NIOSH HEALTH HAZARD EVALUATION REPORT:

HETA 2002-0408-2915
Agrilink Foods Popcorn Plant
Ridgway, Illinois

October 2003

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 authorize the Secretary of Health and Human Services, following a written request from any employer 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 disease.

Mention of company names or products does not constitute endorsement by NIOSH.

ACKNOWLEDGMENTS AND AVAILABILITY OF REPORT

This report was prepared by Nancy Sahakian, Kyoo Choe, Randy Boylstein, and Patty Schleiff of the RDHETAP, Division of Respiratory Disease Studies (DRDS). Desktop publishing was performed by Terry Rooney. Review and preparation for printing were performed by Penny Arthur.

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Highlights of NIOSH Health Hazard Evaluation

Evaluation of Agrilink Popcorn Plant: Fixed Airways Obstruction and Artificial Butter Flavorings

In September 2002 NIOSH received a Health Hazard Evaluation request from employees at the Agrilink Microwave Popcorn Plant in Ridgway, Illinois who were concerned about respiratory health effects potentially associated with artificial butter flavoring exposure. NIOSH investigated this plant to determine if workers were at risk for respiratory disease from occupational exposure and to identify needed prevention measures.

What NIOSH Did

- We took area air samples from six different plant locations and performed quantitative tests for diacetyl and other volatile organic compounds.
- We took personal breathing zone air samples from workers in eight different job categories and tested these for ketones.
- We administered a computerized health questionnaire to employees.
- We performed spirometry tests and repeated this test and performed lung diffusing capacity for carbon monoxide on workers who had an abnormal spirometry test result.

What NIOSH Found

- Diacetyl concentrations were highest near the mixing tanks and microwave popcorn packaging line, and in the quality control room.
- Diacetyl concentrations varied widely during the two days tested.
- Plant employees, overall, had about a 2 times greater rate of airways obstruction, compared to national rates.
- Plant employees aged 17 to 39 had about a 3 times greater rate of chronic cough, compared to national rates.
- Plant employees aged 40 to 69 who had never smoked had about a 2 times greater rate of shortness of breath, compared to national rates.

What Agrilink Plant Managers Can Do

This plant closed its microwave and plain popcorn packaging operation on January 30, 2003. If the plant reopens, we suggest the following:

- Substitute currently used artificial butter flavorings with products that release lower levels of diacetyl and other volatile organic compounds.
- Enclose and isolate all mixing and nurse tanks and connect tanks to local exhaust ventilation.
- Maintain the mixing tank room under negative pressure relative to the rest of the plant.
- Install local exhaust ventilation for microwave ovens used for quality control testing of product.
- Make respiratory protection mandatory for mixers and quality control workers.
- Obtain baseline spirometry on all new workers.
- Perform spirometry testing every three to four months on mixers, quality control workers, and previously exposed workers (includes microwave popcorn packagers). Remove from exposure and refer for further medical evaluation workers who have newly identified abnormal or rapidly falling lung function.

What Agrilink Employees Can Do

- Plant workers who have been identified as having abnormal spirometry tests should be evaluated for possible work-related lung disease and should have yearly spirometry performed for at least two years.
- Plant workers who had normal spirometry tests should have the test repeated yearly for two years.

CDC Workplace Safety and Health

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 1-513/841-4252 and ask for HETA Report 2002-0408-2915

National Institute for Occupational Safety and Health NIOSH

Health Hazard Evaluation Report 2002-0408-2915
Agrilink Foods Popcorn Plant
Ridgway, Illinois
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SUMMARY

In September 2002, the National Institute for Occupational Safety and Health (NIOSH) received a request for a health hazard evaluation (HHE) from employees at Agrilink Foods Popcorn Plant, Ridgway, Illinois. The respiratory health concerns cited in the request included cough, shortness of breath, and chest pain; and exposure concerns included butter flavorings, coloring agents, and salt.

We conducted a walk-through survey October 22-23, 2002 and an industrial hygiene survey November 5-6, 2002. Average area diacetyl air levels in the mixing tank area, microwave popcorn packaging line, and quality control room were 0.60, 0.33, and 0.19 parts per million parts air by volume, respectively. Average personal diacetyl air levels for the mixer, microwave popcorn packaging line machine operator, and quality control workers were 0.37, 0.64, and 0.06 parts per million parts air by volume, respectively.

On November 19-21, 2002, 35 current workers (73%) participated in health questionnaire interviews and spirometry and lung diffusing capacity testing. Comparisons to national data were performed which controlled for race, age group, and smoking status. These comparisons demonstrated that plant employees aged 17 to 39 had about a 3 times greater rate of chronic cough, and plant employees aged 40 to 69 who had never smoked had about a 2 times greater rate of shortness of breath. We supplemented our 35 spirometry test results with company results for individuals who did not volunteer in our study, and used spirometry tests for 41 workers for our analysis. Plant employees overall and plant employees aged 40 to 69 had about a 2 times greater rate of airways obstruction, compared to national rates. Despite the small number of workers in this study, we were able to demonstrate statistical significance for the elevated airways obstruction rate in workers aged 40 to 69. None of the tested workers with obstruction demonstrated reversibility with the administration of bronchodilator.

The survey findings are best explained by work-related bronchiolitis obliterans due to exposures arising from the open configuration of the mixing tanks which allowed volatile organic compounds (VOCs) to be disseminated to other areas of the plant, as well as due to the quality control process where many bags of microwave popcorn were popped in a small room with minimal general dilution ventilation.

We demonstrated that the prevalence of obstructive lung disease was elevated at this microwave popcorn plant, compared to national rates. Findings in other microwave popcorn plants and animal studies confirm the association of bronchiolitis obliterans, a rare disease of the small airways of the lung, with exposure to artificial butter flavoring agents. Recommendations for engineering controls, use of personal protective equipment, medical surveillance, and medical treatment of affected workers are provided in this report.

Keywords: 2099 (Food Preparations, not elsewhere classified); Bronchiolitis obliterans, Diacetyl, Fixed Obstructive Airways Disease, Chronic Obstructive Pulmonary Disease, Artificial Butter Flavorings, Microwave Popcorn, Popcorn, Flavorings.

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INTRODUCTION

On September 10, 2002 the National Institute for Occupational Safety and Health (NIOSH) received a request for a health hazard evaluation (HHE) from employees at the Agrilink Foods Popcorn Plant, Ridgway, Illinois. The request listed adverse health effects, including cough, shortness of breath, chest pain, headaches, sore throat and rash thought to be due to exposure to butter flavorings, coloring agents, and salt.

NIOSH responded with a walk-through survey on October 22-23, 2002. We conducted an industrial hygiene survey on November 5- 6 and a medical survey on November 19-21. The plant closed in February 2003.

BACKGROUND

NIOSH was first informed of the problem of bronchiolitis obliterans in microwave popcorn plant workers in 2000 when a cluster of 8 cases of former workers at a plant (referred to as the sentinel plant) in Missouri was reported by a physician to the State Department of Health. NIOSH responded by performing a cross-sectional survey and found increased rates of respiratory symptoms and airways obstruction among the current workforce.

The clinical features of the index cases in the sentinel microwave popcorn plant are similar to those of constrictive bronchiolitis, which occurs with chemical exposures. Four of the index cases who have severe disease have been placed on lung transplant waiting lists.[1,2] The main respiratory symptoms include cough (usually without phlegm) and shortness of breath on exertion. Symptoms usually develop gradually but may require only a few months of exposure in some workers. Symptoms generally do not improve much when the worker goes home at the end of the workday or on weekends or vacations. Some affected workers have fever, night sweats, and/or weight loss. Spirometry tests generally show fixed airways obstruction. However, preliminary results from several microwave popcorn plants indicate that restrictive lung disease may also be involved. Some workers show evidence of fixed airways obstruction on spirometry before they develop symptoms of lung disease. Most affected workers have not improved with medical treatment. While most have had less cough months to years after cessation of exposure to butter flavoring, shortness of breath on exertion has persisted.

NIOSH has subsequently investigated the occurrence of this rare lung disease in workers at other microwave popcorn plants. Those investigations, and animal studies conducted at NIOSH, have shown that inhalation of artificial butter flavoring vapors may lead to lung disease under some working conditions. The investigations conducted so far indicate that the highest risk to workers in microwave popcorn production is from mixing room and quality control activities.

The Agrilink Foods Popcorn Plant in Ridgway, Illinois began operation in 1952. Initially they packaged only plain kernel popcorn. Microwave popcorn production began in 1986. At the time of this investigation, the plant employed 48 workers. They had one mixer, two machine operators, one carton placer, two bag placers, 19 general laborers who packaged and packed both microwave popcorn and plain kernel popcorn, three supervisors, two quality control workers, five maintenance and sanitation workers, four fork lift operators who worked primarily in the warehouse, five dump station attendants and process operators, and three office workers who worked in a separate building. Plant operations ran ten hours per day, four days per week.

Popcorn arrives by truck and is air-cleaned after unloading. This operation is overseen by the dump station attendants. The corn is then transferred to the gravity table where it undergoes further air-cleaning. This process is overseen by the process operators. The corn is then transferred, using an air vacuum system, to the plant and is sent either to the microwave popcorn, polyethylene bag, or bulk (10- or 50-pound) packaging lines.

Figure 1A and 1B illustrates the floor plan of the plant. In the polyethylene packaging line (poly line), plain kernel corn is machine-packaged into polyethylene bags. In the 10-pound and 50-pound bulk packaging lines, plain kernel corn is dumped into paper sacks that are then sealed by the worker. After packaging the bags are either packed in boxes or stacked on pallets and wrapped with plastic sheeting, and then transported to the warehouse by a fork lift.

There were three microwave popcorn production lines but only two were currently running at the time of our environmental evaluation. Microwave popcorn was packaged by machines on the lines, with workers overseeing the process. Paper bags are manually loaded at the front of the line by the bag tender. The bags are then pneumatically opened and popcorn kernels are dropped into the bags. A conveyer belt carries the bags further down the line where a nozzle injects heated soybean oil and flavorings into the bag. The machine operator oversees this process. The bag is then automatically sealed, folded in half, and enclosed in a plastic wrap. Three popcorn bags are packed into small consumer-sized boxes by general laborers. Further down the line general laborers hand-pack these microwave popcorn packages into larger boxes. Boxes are stacked on pallets, wrapped with plastic sheeting, transported to the warehouse by a fork lift, and stored until shipping.

Two quality control workers pop plain kernel and microwave popcorn in a small room (approximately 10 feet by 10 feet) on the second floor of the plant, to monitor the quality of the product. Approximately 60 bags of microwave popcorn with artificial flavoring are popped per 10 hour shift. After the microwave popcorn is popped, the bag is opened and its contents are poured into a sieve to count the number of un-popped corn kernels and then the contents are transferred to a tall graduated cylinder to measure the popped corn volume.

Maintenance personnel keep the lines operating and sanitation workers sweep up popcorn kernels that have dropped onto the production floor. Office personnel work in a separate building and visit the microwave production building only occasionally.

The plant produced four varieties (A-D) of microwave popcorn. The particular variety of microwave popcorn that was produced on any particular day depended on shipping schedules. One variety used an oil slurry made up of soybean oil and salt. The other three varieties used an oil slurry consisting of soybean oil, salt, a coloring agent, and one of two different varieties of artificial butter flavorings. One artificial butter flavoring was a paste and the other was a liquid.

Two microwave popcorn packaging lines were running on the first day of the industrial hygiene survey (microwave popcorn flavor A on one line and microwave popcorn flavor B on the second line). Only one line was operated on the second day (microwave popcorn flavor B). Flavor A used the liquid artificial butter flavoring and flavor B used the paste artificial butter flavoring.

Two to three times daily, a combination of salt, butter-flavoring, and coloring agent was added by the mixer to heated soybean oil in two of three approximately 800 gallon mixing tanks by raising the tank lid and pouring in the pre-measured ingredients. At the time of our visits all three tanks were full of heated soybean oil, but only two tanks were being used in production and contained artificial butter flavoring. Mixing was accomplished by a rotating blade inside the mixing tank. The flavored, heated soybean oil was then pumped into three smaller nurse tanks each positioned at the head of a microwave popcorn line.

METHODS

Industrial Hygiene Evaluation

During the walk-through and industrial hygiene surveys, ventilation and air-flow patterns were assessed using smoke tubes (Air Current Kit, Draeger Safety, Inc., Pittsburgh, PA). Temperatures of the soybean oil in the mixing and nurse tanks were measured using an infrared non-contact thermometer (Raynger® ST, Raytek Corp., Santa Cruz, CA).

We obtained 6-hour quantitative and semi-quantitative area air samples on both days of the industrial hygiene survey from six sampling locations in the plant: mixing tank area; bag-tender station on the microwave production packaging line (near the nurse tanks); packing area; poly line; stencil area; and quality control room. The area air samples were analyzed quantitatively for diacetyl, acetoin, 2-nonanone, acetaldehyde, acetic acid, total volatile organic compounds, and total (respirable and non-respirable) and respirable dust, and semi-quantitative analyses were performed to assess the types of volatile organic compounds present in the air.

Ketones (diacetyl, acetoin, and 2-nonanone) were collected on carbon molecular sieve (CMS) tubes at a flow rate of 75 milliliters per minute (mL/min). These ketones were analyzed quantitatively by gas chromatography (GC) according to NIOSH Method 2557.[3] Acetic acid was collected on silica gel sorbent tubes at a flow rate of 500 mL/min and analyzed by high pressure liquid chromatography (HPLC) according to NIOSH Method 7903.[3] Acetaldehyde was collected on XAD-2 tubes at a flow rate of 30 mL/min and analyzed by GC according to NIOSH Method 2018.[3] Total VOCs were collected on charcoal sorbent tubes at a flow rate of 100 mL/min and the samples were analyzed by GC following NIOSH Method 1550.[3] Total dust samples were collected at a flow rate of 2.0 liters/min on closed-face filter cassettes using 37-mm poly vinyl chloride (PVC) filters with a pore size of 5 micrometers (μm). Respirable dust samples were collected at 4.2 liters/min on similar filters with BGI Respirable/Thoracic Cyclones™ (BGI Inc., Waltham, MA). The cyclone cut-off size was 4 μm (this allows most particles smaller than 4 μm in aerodynamic diameter to be collected) for the 4.2 liters/min flow rate. The filters were analyzed gravimetrically according to NIOSH Methods 0500 and 0600,[3] respectively.

