for respirable dust concentrations on 4/12/2006 with no powdered flavor application.



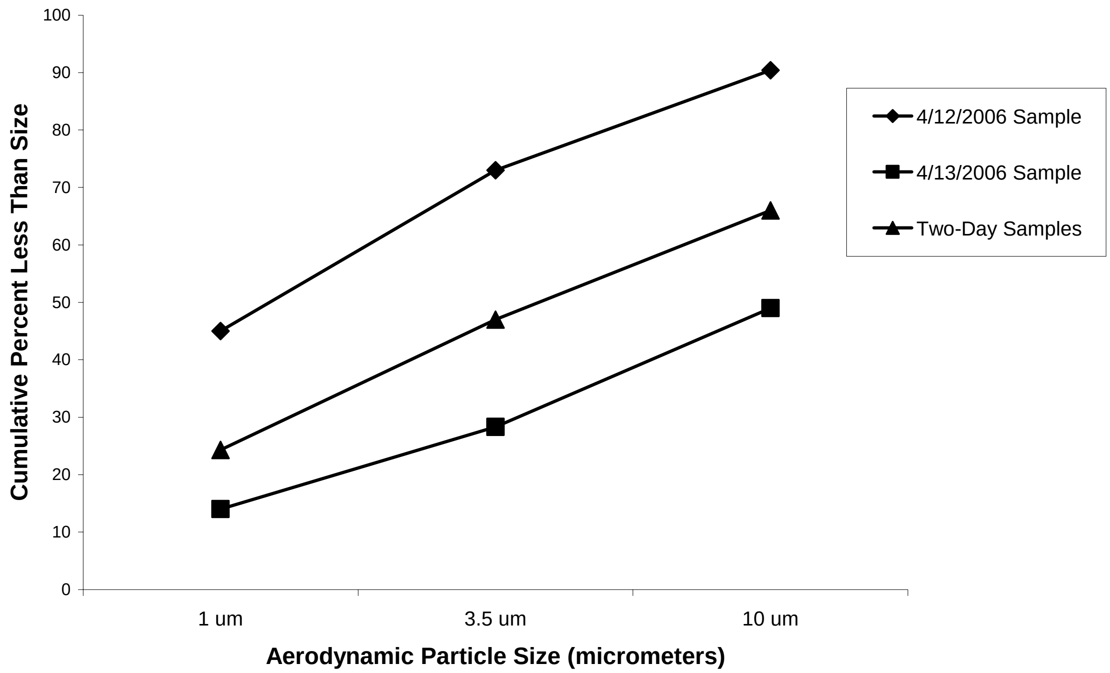
* Real-time concentrations of respirable particles are reported in units of mg/m^3 as determined by optical measures; consequently, these concentrations are not always equivalent to particle concentrations made using gravimetric analyses.

Figure 5-B. Real-time air sampling for respirable dust concentrations on 4/13/2006 with powdered flavor application.



* Real-time concentrations of respirable particles are reported in units of mg/m^3 as determined by optical measures; consequently, these concentrations are not always equivalent to particle concentrations made using gravimetric analyses.

Figure 6. Aerodynamic size distribution of airborne particles during popcorn popping, based on gravimetric analyses



APPENDIX A
Clinical Interpretation of Pulmonary Tests

There are two major categories of lung disease based on ventilatory function—obstructive airways diseases and restrictive lung disease. In obstructive airways disease, airflow through the airways is reduced due to effective narrowing of the airways. Examples of obstructive airways disease include asthma, emphysema, and bronchiolitis obliterans. In restrictive disease, lung volumes are reduced due to scarring, displacement of normal lung tissue by other disease processes, or by neuromuscular weakness, among other causes. Examples of restrictive lung disease include lung diseases associated with connective tissue diseases, silicosis, and coal workers' pneumoconiosis.

Spirometry measures include: forced expiratory volume in one second (FEV_1), the maximal amount of air that can be forcefully exhaled in one second; forced vital capacity (FVC), the maximal amount of air that can be forcefully exhaled; and the forced expiratory flow rate over the middle 50% of the FVC (FEF_{25-75}). Spirometry results are considered consistent with airways obstruction when both the FEV_1 and FEV_1/FVC ratio are below their respective lower limits of normal as expected for an asymptomatic person who has never smoked and who is of the same sex, age, height, and race. Spirometry results are considered consistent with restriction when the FEV_1/FVC ratio is in the normal range and the FVC is below the lower limit of normal. In the absence of results of other tests that can help distinguish between obstruction and restriction, spirometry results are considered consistent with a mixed pattern of obstruction and restriction when both the FEV_1/FVC ratio and the FVC are below their respective lower limits of normal. Airways obstruction that significantly improves with the administration of bronchodilator is consistent with asthma. Airways obstruction that does not resolve with a bronchodilator and a several week course of oral corticosteroids (fixed airways obstruction) is consistent with chronic obstructive pulmonary disease (including emphysema, bronchiolitis obliterans, or, in some cases, long-standing asthma).

Plethysmography measures include: total lung capacity (TLC), the maximal amount of air that the lungs can hold; residual volume (RV), the amount of air that remains in the lungs after a forceful and complete exhalation; and airways resistance (R_{aw}). Lung volumes measured by plethysmography can help distinguish between obstruction and restriction when spirometry results indicate a mixed pattern. A low TLC and low RV are consistent with restriction. A high TLC, high RV, or high RV/TLC ratio suggests trapping of air in the lungs, which is consistent with airways obstruction.

Mildly low TLC and FVC may also be caused by obesity. Obesity is defined as a body mass index (BMI) [calculated as weight in kilograms ÷ (height in meters)^2] greater than or equal to 30.

DLCO measures the transfer of gas from inhaled air into the blood stream. Accurate measurement and interpretation of DLCO is challenging. Generally, in asthma and bronchiolitis obliterans, the DLCO, DLCO corrected for hemoglobin, carboxyhemoglobin and altitude, and the DLCO corrected for lung volume are usually normal. However, as has been observed in affected microwave popcorn workers, some individuals with bronchiolitis obliterans can have low DLCO values. In emphysema and restrictive lung disease, all DLCO values are usually low.

Some abnormalities on chest radiographs include scarring (which is seen in restrictive lung disease), bronchial wall thickening (which can be seen in asthma and bronchiolitis obliterans syndrome), and accentuation of bronchovascular markings (which can be due to inflammation or fluid collection around the airways). Peribronchial inflammation can be caused by asthma and bronchiolitis, and peribronchial fluid collection can be caused by congestive heart failure.

High resolution computed tomography of the chest can show a non-localized (diffuse) increase in airspace or an increase in airspace which is patchy in distribution (mosaic pattern) on the inspiratory views. When present, air trapping is typically more evident on expiratory views. All of these findings are consistent with both severe asthma and bronchiolitis obliterans. However, one hospital study has demonstrated that the presence of a mosaic pattern on the inspiratory view is statistically more likely to be found in patients with bronchiolitis obliterans than in patients with severe asthma.[35]

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