Semi-quantitative air samples were collected on thermal desorption tubes at a flow rate of 15 mL/min and were analyzed by gas chromatography with a mass selective detector according to NIOSH Method 2549.[3]

We used three Grimm optical particle counters (OPC) (Grimm Technologies, Inc., Douglasville, GA) to measure real-time airborne particle concentrations and three Q-Traks (TSI Inc., St. Paul, MN) to measure real-time temperature, relative humidity (RH), carbon monoxide (CO), and carbon dioxide (CO_2) from three locations: mixing tank area; poly line area; and stencil area. The Grimm OPC and Q-Trak measurements were over six and eight hour periods, respectively.

We also obtained personal air samples for ketones, using the same sampling method as for area samples, from 10 workers on each of the two days of the survey, for eight different job titles: mixer (also performed packing and fork lift work); machine operator; bag tender; microwave line packager/packer/poly line/bulk packager; maintenance worker; quality control worker; fork lift operator; and stenciler. Sampling times ranged from six to eight hours. Personal air samples were analyzed for diacetyl, acetoin, and 2-nonanone.

The minimum detectable concentration (MDC) was calculated for all industrial hygiene measurements. For values below the MDC, one half of this value was used in the calculation of average values.

Bulk samples of the two butter flavoring agents used by the plant were obtained and analyzed semi-quantitatively. Samples were heated to 50 ºC for 10 minutes and the released organic compounds were measured by gas chromatography with a mass selective detector.

Medical Evaluation

All current employees in all areas of the plant were invited to participate in the survey. After obtaining signed informed consent from participants, NIOSH interviewers administered a standardized questionnaire to collect information on symptoms, medical diagnoses, smoking history, work history at the plant, and work-related exposures. This health questionnaire (Appendix A) included questions abstracted from the American Thoracic Society (ATS) standardized respiratory symptom questionnaire[4] and the 3rd National Health and Nutrition Examination Survey (NHANES III)[5] (Table 1).

Spirometry

NIOSH technicians performed lung function testing with spirometry on all individuals. We used a dry rolling-seal spirometer interfaced to a personal computer and used testing procedures that conformed to the American Thoracic Society's recommendations for spirometry.[6] We chose the largest forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) from a minimum of three trials. We calculated predicted values and lower limits of normal using reference values[7] generated from NHANES III. Test results were compared to the lower limit of normal values to identify participants with abnormal spirometry patterns of obstruction and restriction.[8] We defined obstruction as a FEV1/FVC ratio below the lower limit of normal with a FEV1 also below the lower limit of normal. Borderline obstruction was defined as a FEV1/FVC ratio below the lower limit of normal with a FEV1 lower than predicted but above the lower limit of normal. Restriction was defined as a FVC below the lower limit of normal with a normal FEV1/FVC ratio. Abnormal spirometry was defined as borderline obstruction, obstruction, or restriction. If the spirometry was normal, no further tests were performed. If the spirometry test result was abnormal, we gave a bronchodilator medication to help open the airways (2 puffs of albuterol from a metered dose inhaler) and repeated the spirometry test. If there was substantial improvement in spirometry after the use of the bronchodilator, we determined the lung condition to have a bronchodilator response. Substantial improvement was defined as a 12% increase in the FEV1 of at least 200 mL.

DLCO

If the spirometry test was abnormal, we tested lung diffusing capacity for carbon monoxide (DLCO). This measurement reflects the ease with which a gas passes across the lung tissue and into the bloodstream. We used commercial systems purchased from Jaeger and Medical Graphics and standard guidelines for performing the test.[9] We compared DLCO results to reference values determined from a sample of non-smoking adults from the state of Michigan[10] and defined them as abnormal if the observed DLCO was less than the calculated lower limit of normal.

Spirometry Test Quality Rating

The company had performed spirometry tests on all 47 employees who were present at their Ridgway, Illinois microwave popcorn plant on August 20, 2002. We rated these spirometry tests for quality on an A to F scale, using the 1995 recommendations of the American Thoracic Society.[6] Criteria included reproducibility of curves, absence of cough and hesitation, and an expiration of at least six seconds.

Computed Tomography and Thoracoscopic Lung Biopsy Results

We reviewed medical test results ordered by private physicians on six patients. Computed tomography (CT) films of the chest on five workers and pathology slides from open lung biopsies from four workers were sent to and reviewed by a pulmonary radiologist and a pulmonary pathologist, respectively.

Statistical Analyses

We used computerized questionnaires and program modules provided by the SAS Institute, Inc. for all statistical analyses.[11] Poisson distribution and the Chi-Square and Fisher's Exact tests were used to determine statistical significance. We considered probability (p) values less than 0.05 as statistically significant (i.e., unlikely to be due to chance).

We first performed analyses using NIOSH data alone. In order to achieve a larger sample size and a more representative sample, we repeated the analyses with a combined set of NIOSH's and the company's spirometry test results. We reviewed company spirometry test results for individuals who did not participate in our survey and excluded results that were of unacceptable quality (D or F). Because the smoking status classification on the company spirometry records did not differentiate between never-smokers and current nonsmokers, we only included those who were listed as "Smoker: Yes" (to avoid misclassifying former smokers as never-smokers). We did not include those less than 40 years of age because of the small number of individuals in this category and the small cell numbers this would generate. Participants were categorized as to work history, and their spirometry test results were compared using a crude odds' ratio.

We did side by side comparisons of symptom and medical diagnosis proportions from the sentinel microwave popcorn plant investigated in 2000 and the Agrilink popcorn plant. We repeated the analysis and compared Agrilink workers with normal spirometry to Agrilink workers with borderline obstruction or obstruction on spirometry.

We compared prevalence rates for respiratory symptoms, self-reported medical diagnoses, and obstructive spirometry test results in Agrilink workers to prevalence rates in the 3rd National Health and Nutrition Examination Survey (NHANES III) participants. We compared numbers of workers with the symptom, medical diagnosis, or spirometry obstruction (number observed), to the number expected based on national data from NHANES III (number expected). A ratio of the number observed to the number expected greater than one indicates an increased proportion of disease in Agrilink workers compared to the general public. If the ratio is greater than one and the confidence interval (CI) excludes one, then the difference is statistically significant and we are at least 95% certain that the higher proportion of disease in the workers is not due to chance. All comparisons were controlled for race, age group (17 to 39 years of age versus 40 to 69 years of age), and smoking status (ever-smokers versus never-smokers).

RESULTS

Industrial Hygiene Results

Engineering Controls, Ventilation, and Personal Protective Equipment

Containers of liquid artificial butter flavoring were stored in the warehouse and containers of artificial butter flavoring paste were stored in a storage room cooled by air-conditioning. Butter flavorings and coloring agents were carried as needed to a weighing area where they were poured into a weighing container and blended in another container (using a blender). An oven-range hood was the only ventilation for this operation. The hood was several feet above the scale and was not effective at controlling emissions during the measuring and blending processes. After use, the containers of artificial butter flavoring and artificial coloring were returned to their original locations and the blended mixture was added to the mixing tanks.

Mixing tanks were not enclosed. There were holes on the mixing tank lids which were larger than the pipe diameters currently in use, so that there was no seal. There were one to three open 3-inch diameter holes on each nurse tank lid. The mixing tanks were approximately 35, 30, and 20 feet from the poly line, 10-pound, and 50-pound packaging areas, respectively. Using smoke tubes, we determined that air movement through the plant generally flowed from the mixing tank area across the adjacent microwave production packaging area and up to the third floor where a large exhaust fan was installed. No local exhaust ventilation existed in the mixing tank area or in the quality control room. A general exhaust fan near the mixing tank area drew air from only the surrounding area. The quality control room was approximately 10 feet by 10 feet in size with two doors to the room, which were both kept open. There was a small ceiling general exhaust vent in this room.

Following our walk-through survey, 4-inch PVC pipe was connected to each of the mixing and nurse tank lids to exhaust vapors generated inside the tanks. These pipes were connected to a large industrial fan located on the 2nd floor. This local exhaust ventilation system efficiently exhausted butter flavoring vapors generated inside the mixing and nurse tanks to the outside of the building. Smoke from smoke tubes was drawn into the tanks through the holes in the lid, demonstrating that there was effective negative pressure within this system. This newly installed industrial fan was not operated during our industrial hygiene survey, to better approximate conditions that existed prior to its installation.

Respiratory protection for mixers (air purifying respirators with organic vapor and particulate cartridges) was implemented several weeks before our initial visit.

Environmental Measurements

The temperature of one mixing tank actively in use was 142 degrees Fahrenheit (°F) during the morning of our walk-through survey and 129 °F during the afternoon of our industrial hygiene survey. Other mixing tanks had temperatures of 101 and 134 °F during the morning of our walk-through survey. Nurse tank temperatures ranged from 112 to 132 °F during the morning of our walk-through survey and 106-114 °F during the afternoon of the industrial hygiene survey (Table 2).

The results of semi-quantitative air sampling analyses for VOCs in six areas in the plant for each of the two days sampled showed up to 88 different VOCs. The predominant compounds identified in the mixing area included diacetyl, methyl ethyl ketone (MEK), acetoin, methanol, and ethanol (Figures 2A and 2B). The results of all other areas such as microwave popcorn production line, packing area, poly line, and stencil area showed patterns similar to the mixing area. In the quality control room the predominant compounds included diacetyl, MEK, acetoin, propane, methanol, isobutane, 2-nonanone, tridecane, and tetradecane (Figures 3A and 3B).

Predominant compounds in the butter flavoring bulk sample analyses were diacetyl, acetoin, butyric acid, and 2-nonanone (Figures 4A and 4B).

Area ketone concentrations, in parts per million parts air by volume (ppm), are presented in Table 3. Two ketones, diacetyl and acetoin, which were major constituents of the butter flavorings, had the highest concentration of any of the individually quantified volatile organic compounds. Both of these ketones had levels highest near the mixing tank and in the microwave popcorn packaging area. Diacetyl concentrations varied widely from day 1 to day 2 in all areas of the plant and were higher on day 2. On day 2 the number of microwave popcorn packaging lines was reduced from two to one and only one of the two popcorn flavors that were used the previous day was used. Average diacetyl levels near the mixing tanks, microwave popcorn packaging line, and quality control room were 0.605 ppm, 0.326 ppm, and 0.186 ppm, respectively. 2-nonanone concentrations were below the minimum detectable concentration (MDC) of 0.003 ppm.

Table 4 lists the acetaldehyde, acetic acid, and total volatile organic compound levels in ppm and milligrams per cubic meter of air (mg/m^3), by work area. The concentrations of these chemicals varied substantially from day 1 to day 2 and by work area. Average acetaldehyde concentrations for the packing area, quality control room and poly line were 0.730, 0.194, and 0.136 ppm. Average acetic acid concentrations for the microwave packaging line, quality control room, and poly line were 0.234, 0.224, and 0.439 ppm, respectively.

Personal diacetyl measurements (Table 5) showed sizable daily variation with higher levels on day 2, except for the general laborer, quality control worker, and fork lift operator categories. General laborers rotated between three to four jobs (microwave popcorn line packaging, packing, poly line, and 10-pound bulk packaging). Average personal diacetyl levels for bag tender, quality control worker, and stenciler were 0.358, 0.064, and 0.026 ppm, respectively, compared to average area diacetyl levels of

0.326, 0.186, and 0.014 ppm. All levels for 2-nonanone were below the MDC.

Table 6 compares average area diacetyl levels at the Agrilink plant during our November 2002 survey with levels at the sentinel plant during the initial November 2000 and subsequent November 2001 surveys. Between these two test dates, the sentinel plant enclosed the mixing tanks in a separate room and installed local exhaust ventilation from the tanks to the outside.

Average total dust (particles collected with no size-selective device other than the filter cassette), and respirable dust (particles collected on filters through cyclones with a 50% cut at 4 μm) were measured. Gravimetrically measured average total dust levels were highest in the mixing tank area. The average total dust levels in the mixing tank area, microwave packaging line, quality control room, and poly line were 1.10, 0.75, 0.59, and 0.49 mg/m^3, respectively. The average respirable dust level (measured gravimetrically) was highest in the quality control area (0.62 mg/m^3) with levels in the mixing tank area and microwave packaging line, of 0.48 and 0.42 mg/m^3, respectively (Table 7).

Real-time concentrations of coarse and respirable airborne particles monitored with the Grimm OPCs are illustrated in Figures 5A and 5B. (Coarse particles here are defined as particles having an optical diameter of 4 to 20 μm and respirable particles are defined as particles having an optical diameter of 0.4 to 4 μm.) Coarse and respirable particles remained constant throughout most of the day, but varied by work area. The concentrations of coarse particles were highest in the poly line, intermediate in the mixing area, and lowest in the stencil area (Figure 5A). Respirable particle concentrations were highest in the mixing area (probably due to the oil mist or vapors generated from the mixing and nurse tanks), intermediate in the poly line, and lowest in the stencil area (Figure 5B).

The temperature inside the plant in the three monitored areas (mixing tank area, poly line area, and stencil area) remained generally between 65 and 78 ^{o}F with a number of abrupt changes in the temperature (Figure 6). Average temperature in the mixing area was slightly higher than in other monitored areas (Table 8). The downward peaks in Figure 6 may be due to occasional opening of the overhead delivery door adjacent to the mixing tanks, and the upward peak in the stencil area may be due to the heat from the fork lift exhaust. The relative humidity (RH) in the three monitored areas generally remained within the 30 to 60% RH range recommended by the American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE)[12] (Figure 7).

Carbon monoxide levels in the monitored areas continuously increased during the morning, peaked at about 10:30 AM, and then decreased very slowly until the end of the work day (Figure 8). The downward peaks in carbon monoxide concentration may be due to occasional opening of the overhead delivery door adjacent to the mixing tanks and the upward peak in the stencil area may be due to fork lift exhaust gas. Average carbon monoxide levels were highest in the poly line, intermediate in the stencil area, and lowest in the mixing area, with a range from 22 to 34 ppm (Table 8). Measured CO levels in the boiler room were as high as 300 ppm. Management was made aware of this elevated CO measurement and was advised to have the boiler checked for leaks. Carbon monoxide levels in the poly line and stencil area were generally below the Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) time-weighted-average (TWA) of 50 ppm but close to or higher than the NIOSH recommended exposure limit (REL) and American Conference of Governmental Industrial Hygienists (ACGIH®) threshold limit value (TLV®) TWAs of 35 and 25 ppm, respectively. [The OSHA PEL and ACGIH® TLV® TWAs are calculated for an 8-hour day, 40 hour week. The NIOSH REL TWAs are calculated for a 10-hour day, 40 hour week]. The main sources of the carbon monoxide were thought to be the fork lifts (which frequently operated in the poly line and stencil area) and the boiler room. Carbon dioxide levels (Figure 9) remained below the OSHA PEL, NIOSH REL, and ACGIH TLV of 5000 ppm with the exception of a single peak in the stencil area, in addition, for the majority of the time the carbon dioxide levels were below the ASHRAE recommended limit for the indoor office environment of 1000 ppm.[12] Average carbon dioxide levels for the three monitored areas ranged from 726 to 809 ppm (Table 8).

Medical Results

Participation

Thirty-five of 48 (73%) current plant employees participated in the survey. This included 29 of 35 (83%) workers currently working on the production floor or in the quality control area, and 6 of 13 (46%) workers currently working in all other areas of the plant.

Symptoms and Physician Diagnoses

Table 9 describes the current workers in terms of age, gender, smoking status, smoking history, number of years worked in the plant, and whether they ever worked in quality control or in mixing. Table 10 contains numbers and percentages of current workers who reported respiratory and non-respiratory symptoms and physician diagnoses.

When compared to expected rates generated from national NHANES III data, plant employees aged 17 to 39 had a 2.9 times greater rate of chronic cough (Table 11). Employees aged 40 to 69 who had never smoked had a 2.5 times greater rate of shortness of breath, when compared to national data. Statistical significance was not achieved in these two comparisons.

Table 12 compares prevalence rates of selected respiratory symptoms ("chronic cough", "shortness of breath compared to others", and "wheeze during the last 12 months, not associated with a cold"), medical diagnoses ("chronic bronchitis" and "asthma"), and obstruction on spirometry in Agrilink workers with rates in the sentinel plant[1,2,13,14] that NIOSH investigated in 2000. Prevalence rates for obstruction on spirometry were comparable between the two plants. However, prevalence rates for listed respiratory symptoms and medical diagnoses were consistently lower among Agrilink workers.

Table 13 compares symptom and medical diagnosis prevalence rates in workers with borderline obstruction or obstruction to workers with normal spirometry. Shortness of breath and wheezing were found in 67% and 33%, respectively, of workers with borderline obstruction or obstruction on spirometry compared to 26% and 11%, respectively, of workers with normal spirometry. Other symptoms had comparable rates.

Spirometry Abnormalities

Using NIOSH spirometry results (replacing one spirometry test result that was of poor quality in our study with the company acceptable-quality test for that individual), eight out of 35 workers (23%) had abnormal spirometry test results: six out of 35 (17%) had borderline obstruction or obstruction, and two out of 35 (6%) had restriction. When we used a combined set (as defined in the methods section) of NIOSH and company spirometry test results, 11 out of 41 (27%) had abnormal spirometry test results: nine out of 41 (22%) had a borderline or obstructive pattern, and two out of 41 (5%) had a restrictive pattern. Eight out of 41 (20%) of Agrilink workers had an obstructive pattern on spirometry compared to 18% of all workers at the Sentinel plant.

Table 14 includes the analysis of 35 spirometry test results NIOSH performed and six performed by the company. We found 2.1 times more cases of airways obstructive among Agrilink workers aged 40 to 69, than would be expected based on national data. For Agrilink workers aged 40 to 69 who were ever-smokers there was a 2.2 times higher rate of airways obstruction, compared to national data. For Agrilink workers overall, there was a 1.6 times higher rate of airways obstruction, compared to national data. The first two comparative ratios were statistically significant.

No statistically significant difference in rates of disease was demonstrated when workers with restrictive disease or workers with any spirometry abnormality were compared to national averages (data not displayed).

Spirometry Abnormalities in Workers Who Worked in Different Areas of the Plant

Table 15 shows that two out of nine (22%) workers who reported having worked in quality control, presently or at some time in the past, had obstructive spirometry test results compared to three out of 25 (12%) workers who never worked in quality control. Workers with obstruction were 2.1 times more likely to have ever worked in quality control than to never have worked in quality control, but this difference was not statistically significant.
Of the 8 workers who reported having worked as mixers and/or mixing tank cleaners, none had obstructive spirometry test results.

Reversibility with Bronchodilator and Diffusing Capacity Results

Of the six workers with borderline obstructive or obstructive spirometry test results on NIOSH testing, five were given bronchodilator. None improved with this treatment. Lung diffusing capacity test results were normal for four of these six workers. Lack of substantial improvement in spirometry with bronchodilator and a normal diffusing capacity supports a diagnosis of bronchiolitis obliterans. However, because individuals with advanced bronchiolitis obliterans may have a decreased diffusing capacity, a low diffusing capacity does not exclude bronchiolitis obliterans as a possible diagnosis.

For the two workers with a restrictive pattern, their DLCO's were both 58% of predicted, their estimated total lung capacities were 59% and 72% of predicted, respectively. Their body mass indices were 22.3 and 19.0 kg/m^2, respectively, suggesting that their restriction was not due to their being overweight.

Computed Tomography (CT) and Thoracoscopic Biopsy Results

Of the five workers for whom we had computed tomographic (radiologic) films, only two had complete studies (both inspiratory and expiratory views, high resolution technique, and thin sections). One out of the two CTs showed diffuse air trapping. Radiological findings included diffuse air trapping (1 worker), possible or probable air trapping (2 workers), emphysema (1 worker), cylindric bronchiectasis (1 worker), and possible bronchiectasis (1 worker).

We received lung biopsy specimens on four workers. Results showed constrictive bronchiolitis (1 worker); granuloma (1 worker); chronic fibrous pleuritis (2 workers); and respiratory bronchiolitis which is commonly seen in smokers (4 workers, all who were current or prior smokers).

DISCUSSION

Nature of the Disease

Bronchiolitis obliterans is a lung disease characterized by inflammation and scarring of the small airways of the lung which can lead to severe, permanent shortness of breath. Known work-related causes include inhalation of nitrogen dioxide, silo gases, ammonia, chlorine, hydrogen fluoride, ozone, phosgene, fly ash, and sulfur dioxide.[15] In occupational settings, an incident of overexposure often results in severe initial symptoms of pulmonary edema, followed by apparent recovery. Persistent shortness of breath occurs weeks later due to bronchiolitis obliterans. Bronchiolitis obliterans has also been reported in cases of hypersensitivity pneumonitis in work settings with aerosols of micro-organisms or chemicals to which workers become sensitized. Apart from work-related exposures, most bronchiolitis obliterans cases are due to bone marrow or lung transplants. When bronchiolitis obliterans develops insidiously, as in the case of post-transplant patients, there are no respiratory symptoms during the early stages of disease; however lung function tests will be abnormal. As the lung function test abnormalities worsen, respiratory symptoms appear. Lung function tests typically show obstruction (a low FEV1/FVC and a low FEV1) that does not improve with use of an inhaled bronchodilator. In moderate to severe disease, increased residual volume may occur. The chest x-ray is usually normal, but a high resolution lung computerized tomography with inspiratory and expiratory views may show nonhomogeneous aeration on the expiratory view. The diagnosis may also be demonstrated by lung biopsy, but the process is patchy in distribution. It is only with great care, special stains, and the examination of many biopsy sections that the typical lesion can be identified. Because the process of obtaining the tissue is invasive and the yield is not certain, it is not reasonable to require a tissue diagnosis solely to confirm a case. Thus, the diagnosis of bronchiolitis obliterans is suspected when the clinical history includes one of the known causes, the more common lung diseases are ruled out, and the above lung function abnormalities are present. Known causes now include flavoring chemicals.[1,2,13,14,16]

CT findings of bronchial wall thickening were seen in 8 out of 8 index cases in the sentinel plant and 0 out of 5 Agrilink plant workers (who were both medically evaluated and allowed us assess to their medical records). Diffuse air trapping was seen in 8 out of 8 index cases in the sentinel plant and 3 (possibly) out of 5 of the Agrilink plant workers. Cylindric bronchiectasis was seen in 5 of 8 index cases in the sentinel plant and 1 of 5 the Agrilink plant workers.

Pathology findings of bronchiolitis (constrictive bronchiolitis, fibroblastic proliferation within the bronchiolar lumen, or chronic bronchiolitis) were seen in 2 out of 3 index cases in the sentinel plant and 2 out of 4 of the Agrilink plant workers (who were both medically evaluated and allowed us assess to their medical records). Granuloma were seen in 2 of 3 index cases in the sentinel plant and 1 of 4 the Agrilink plant workers.

Excessive Rates of Obstructive Lung Disease Compared to National Data

Our analyses revealed a 20% prevalence of obstruction in the workforce of this plant. Since only 15% of adult smokers over age 45 develop chronic obstructive pulmonary disease, and 80% of this workforce smoked, we would expect at most only 12% to have obstruction due to smoking.

Our predicted values for spirometry were inherently corrected for height, age, gender, and race. These same prediction equations were used on spirometry data from our comparison group of NHANES III participants. We further controlled the comparison by controlling for race, age group, and smoking classification. Thus we are confident that an excess of lung disease exists at this plant that is due to occupational exposures.

We identified 8 out of 41 workers who may possibly have bronchiolitis obliterans, based on airways obstruction on spirometry. Three of these individuals had chest CT scans with possible, probable, or definite diffuse air trapping, a finding seen with bronchiolitis obliterans. One other individual (with borderline airways obstruction) had a lung biopsy which demonstrated bronchiolar submucosal fibrosis, which is consistent with constrictive bronchiolitis. Another individual (with a restrictive lung disease) had a CT scan which showed possible basal bronchiectasis. All totaled, we suspect that 10 out of 41 workers may have bronchiolitis obliterans.

Volatile Organic Compound and Dust Exposures

Mixing and nurse (holding) tank temperatures are critical in controlling the amount of volatile organic compounds, including diacetyl, released into the air. The mixing and nurse tank temperatures varied widely at this plant and were shown to exceed the temperature necessary to keep the soybean oil fluid. This would have liberated more of the butter flavoring vapors into the air than would have occurred at a lower temperature. The tank temperatures were higher during our walk-through survey compared to our subsequent industrial hygiene survey. The higher temperatures may be more typical of what were normal historical operating temperatures. The plant had a capacity of running three microwave popcorn packaging lines. Only 1-2 lines were operating at the time of our industrial hygiene survey. Given the fewer number of lines and the lower tank temperatures at the time of our industrial hygiene survey (compared to at the time of our walk-through survey), the volatile organic compound levels we measured may underestimate true historical exposure levels.

The lack of enclosure of the mixing and nurse tanks, holes in the lids of these tanks, and close proximity of the tanks to work stations would have increased production line worker exposure to butter flavoring vapor. Lack of enclosure of the mixing tanks and limited time functioning as a mixer may have decreased exposure of the mixer. The process of blending the flavoring and coloring agents in an open bucket in the weighing room, which had inadequate ventilation, and the only recent use of respiratory protection during the mixing process would have resulted in higher exposures to the mixer than would have occurred had the blending operation been performed in a closed container, local exhaust ventilation been present in the weighing room, and respiratory protection been implemented sooner.

The temperature of the oils and popcorn kernels inside a freshly popped bag of microwave popcorn will greatly exceed the 100 to 140 ^{o}F temperature the soybean oil is maintained at in the mixing and nurse tanks. Because of this temperature difference, it is reasonable to expect that the spectrum of chemicals released during the microwave process in the quality control room is different than that near the mixing tanks and microwave popcorn packaging lines. Hence, diacetyl and acetoin levels may not adequately predict risk in quality control workers who were at increased risk for disease at the sentinel plant.

The levels of acetaldehyde detected were far below the OSHA PEL of 200 ppm as an 8-hour TWA. However because acetaldehyde is a potential occupational carcinogen, NIOSH recommends that levels not exceed the lowest feasible concentration. Acetic acid levels were below the OSHA PEL, NIOSH REL, and ACGIH® TLV® of 10 ppm (as 8-hour and 10-hour TWAs). Exposure limits for diacetyl and acetoin have not been established by NIOSH, OSHA, or ACGIH®. 2-Nonanone levels were below the minimal detectable concentration.

Concentrations of total and respirable particulates in the Agrilink popcorn plant, measured gravimetrically and estimated with Grimm OPC data, were well below the OSHA PELs (8-hour TWA) for particulate dust (that is not otherwise regulated) and respirable dust which are 15 mg/m^3 and 5 mg/m^3, respectively.

Causation

Diacetyl is the major ketone present in artificial butter flavoring. It is a volatile ketone with a buttery flavor. We measured it as a marker of artificial butter flavoring vapor exposure. The hypothesis that artificial butter flavoring causes fixed airways disease, and more specifically bronchiolitis obliterans, is supported by the NIOSH Health Hazard Evaluation of a company that produced flavored corn starch for the baking industry.[17] One of the two young workers in that plant who developed bronchiolitis obliterans suspected cinnabutter as the cause. Investigations at other microwave popcorn plants, including the sentinel plant, have identified fixed airways disease in a number of workers. Several of these workers have had lung biopsies performed which demonstrate bronchiolitis obliterans. The NIOSH investigation at the sentinel plant demonstrated a statistically significant correlation between cumulative diacetyl exposure and rates of obstructive lung disease.

During the November 2000 survey at the sentinel plant, five of the six quality control workers had airways obstruction. Those with airways obstruction were 37 times more likely to work in quality control and 11 times more likely to work as mixers than those without airways obstruction (when controlled for cigarette smoking and age). At Agrilink, those with airways obstruction were 2.1 times more likely to have ever worked in quality control than those without airways obstruction (we did not control for cigarette smoking and age due to the small numbers) and none of the workers who had ever mixed had airways obstruction. We cannot explain the lack of disease in ever-mixers at Agrilink as due to a lower level of ketone exposure because personal air sampling showed that the diacetyl and acetoin exposure of mixers was approximately two to five times greater than for the quality control workers. The absence of disease in this group of workers may more accurately reflect the healthy worker effect, where workers with respiratory symptoms leave employment where there are respiratory irritants and healthy, unaffected workers remain, or where workers with lung disease leave physically demanding jobs and healthy workers remain.

Inhalation studies at NIOSH, using both artificial butter flavoring[18] and diacetyl alone, resulted in damage to respiratory epithelium in the airways of rats.

Limitations

We used a cross-sectional study design which is unable to determine whether exposure preceded the demonstrated lung disease. Had we been able to follow workers from the time they were hired onward (a longitudinal study), we would be better able to conclude that the exposure to butter flavoring caused lung disease in these workers.

This study involved relatively small numbers of workers, even with an 85% participation rate for spirometry testing. Workers had multiple current and former jobs at the plant which made exposure assessment difficult. We compensated for both of these limitations by considering all the workers at the plant and using an external comparison group. Although the small numbers made it more difficult to prove an association between workplace exposure and disease, we were able to demonstrate an increased rate of airways obstruction at this work site, compared to national rates.

Exposure assessment was limited by lack of historical data, lack of peak exposure measurements for mixers during weighing and mixing activities, and the small number of environmental measurements.

CONCLUSIONS

Workers at Agrilink Foods have approximately a two times greater risk of airways obstruction than the general public when race, age, and smoking history are taken into account. Even though statistical significance is difficult to achieve in studies involving small numbers of people, we were able to show statistical significance in this risk calculation. The likelihood that the excess is due to chance is less than 5%.

No reversibility was demonstrated in any workers with borderline obstruction or obstruction, making obstruction due to asthma unlikely. Four workers with borderline obstruction or obstruction had a normal diffusing capacity, making lung disease due to bronchiolitis obliterans more likely in these four individuals. Three workers had air-trapping or possible or probable air-trapping on CT and one worker had cylindric bronchiectasis, both possibly associated with bronchiolitis obliterans. One worker had constrictive bronchiolitis on lung biopsy. Another worker had a granuloma on lung biopsy, possibly due to hypersensitivity pneumonitis.

Average diacetyl concentrations in the mixing tank area (0.60 ppm) and microwave popcorn packaging line (0.33 ppm) were slightly higher to three fold higher than respective levels at the sentinel plant during November 2001. (Mixing tanks were enclosed in a separate room and ventilated to the outdoors at the sentinel plant prior to November 2001)

Studies at other microwave popcorn plants confirmed a relationship between inhalational exposure to butter flavoring agents and airways obstruction. In the Agrilink and the sentinel plants, where there was a lack of isolation of the mixing and storage tanks, there were similar rates of airways obstruction. Animal studies, which demonstrate respiratory epithelial damage in animals exposed to butter flavoring agent vapors, also support an association between butter flavoring agents and respiratory disease.

RECOMMENDATIONS

We make the following recommendations based on the understanding that the Agrilink Foods popcorn plant has closed all microwave popcorn production:

1. All workers should have their spirometry test repeated yearly for the next two years. Workers who currently have abnormal spirometry test results and other workers who later develop a decline in the their lung function should be evaluated by their physicians for occupational lung disease, should be followed by their physicians, and should receive influenza and pneumococcal vaccinations.

2. Former workers, who have not had a spirometry test within two years of leaving employment at the plant, should have this performed. If this test is abnormal, they should be followed by their physicians and should receive influenza and pneumococcal vaccinations. Whether normal or abnormal, the spirometry test should be repeated yearly up to two years from the time that they stopped working at the plant.

If the Agrilink Foods popcorn plant reopens its microwave popcorn production in the future, we would make the following recommendations:

1. Engineering Controls:

- Substitute currently used artificial butter flavorings with products which release lower levels of diacetyl and other volatile organic compounds.
- Enclose or isolate all flavor mixing and holding (nurse) tanks in a separate room, utilizing maximal local exhaust ventilation and an airlock system or double door. Maintain this room under negative pressure relative to the rest of the plant.
- Engineer the addition of flavorings to the mixing tanks as a closed transfer, reducing worker contact with open flavorings and the need for respiratory protection during this activity.
- Install local exhaust ventilation in the measuring room and quality control area (microwave ovens), install a vertical sash in front of the microwave ovens and all testing operation areas, and keep the area behind the sash under negative pressure with respect to the rest of the room. Have quality control workers wait until microwave popcorn bags cool, before opening.
- Minimize dust dispersion by using high efficiency particulate air (HEPA) vacuums instead of dry sweeping when cleaning floors. Avoid spills and promptly clean up when spills occur.
- Replace propane-powered fork lifts with battery-powered fork lifts, to eliminate CO sources inside the plant. Replace the supply fan in the boiler room with an exhaust fan to reduce CO concentration in this room.
- Repeat an industrial hygiene survey following the implementation of the above outlined measures.

2. Respiratory Protection:

- Begin a respiratory protection program for all respirator users to include a written program, medical evaluation, fit testing, cartridge change protocol, and training on proper respirator use and maintenance and on the nature of the health hazard. This respiratory protection program should meet the requirements of the OSHA respiratory protection standard (29 CFR 1910.134).
- Require mandatory use of a NIOSH-certified air-purifying or a supplied air (air line) respirator for mixers and quality control workers. If an air-purifying respirator is chosen, the respirator should be equipped with organic vapor cartridges and particulate filters and be a half- or full-facepiece negative pressure respirator or a powered air-purifying respirator (PAPR). If a half-facepiece respirator is used, then goggles should be worn by

mixers to provide eye protection. Mixers should use respiratory protection when handling open containers of flavorings, when entering rooms where flavorings are stored, when entering the mixing room, or when working on the nurse tanks. Quality control workers should use respiratory protection when in the quality control rooms.

3. 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 their spirometry technician has attended a NIOSH certified spirometry course, and that routine calibrations of their spirometer are performed as recommended by the American Thoracic Society.
- Perform spirometry tests every 3-4 months on mixers, quality control workers, and previously exposed workers (prior mixers and quality control and microwave packaging line workers). This will identify workers with rapidly falling lung function who should receive more intense surveillance, education on health effects of artificial flavorings, and who should be removed from further exposure.
- Encourage mixers and quality control and production floor workers to report respiratory symptoms to the person responsible for worker safety in the plant.
- 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 measures to prevent further injury or progression, including respiratory protection and relocation or exposure restriction.

4. Continued Communication with NIOSH:

- Contact NIOSH if the microwave popcorn line is restarted so that we can update you on medical and environmental surveillance recommendations.

REFERENCES

1. Kreiss K, Gomaa A, Kullman G, et al. [2002]. Clinical bronchiolitis obliterans in workers at a microwave-popcorn plant. N Engl J Med 347 (5):330-338.

2. Akpinar-Elci M, Kanwal R, Kreiss K [2002]. Bronchiolitis obliterans syndrome in popcorn plant workers [Abstract]. Am J Respir Crit Care Med 165:SupplA526.

3. NIOSH [1994]. NIOSH manual of analytical methods (4th edition). Washington, DC: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. Publication No. 94-113.

4. Ferris BG [1978]. Epidemiology standardization project. Am Rev Resp Dis 118 (6 Pt 2):1-53.

5. CDC [1996]. Third National Health and Nutrition Examination Survey, 1988-1994, NHANES III Examination Data File [CD-ROM]. Hyattsville, Maryland: U.S. Department of Health and Human Services, Public Health Service, CDC. (Public use data file documentation No. 76300.)

6. American Thoracic Society [1995]. Standardization of spirometry: 1994 update. Am J Resp Crit Care Med 152:1107-1136.

7. Hankinson JL, Odencrantz JR, Fedan KB [1999]. Spirometric reference values from a sample of the general U.S. population. Am J Resp Crit Care Med 159:179-187.

8. American Thoracic Society [1991]. Lung function testing: selection of reference values and interpretive strategies. Am Rev Resp Dis 144:1202-1218.

9. American Thoracic Society [1995]. Single-breath carbon monoxide diffusing capacity: recommendations for a standard technique – 1995 update. Am J Resp Crit Care Med 152:2185-2198.

10. Miller A, Thornton JC, Warshaw R, et al. [1983]. Single-breath diffusing capacity in a representative sample of the population of Michigan, a large industrial state. Am Rev Resp Dis 127:270-277.

11. SAS Institute, Inc. [1999]. SAS/STAT User's Guide, version 8. Cary, NC: SAS Institute, Inc.

12. ASHRAE [2001]. Ventilation for acceptable indoor air quality. American Society of Heating, Refrigerating, and Air-Conditioning Engineers. Atlanta, GA:ASHRAE 62-2001.

13. Simoes E, Phillips P, Maley R, et al. [2002]. Fixed obstructive lung disease in workers at a microwave popcorn factory – Missouri, 2000-2002. MMWR 51 (No. 16): 345-347.

14. Parmet AJ, Von Essen S [2002]. Rapidly progressive, fixed airway obstructive disease in popcorn workers: a new occupational pulmonary illness? J Occup Environ Med 44:216-218.

15. King TE [1998]. Bronchiolitis. In: Fishman AP, ed. Fishman's pulmonary diseases and disorders. New York, NY: McGraw-Hill, pp. 825-847.

16. Lockey J, McKay R, Barth E, et al. [2002]. Bronchiolitis obliterans in the food flavoring manufacturing industry [Abstract]. Am J Respir Crit Care Med 165:Suppl:A461.

17. NIOSH [1986]. Health hazard evaluation and technical assistance report: International Bakers Services, Inc., South Bend, Indiana. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 85-171-1710.

18. Hubbs AF, Batelli LA, Goldsmith WT, et al. [2002]. Necrosis of nasal and airway epithelium in rats inhaling vapors of artificial butter flavoring. Toxicol Appl Pharmacol 185:128-135.

Table 1. Questions used to define symptoms and diagnoses in Agrilink survey (November 2002) compared to the sentinel plant survey (November 2000) and the American Thoracic Society – Division of Lung Disease (ATS-DLD) and NHANES III questionnaires.

Health Condition	Agrilink Survey	Sentinel Survey	ATS-DLD	NHANES III
Shortness of breath	Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?		13A Are you troubled by shortness of breath when hurrying on the level or walking up a slight hill?	L5 Same question as Agrilink survey
Shortness of breath compared to others	Are you troubled by shortness of breath when walking with people of your own age on level ground?	Same question as Agrilink survey	13B Do you have to walk slower than people of your age on the level because of breathlessness?	
Regular trouble breathing	During the last 12 months have you had any trouble with your breathing but it always gets completely better?			
Chronic cough	Do you usually cough on most days for 3 consecutive months or more during the year?	Same question as Agrilink survey	7E Do you usually have a cough like this on most days for 3 consecutive months or more during the year?	L1 Same question as Agrilink survey
Wheezing in chest	During the last 12 months, have you had (this) wheezing or whistling in your chest when you did not have a cold?	Same question as survey		L6 Have you had wheezing or whistling in your chest at any time in the past 12 months
Episodes of bronchitis	Since working at this plant, have you ever had attacks of bronchitis and was it confirmed by a doctor?		17B Have you ever had attacks of bronchitis and was it confirmed by a doctor?	
Chronic bronchitis	Have you ever had chronic bronchitis and was it confirmed by a doctor?	Same question as Agrilink survey	18C Same question as Agrilink survey	
Asthma	Have you ever had asthma and was it confirmed by a doctor?	Same question as Agrilink survey	20C Same question as Agrilink survey	C1e Has a doctor ever told you that you had asthma?

Table 2. Mixing and nurse tank temperatures in degrees Fahrenheit, Agrilink and sentinel plants.

Type of Tank	Agrilink (°F)		Sentinel Plant (°F)
	Oct 22, 2003	**Nov 5, 2003**	**March 2002**
Nurse Tank Temperature	#1 117 #2 132 #3 112	#1 106 #3 113-114	112-125
Mixing Tank Temperature	#1 142 #2 134 #3 101	#1 129	129-130

Table 3. Ketone concentrations in parts per million parts air by volume (ppm) in six work areas, Agrilink, November 5 and 6, 2002.

Sampling Location	**Diacetyl** (ppm)			**Acetoin** (ppm)		
	Day 1	**Day 2**	**Average**	**Day 1**	**Day 2**	**Average**
Mixing Tank Area	0.337	0.874	0.605	0.226	0.349	0.288
Microwave Packaging Line	0.242	0.411	0.326	0.154	0.206	0.180
QC Room	0.102	0.270	0.186	0.123	0.172	0.148
Poly Line	0.063	0.126	0.095	0.061	0.061	0.061
Packing Area	0.004	0.137	0.071	0.050	0.075	0.063
Stencil Area	ND	0.027	0.014	0.021	0.026	0.023

ND: not detectable
Minimum detectable concentrations for diacetyl and acetoin were 0.003 ppm.
All 2-nonanone concentrations were below the minimum detectable concentration of 0.003 ppm.

Table 4. Concentrations of acetaldehyde, acetic acid, and total volatile organic compounds in parts per million parts air by volume (ppm) and milligrams per cubic meter of air (mg/m^3) in six work areas, Agrilink, November 5 and 6, 2002.

Work Area	**Acetaldehyde** (ppm)			**Acetic Acid** (ppm)			**Total VOCs** (mg/m^3)		
	Day 1	**Day 2**	**Avg.**	**Day 1**	**Day 2**	**Avg.**	**Day 1**	**Day 2**	**Avg.**
Mixing Tank Area	ND	ND	0.009	0.129	0.249	0.189	3.056	1.722	2.389
Microwave Packaging Line	0.139	ND	0.074	0.129	0.339	0.234	3.333	3.056	3.194
QC Room	0.139	0.248	0.194	0.181	0.268	0.224	11.667	1.397	6.532
Poly Line	0.108	0.164	0.136	0.656	0.222	0.439	2.139	2.389	2.264
Packing Area	1.295	0.164	0.730	0.102	0.271	0.187	1.694	1.972	1.833
Stencil Area	0.072	0.144	0.108	ND	0.226	0.116	1.028	1.111	1.069

Avg.: average ND: Not detectable.
Minimum detectable concentrations for acetaldehyde, acetic acid, and total VOCs were 0.018 ppm, 0.011 ppm, and 0.125 mg/m^3, respectively.

Table 5. Ketone personal air sampling measurements in parts per million parts of air by volume (ppm), by day sample obtained, for workers with eight different job titles, Agrilink, November 5 and 6, 2002.

Job Titles	Number of Workers	Diacetyl		Acetoin	
		Average	Daily Values	Average	Daily Values
Mixer/ Packer/ Forklift Operator	1	0.371	(11/5) 0.371	0.237	(11/5) 0.237
Machine Operator	2	0.640	(11/5) 0.328 (11/6) 1.183 (11/6) 0.408	0.283	(11/5) 0.169 (11/6) 0.501 (11/6) 0.180
Bag Tender	1	0.358	(11/5) 0.330 (11/6) 0.386	0.176	(11/5) 0.177 (11/6) 0.174
General Laborer (Microwave Line, Packer, 10-Pound Bulk Packager, Poly line Worker)	3	0.081	(11/5) 0.073 (11/5) 0.152 (11/5) 0.090 (11/6) 0.070 (11/6) 0.063 (11/6) 0.040	0.059	(11/5) 0.072 (11/5) 0.094 (11/5) 0.065 (11/6) 0.038 (11/6) 0.039 (11/6) 0.047
Maintenance	1	0.092	(11/5) 0.054 (11/6) 0.130	0.070	(11/5) 0.071 (11/6) 0.068
Quality Control	1	0.064	(11/5) 0.110 (11/6) 0.017	0.099	(11/5) 0.107 (11/6) 0.091
Forklift Operator	1	0.002	(11/5) ND (11/6) ND	0.005	(11/5) 0.008 (11/6) ND
Stenciler	1	0.026	(11/5) 0.016 (11/6) 0.037	0.024	(11/5) 0.026 (11/6) 0.023

ND: Not detectable.
Minimum detectable concentration for diacetyl and acetoin was 0.003 ppm.
All 2-nonanone concentrations were below the minimum detectable concentration of 0.003 ppm.

Table 6. Comparison of average area diacetyl concentrations in parts per million parts of air by volume (ppm) in three work areas in the Agrilink and sentinel plants.

Work Area	Agrilink Plant (November 2002)	Sentinel Plant (November 2000)	Sentinel Plant (November 2001)
Mixing Tank Area/ Mixing Room	0.60	37.8	0.52
Microwave Packaging Line	0.33	1.68	0.10
Quality Control Room	0.19	0.54	0.11

Table 7. Concentrations of total and respirable dust in milligrams per cubic meter air (mg/m^3) measured by gravimetric method in six work areas, Agrilink, November 5 and 6, 2002.

Work Area	**Total Dust** (mg/m^3)			**Respirable Dust** (mg/m^3)		
	Day 1	**Day 2**	**Average**	**Day 1**	**Day 2**	**Average**
Mixing Tank Area	0.78	1.42	1.10	0.42	0.53	0.48
Microwave Packaging Line	0.56	0.94	0.75	0.31	0.53	0.42
QC Room	0.69	0.49	0.59	0.69	0.55	0.62
Poly Line	0.31	0.67	0.49	0.28	0.33	0.30
Packing Area	0.47	0.50	0.48	0.27	0.44	0.36
Stencil Area	0.33	0.75	0.54	0.18	0.42	0.30

Table 8. Temperature, relative humidity, carbon monoxide, and carbon dioxide, measured with direct reading instrument (Q-Trak), in three work areas, Agrilink, November 6, 2002.

Work Area	Temperature (^oF)		Relative Humidity (%)		Carbon Monoxide (ppm)		Carbon Dioxide (ppm)	
	Avg.	SD	Avg.	SD	Avg.	SD	Avg.	SD
Mixing Tank Area	75.0	2.8	30.5	2.6	21.7	7.9	751	171
Poly Line Area	73.1	3.0	33.3	3.6	33.5	13.1	809	288
Stencil Area	70.1	3.8	34.5	4.2	28.9	12.6	726	336

^oF: degrees Fahrenheit; ppm: parts per million parts of air by volume; Avg.: average;
SD: standard deviation

Table 9. Demographics of participants, Agrilink, November 2002.

Demographics	All participants (N=35)
Age – Mean – Median – Range	 49 yrs 50 yrs (26-65) yrs
Gender – Males – Females	 16 (46%) 19 (54%)
Smoking Status – Smokers (current and former smokers) – Never	 28 (80%) 7 (20%)
Pack-year (N=28 smokers) – Mean – Median – Range	 20.2 16 (0.1-52.5)
Tenure* – Mean – Median – Range	 15yrs 15yrs (2-28) yrs
Had ever worked in quality control?	10 (29%)
Had ever worked in mixing?	6 (17%)

*Maximum number of years exposed to butter flavoring vapors was 16 years, as the plant began microwave popcorn production in 1986.

Table 10. Prevalence of reported symptoms and physician diagnoses among participants, Agrilink, November 2002.

Respiratory Symptoms	Number (N=35)	Percentage
Any breathing troubles	5	14%
Shortness of breath (onset after hire) - Hurrying on level ground or walking up a slight hill - Walking with people of same age	10 3	29% 9%
Usual cough (onset after hire)	6	17%
Chronic cough (onset after hire)	3	9%
Wheeze (onset after hire)	11	31%
Wheeze aside from a cold (onset after hire)	5	14%
Systemic Symptoms		
Fever or chills	3	9%
Night sweats	7	20%
Unusual fatigue	4	11%
Other Symptoms		
Nasal irritation	21	60%
Eye irritation	14	40%
Skin irritation	4*	12%
Physician Diagnoses		
Episode(s) of bronchitis since hire	7	20%
Chronic bronchitis since hire	0	0%
Asthma since hire	1	3%
Pneumonia while working at plant	5*	15%

* One individual did not answer this question, resulting in a denominator of 34.

Table 11. Respiratory symptoms, by smoking status and age, among current workforce compared to expected numbers from the national NHANES III survey*, Agrilink, November 2002.

Symptoms	Age Group (and Smoking Status where Applicable)	# Workers in Age and Smoking Category	Number Observed	Number Expected	Ratio Observed/Expected (95% Confidence Interval)
Shortness of Breath	17-39	6	1	1.3	0.8 (0.1-4.4)
	40-69				
	Ever Smokers	23	9	7	1.3 (0.7-2.4)
	Never Smokers	6	3	1.2	2.5 (0.8-7.4)
	Ever and Never Smokers	29	12	8.2	1.5 (0.8-2.6)
	All	35	13	9.5	1.4 (0.8-2.3)
Chronic Cough	17-39	6	2	0.7	2.9 (0.8-10.4)
	40-69	29	1	3.9	0.3 (0.0-1.4)
	All	35	3	4.6	0.7 (0.2-1.9)
Wheeze or Whistling in the Last 12 Months	17-39	6	2	1.5	1.3 (0.4-4.9)
	40-69	29	3	5.8	0.5 (0.2-1.5)
	All	35	5	7.3	0.7 (0.3-1.6)
Asthma	17-39	6	0	0.6	0 (0.0-6.4)
	40-69	29	2	2.4	0.8 (0.2-3.0)
	All	35	2	3.0	0.7 (0.2-2.4)

* Controlled for race, age, and smoking status

Table 12. Prevalence of respiratory symptoms, medical diagnoses, and obstructive spirometry abnormality, Agrilink (November 2002), compared to the sentinel plant (November 2000).

Respiratory Symptoms	Agrilink Plant	Sentinel Plant
Chronic cough	3/35 (9%)	28/117 (24%)
Shortness of breath compared to others	3/35 (9%)	61/112 (54%)
Wheeze during last 12 months not associated with a cold	5/35 (14%)	36/116 (31%)
Chronic bronchitis diagnosis	1/35 (3%)	14/117 (15%)
Asthma diagnoses	2/35 (6%)	17/117 (15%)
Obstruction on spirometry	8/41 (20%)	21/116 (18%)

Table 13. Prevalence of symptoms and medical diagnoses, among current workforce, by NIOSH spirometry results, Agrilink, November 2002.

Health Condition	Borderline Obstruction or Obstruction on Spirometry (N = 6)		Normal Spirometry (N=27)	
	Number	Percent	Number	Percent
Respiratory Symptoms				
Shortness of breath	4	67%	7	26%
Regular trouble breathing	0	0%	1	4%
Wheezing in chest	2	33%	3	11%
Systemic Symptoms				
Fever or chills	0	0%	2	7%
Night sweats	1	17%	4	15%
Unusual fatigue	1	17%	2	7%
Medical Diagnoses				
Episodes of bronchitis	1	7%	4	15%
Chronic bronchitis	0	0%	1	4%
Asthma	1	17%	1	4%

Two workers (one with restrictive lung disease and one with an uninterpretable spirometry) were excluded.

Table 14. Airways obstruction spirometry abnormalities among current workforce, by smoking status and age, Agrilink, August and November 2002, compared to expected numbers from the NHANES III survey*.

Spirometry	Current and former smokers				Never smokers				All participants			
	N	Exp	Obs	Ratio Obs/Exp (95% CI)	N	Exp	Obs	Ratio Obs/Exp (95% CI)	N	Exp	Obs	Ratio Obs/Exp (95% CI)
NIOSH												
17-39 yrs old	5	0.2	0	0 (0.0-19.2)	1	0.0	0	--	6	0.2	0	0 (0.0-19.2)
40-69 yrs old	22 §	2.8	5	1.8 (0.8-4.2)	6	0.2	0	0 (0.0-19.2)	28 §	3.0	5	1.7 (0.7-3.9)
Total	27 §	3.0	5	1.7 (0.7-3.9)	7	0.2	0	0 (0.0-19.2)	34 §	3.2	5	1.6 (0.7-3.7)
NIOSH and Company (A/B/C) †												
40-69 yrs old	29	3.7	8	2.2 (1.1-4.3)	6	0.2	0	0 (0.0-19.2)	35	3.9	8	2.1 (1.0-4.0)¶
NIOSH and Company (A/B) ‡												
40-69 yrs old	26	3.4	7	2.1 (1.0-4.2)	6	0.2	0	0 (0.0-19.2)	32	3.6	7	1.9 (0.9-4.0)

N: number; Exp: number expected; Obs: number observed; CI: confidence interval

* Controlled for race, age, and smoking status

† Includes A, B, and C quality company spirometry results

‡ Includes A and B quality company spirometry results

§ Because of poor spirometry test reproducibility for one individual the denominator was reduced to 34. A better quality spirometry test on this individual, performed by the company, demonstrated a restrictive pattern.

¶ Statistically significant (lower limit of confidence limit was rounded off from 1.04)

Table 15. Prevalence of obstructive spirometry abnormalities among participants (NIOSH spirometry results) by work history, Agrilink, November 2002.

Work History	Total Number	Number and Percentage with Obstructive Spirometry Abnormalities
Ever Worked in Quality Control	9	2 (22%)*
Never Worked in Quality Control	25	3 (12%)*
Ever Worked in Mixing	6	0 (0%)
Ever Worked in Mixing and/or Cleaning Mixing Tanks	8	0 (0%)

*Differences among workers who ever and never worked in quality control were not statistically significant.

Figure 1A. Floor plan of the 1st floor of the Agrilink Popcorn Plant, November, 2002.

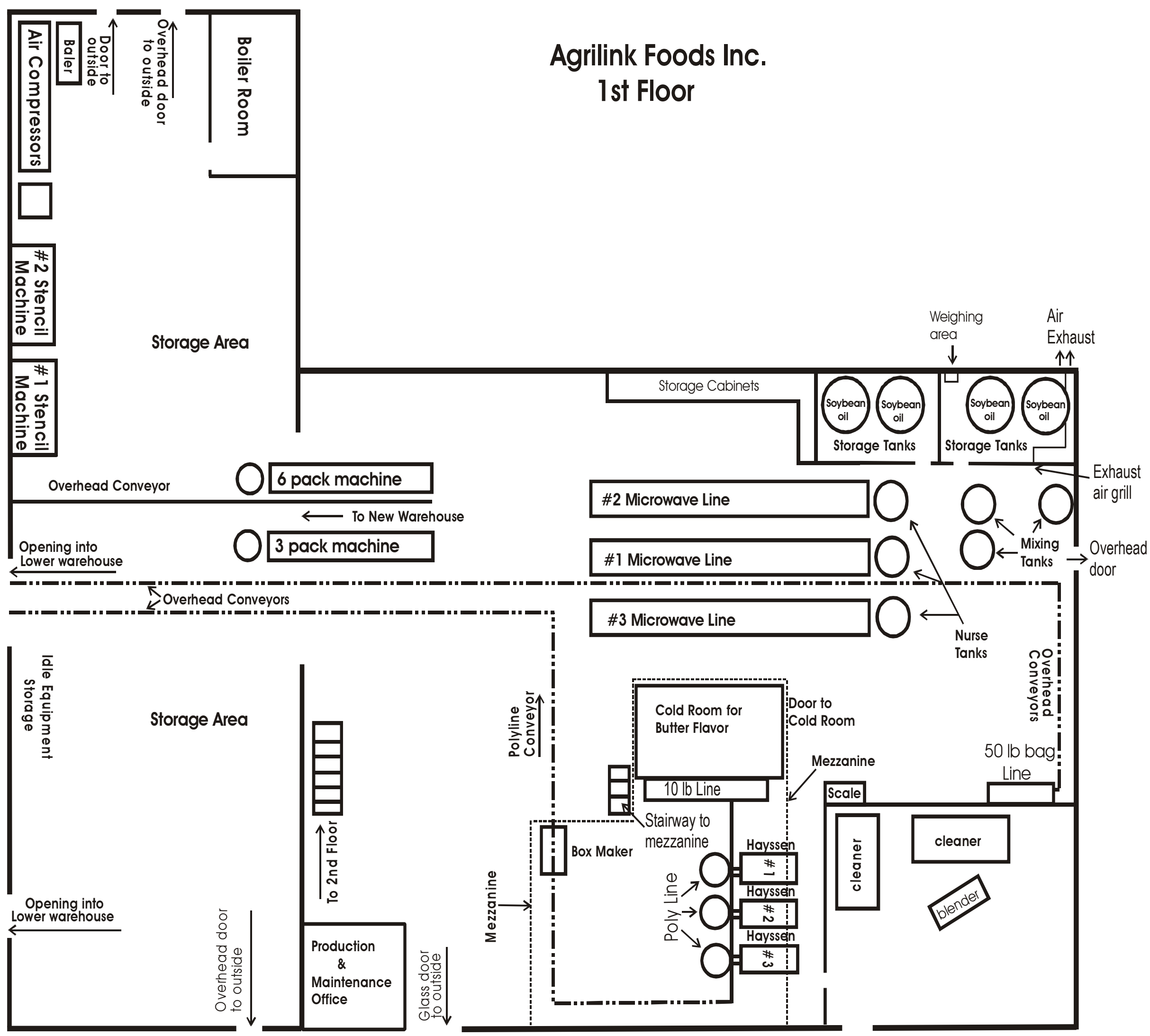


Figure 1B. Floor plan of the 2nd floor of the Agrilink Popcorn Plant, November, 2002.

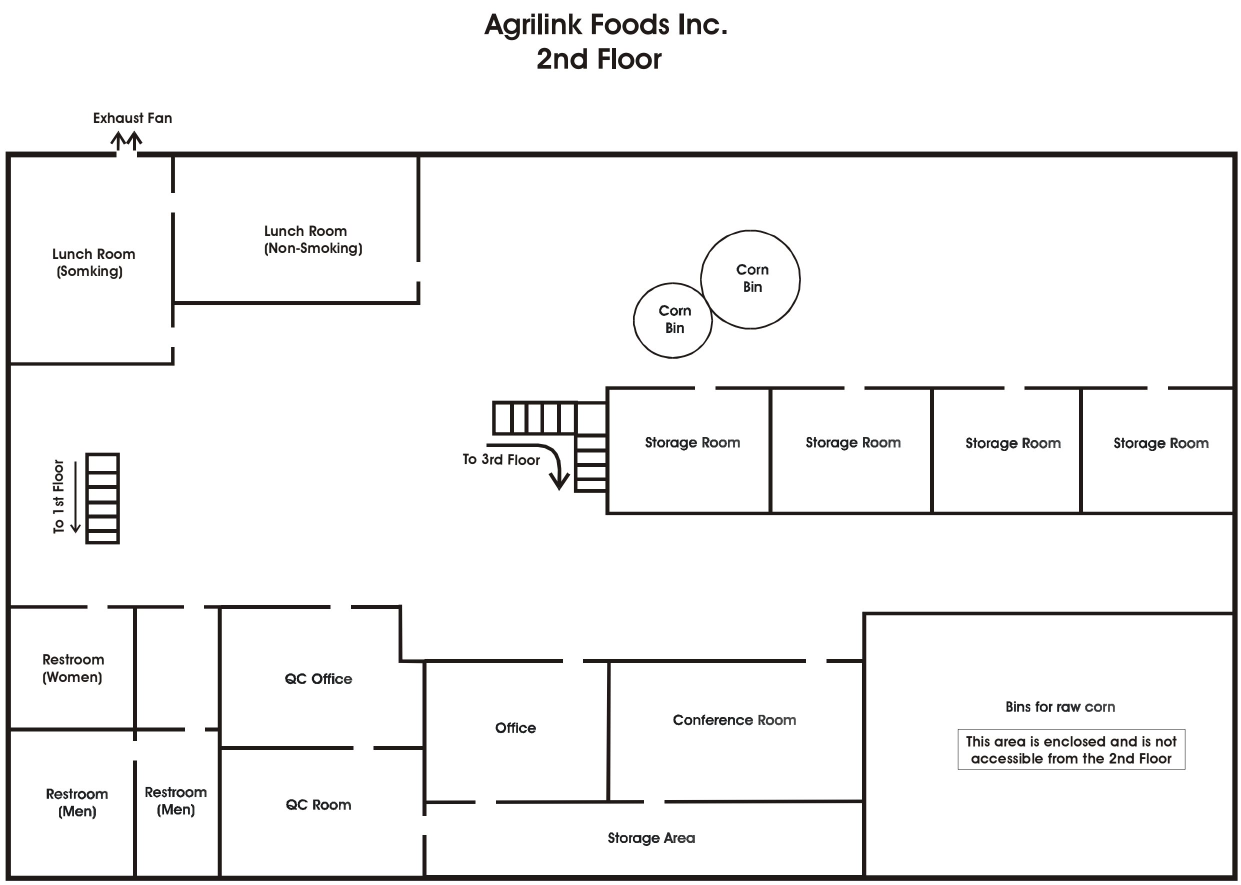
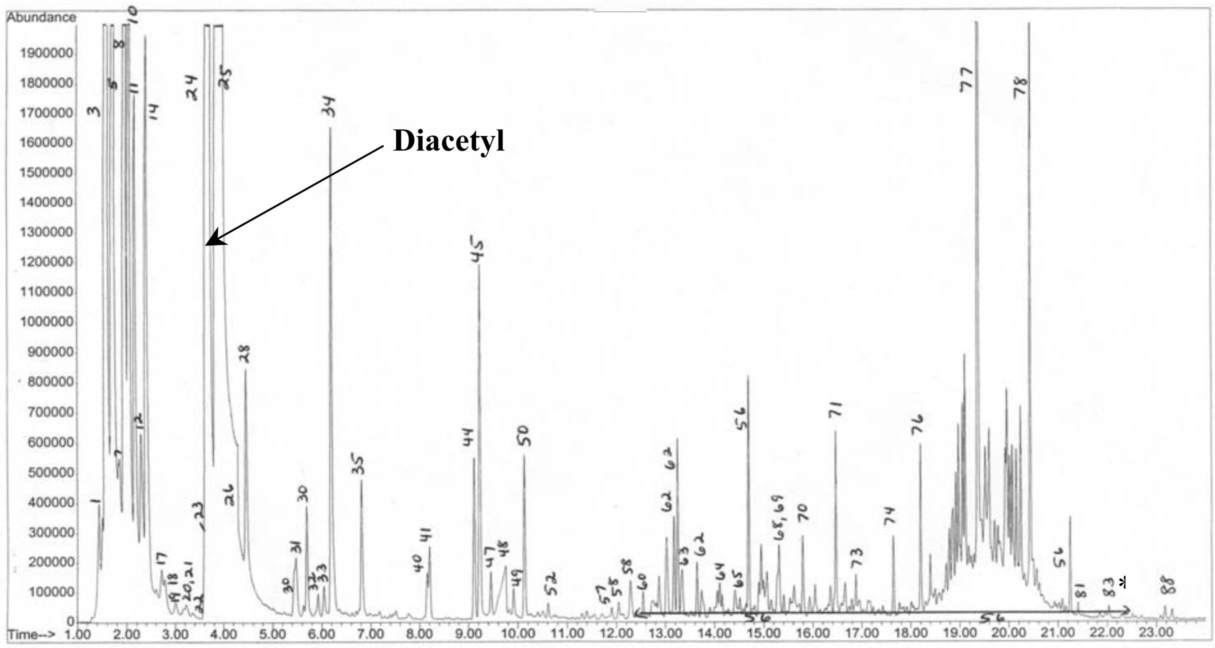
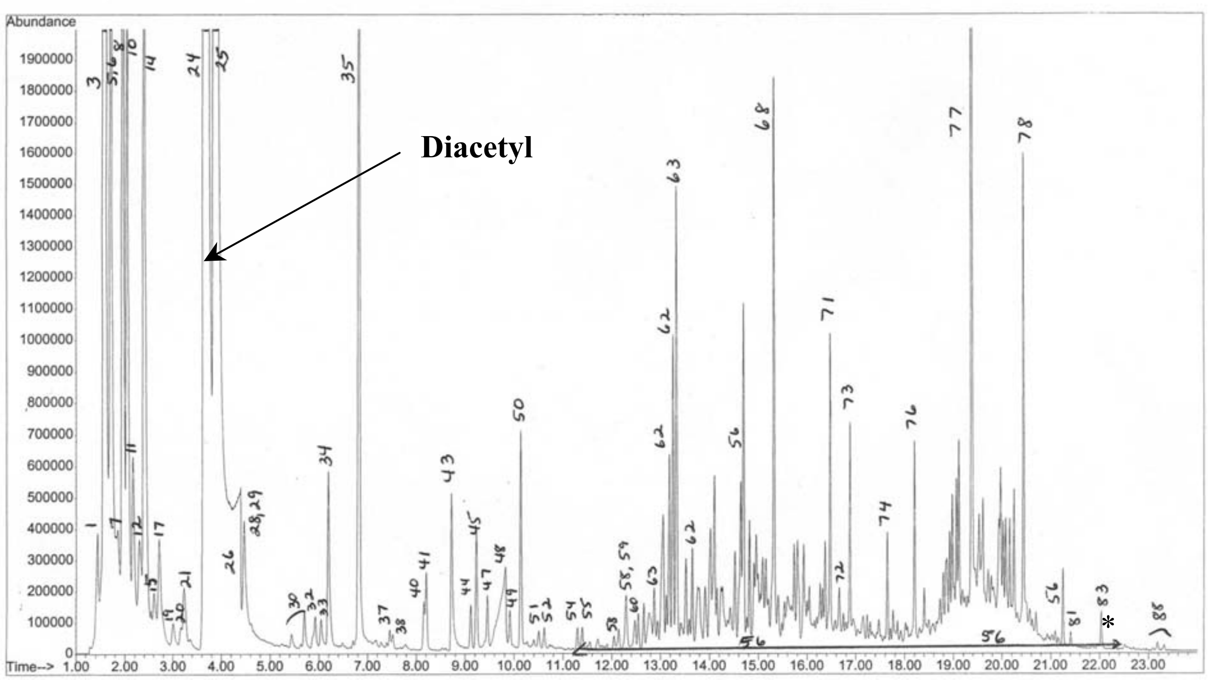


Figure 2A. Qualitative analysis of mixing area air sample, Agrilink, November 5, 2002.



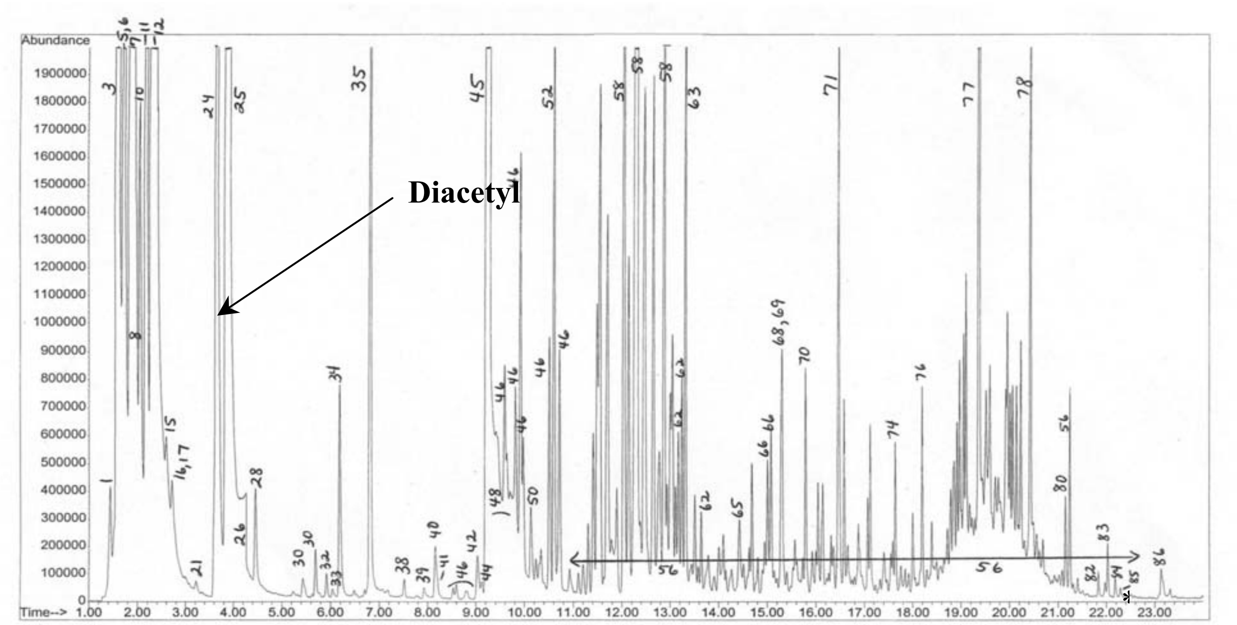
* arrow denotes compounds ranging from C_9 - C_{16}, mostly branched alkanes and aliphatic hydrocarbons. Peaks are identified by number in Identification Key labeled "Room Air" on subsequent page.

Figure 2B. Qualitative analysis of mixing area air sample, Agrilink, November 6, 2002.



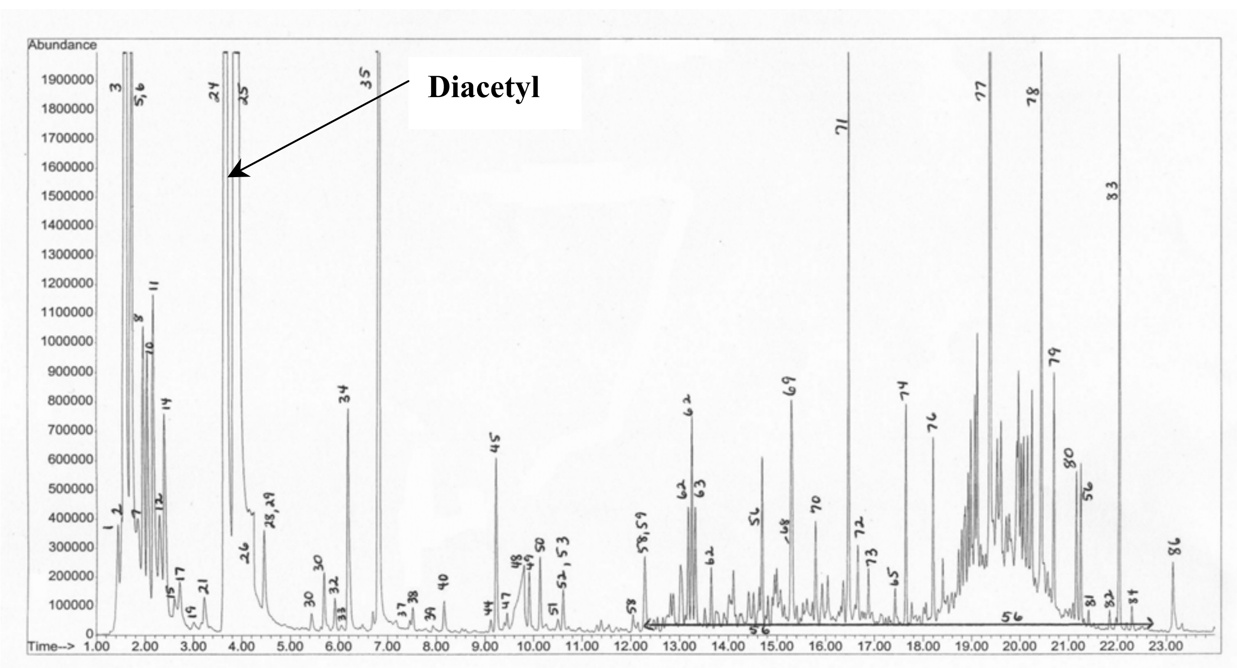
* arrow denotes compounds ranging from C_9 - C_{16}, mostly branched alkanes and aliphatic hydrocarbons. Peaks are identified by number in Identification Key labeled "Room Air" on subsequent page.

Figure 3A. Qualitative analysis of quality control room air sample, Agrilink, November 5, 2002.



* arrow denotes compounds ranging from C_9 - C_{16}, mostly branched alkanes and aliphatic hydrocarbons. Peaks are identified by number in Identification Key labeled "Room Air" on subsequent page.

Figure 3B. Qualitative analysis of quality control room air sample, Agrilink, November 6, 2002.



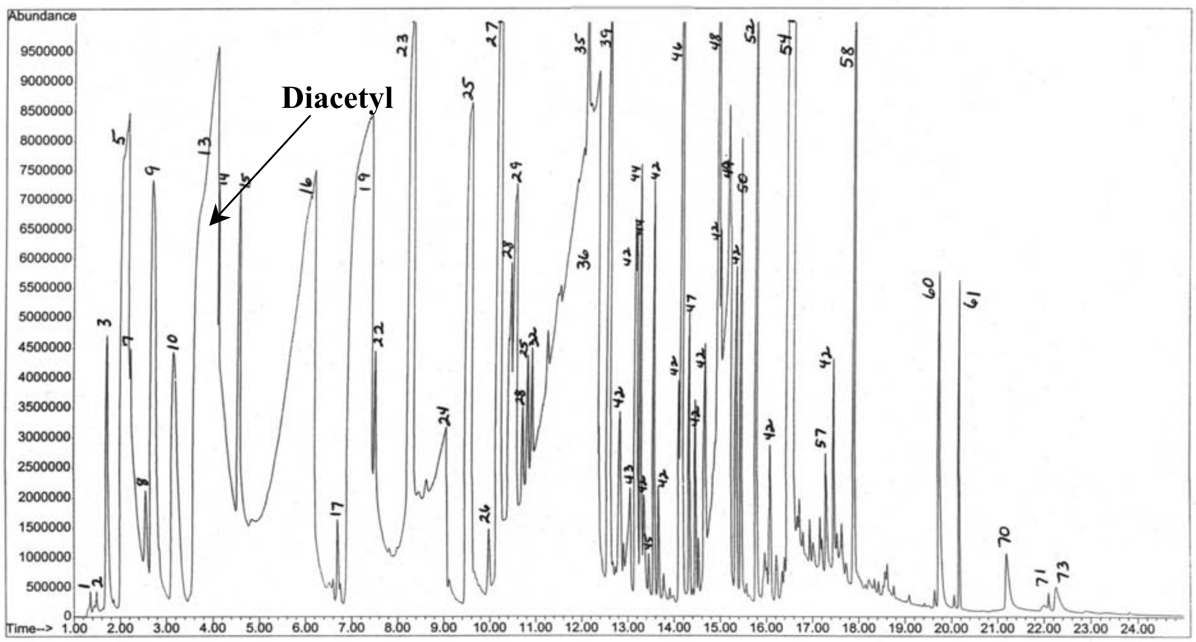
* arrow denotes compounds ranging from C_9 - C_{16}, mostly branched alkanes and aliphatic hydrocarbons. Peaks are identified by number in Identification Key labeled "Room Air" on subsequent page.

Thermal Desorption Tube Peak Identification Key (Room Air), Agrilink, November 2002

No.	Chemical Compound	No.	Chemical Compound
1	Air, CO_2*	45	Toluene*
2	Formaldehyde **	46	C8 Aliphatic hydrocarbons
3	Propane	47	2,3-Hexanedione
4	Chloromethane	48	Butyric acid
5	Methanol*	49	Hexanal*
6	Isobutane	50	Ethyl butyrate
7	Butane/butene	51	Butyl acetate
8	Methyl bromide	52	Octane
9	Bromoethane	53	Furfural
10	Ethanol*	54	Hexamethylcyclotrisiloxane*
11	Acetonitrile*	55	1-Propoxy-2-propanol
12	Acetone	56	C9-C16 (mostly branched alkanes and aliphatic hydrocarbons, some C9-C10 alkyl benzenes)
13	Isopentane*	57	Propylene glycol methyl ether acetate*
14	Isopropanol*	58	Ethyl benzene/xylene isomers
15	Pentane*	59	Meso-2,3-butanediolacetate?
16	t-Butanol*	60	Methyl amyl ketone
17	Dimethyl sulfide	61	Butyl cellosolve
18	Methyl acetate	62	Acetoin dimers, oligomers
19	Nitromethane/carbon disulfide/1,1,2-trichloro-1,2,2-trifluoroethane	63	Nonane
20	Isobutanal	64	α-Pinene
21	1-Propanol	64A	Camphor
22	2-Butenal	65	Fatty acid (hexanoic)
23	3-Buten-2-one	66	Methyl styrene isomer
24	Diacetyl (2,3-butanedione)	67	C8-C10 aliphatic aldehydes*
25	Methyl ethyl ketone (MEK)	68	Decane
26	Acetic acid	69	p-Dichlorobenzene
27	Hexane*	70	Limonene plus hydrocarbon
28	2-Ethyl-2-methyl oxirane?	71	2-Nonanone
29	Ethyl acetate	72	Nonanal*
30	Aliphatic, oxygen compounds, MW86 (methoxybutene?)	73	Undecane
31	1,1,1-Trichloroethane	74	Decamethylcyclopentasiloxane*
32	Benzene*/butanol/isopropyl acetate	75	Naphthalene
33	3-Methyl-3-buten-2-one	76	Dodecane
34	1-Methoxy-2-propanol	77	Tridecane
35	Acetoin (3-hydroxy-2-butanone)	78	Tetradecane
36	Isooctane	79	Dimethylphthalate*
37	Propyl acetate	80	delta-Decalactone
38	Heptane*	81	Pentadecane
39	Propylene glycol	82	Propyl benzamide?
39A	3-Hydroxy-3-methyl-2-butanone	83	Diethylphthalate*
40	Methyl isobutyl ketone/methyl cyclohexane*	84	Methyl propionic acid ester*
41	1,1-Diethoxyethane	85	delta-Undecalactone
42	t-Butyl peroxide?	86	delta-Dodecalactone
43	N,N-Dimethylformamide	87	Hexadecane
44	2,2-Dimethoxybutane	88	Aliphatic, MW 230 compounds?

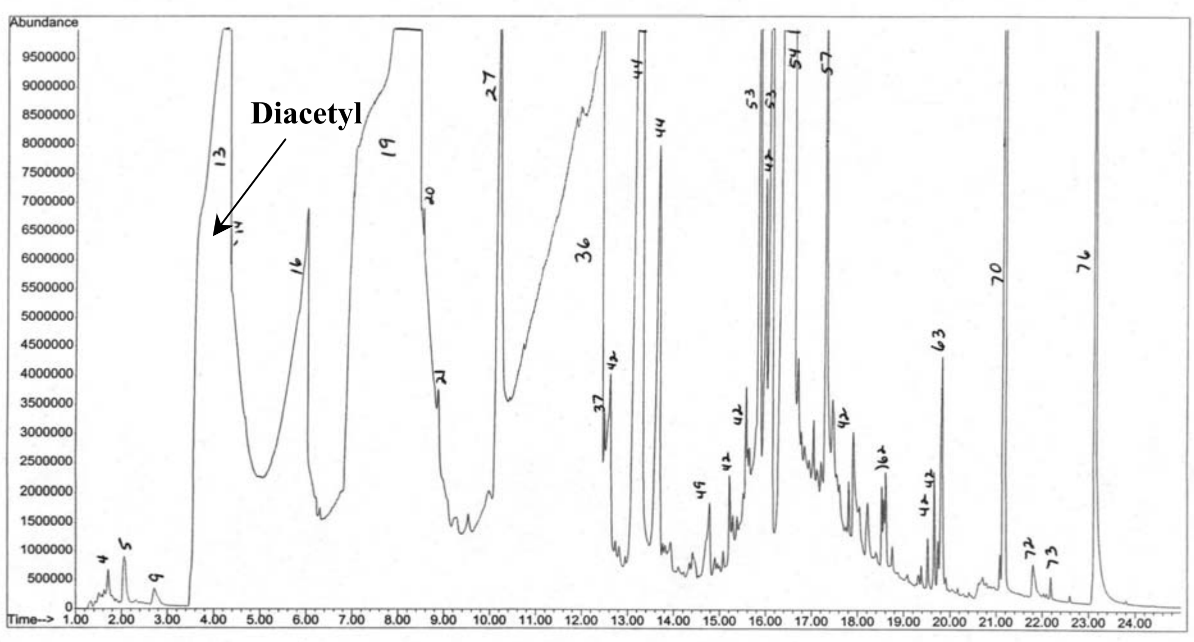
*Also present on some media and/or field blanks; ** May be present as a thermal desorption product and/or impurity from methanol.

Figure 4A. Qualitative analysis of the liquid microwave popcorn butter flavoring bulk sample heated to 50 degrees Centigrade, Agrilink, October 2002.



Peaks are identified by number in Identification Key labeled "Bulk Samples" on subsequent page.

Figure 4B. Qualitative analysis of the paste microwave popcorn butter flavoring bulk sample heated to 50 degrees Centigrade, Agrilink, October 2002.



Peaks are identified in Identification Key labeled "Bulk Samples" on subsequent page.

Thermal Desorption Tube Peak Identification Key
(Bulk Samples, Heated to 50°C, Headspace), Agrilink, November 2002.

No.	Chemical Compound	No.	Chemical Compound
1	Air*/CO_2*	40	C_7-C_{10} aliphatic aldehydes*
2	Formaldehyde	41	α-Pinene
3	Acetaldehyde**	42	Aliphatic esters/oxygen compounds
4	Methanol*	43	Valeric acid
5	Ethanol	44	Acetoin oligomers
6	Propanal	45	Methyle caproate
7	Acetonitrile*	46	Butyl isobutyrate
8	Ethyl vinyl ether?	47	Diethoxybutanone?
9	Dimethyl sulfide	48	Ethyl caproate
10	Isobutanal	49	Caproic acid (hexanoic acid)
11	Pentane*	50	Acetyl pyridine
12	Methylene chloride	51	Decane
13	Diacetyl (2,3-butanedione)	52	Limonene
14	Methyl ethyl ketone (MEK)	53	$C_{18}H_{14}O_4$ isomers, dihydroxy-dimethyl-hexan-dione?
15	Ethyl acetate	54	2-Nonanone
16	Acetic acid	55	Maltol
17	2-Methyl-1, 3-dioxolane?	56	Undecane
18	Pentanal	57	M.W.138 compounds/ethyl resorcinol?
19	Acetoin (3-hydroxy-2-butanone)	58	Ethyl caprylate
20	3-Hydroxy-3-methyl-2-butanone	59	Isobornyl isovalerate?
21	1-Hydroxy-2-butanone	60	Coconut aldehyde (gamma-nonalactone)
22	Ethyl propionate	61	Ethyl caprate
23	1,1-Diethoxyethane	62	Nitrogen compounds?
24	Propionic acid	63	Capric acid (decanoic acid)
25	Acetoin derivatives?	64	Dodecane
26	Hexanedione	65	Tridecane
27	Ethyl butyrate	66	Vanillin
28	Alkyl dioxolanes?	67	Dimethylphthalate*
29	Ethyl lactate	68	gamma-Decalactone
30	Amyl alcohol	69	Silicone compound?
31	Toluene	70	delta-Decalactone
32	Methyl pentenal?	71	Ethyl laurate
33	Hexanal*	72	Lauric acid (dodecanoic acid)
34	Perchloroethylene	73	delta-Undecalactone
35	1,1-Diethoxybutane	74	Diethylphthalate*
36	Butyric acid	75	Methyl propionic acid ester*
37	Dimethylsulfoxide (DMSO)	76	delta-Dodecalactone
38	Xylene	77	Isoamyl salicylate?
39	Methyl amyl ketone (MAK)		

*Sometimes present in media and/or system blanks
**May be present as a thermal decomposition product and/or impurity of ethanol

Figure 5A. Real-time monitoring of concentration of airborne coarse particles (optical diameter = 4-20 μm) in particles per cubic meter, at three work areas, Agrilink plant, November 6, 2002.

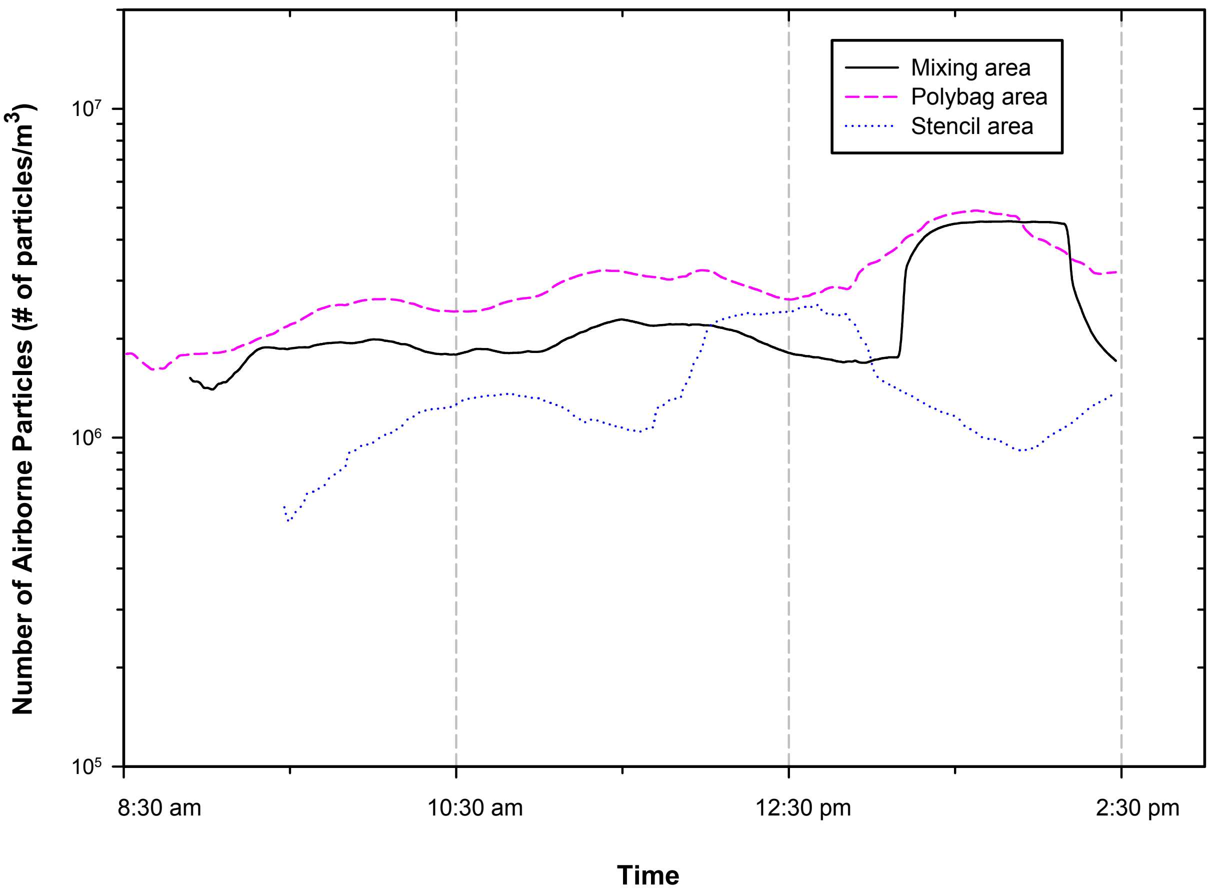


Figure 5B. Real-time monitoring of concentration of airborne respirable particles (optical diameter = 0.4-4 μm) in number of particles per cubic meter, at three work areas, Agrilink plant, November 6, 2002

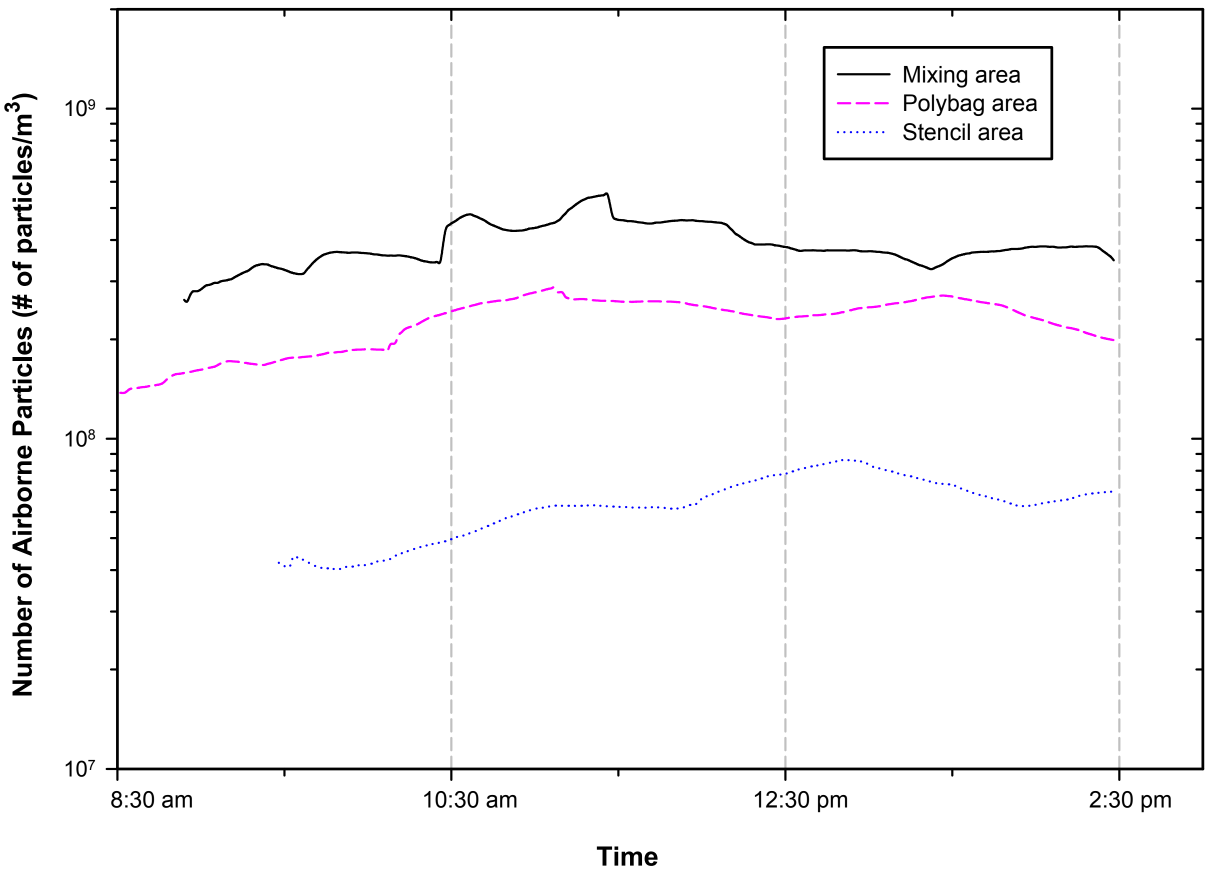


Figure 6. Real-time monitoring of temperature at three work areas, Agrilink plant, November 6, 2002.

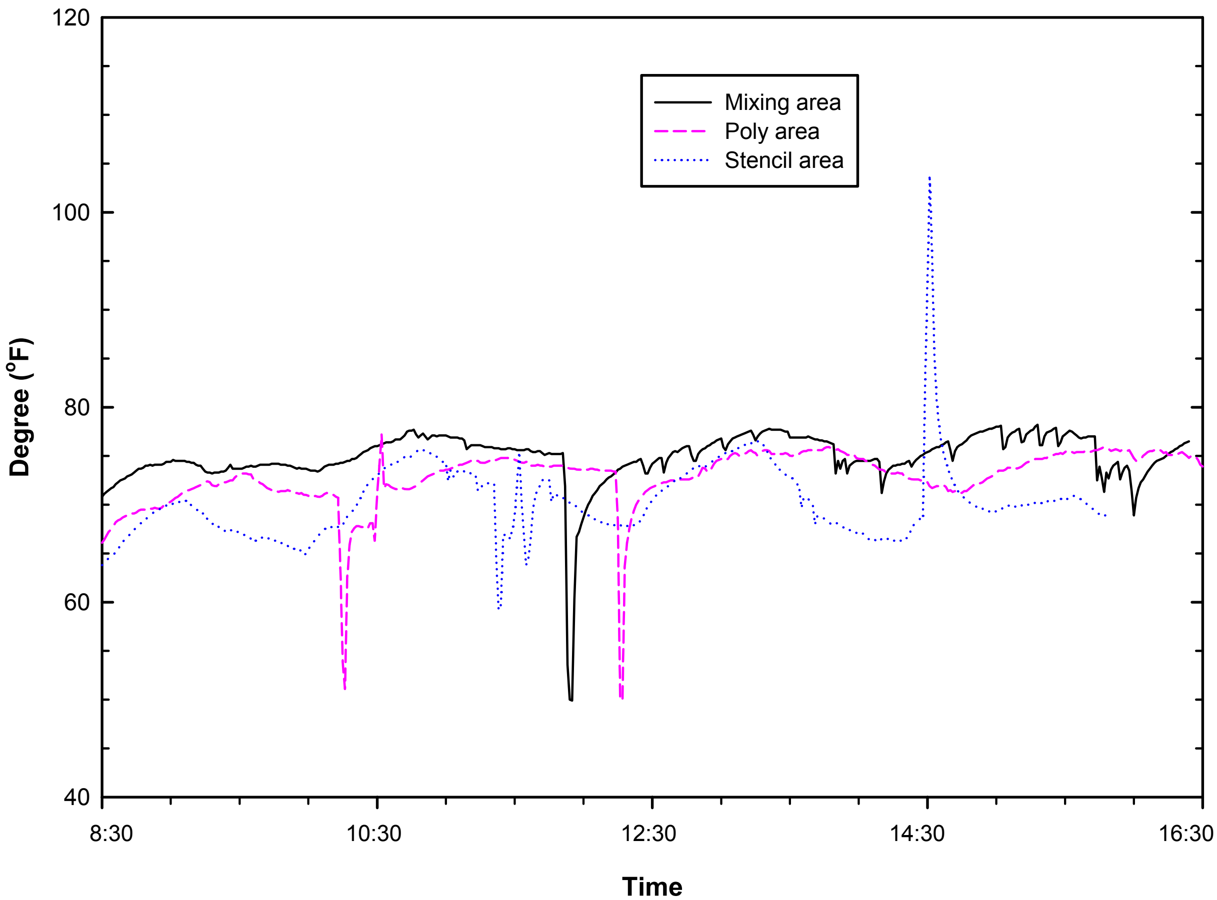


Figure 7. Real-time monitoring of relative humidity at three work areas, Agrilink plant, November 6, 2002.

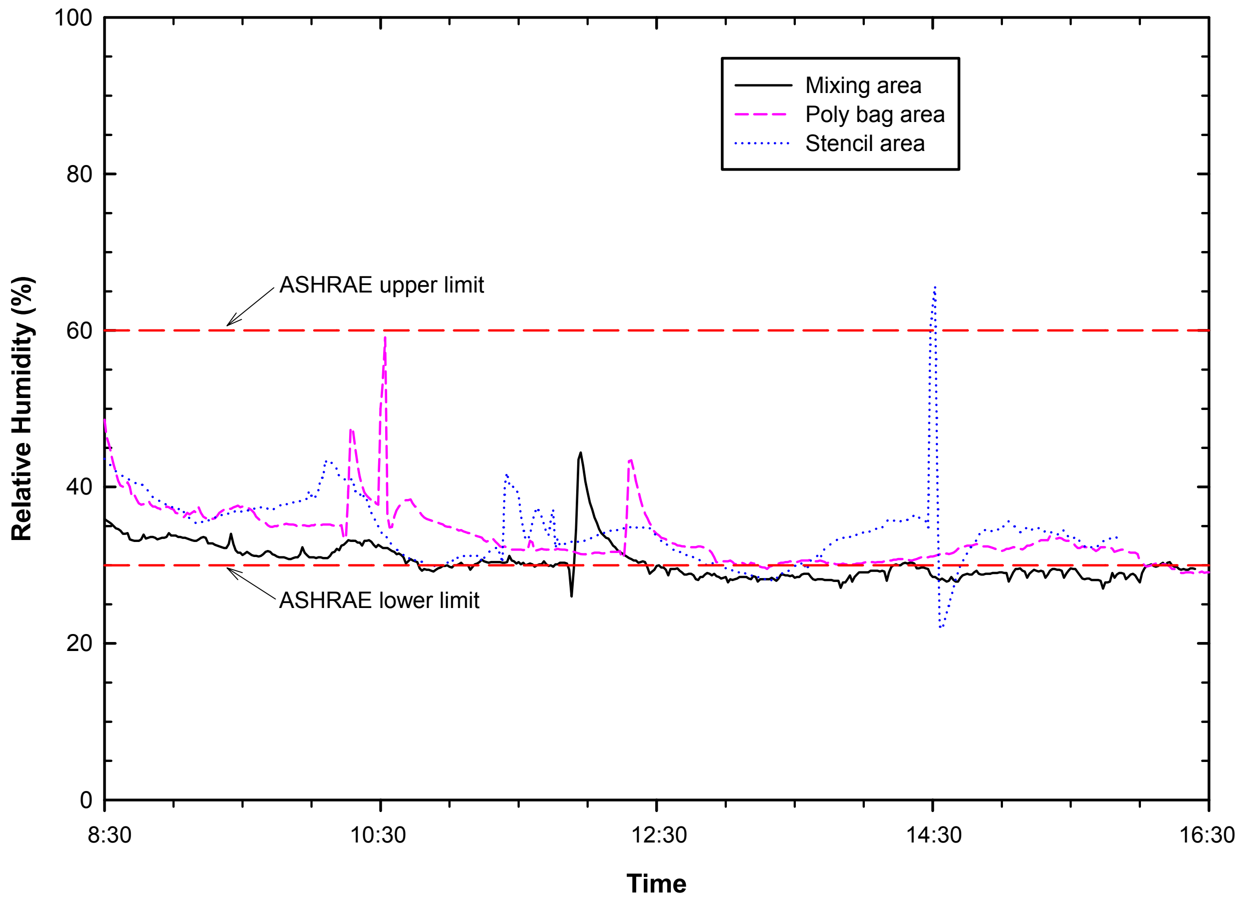


Figure 8. Real-time monitoring of CO at three work areas, Agrilink plant, November 6, 2002

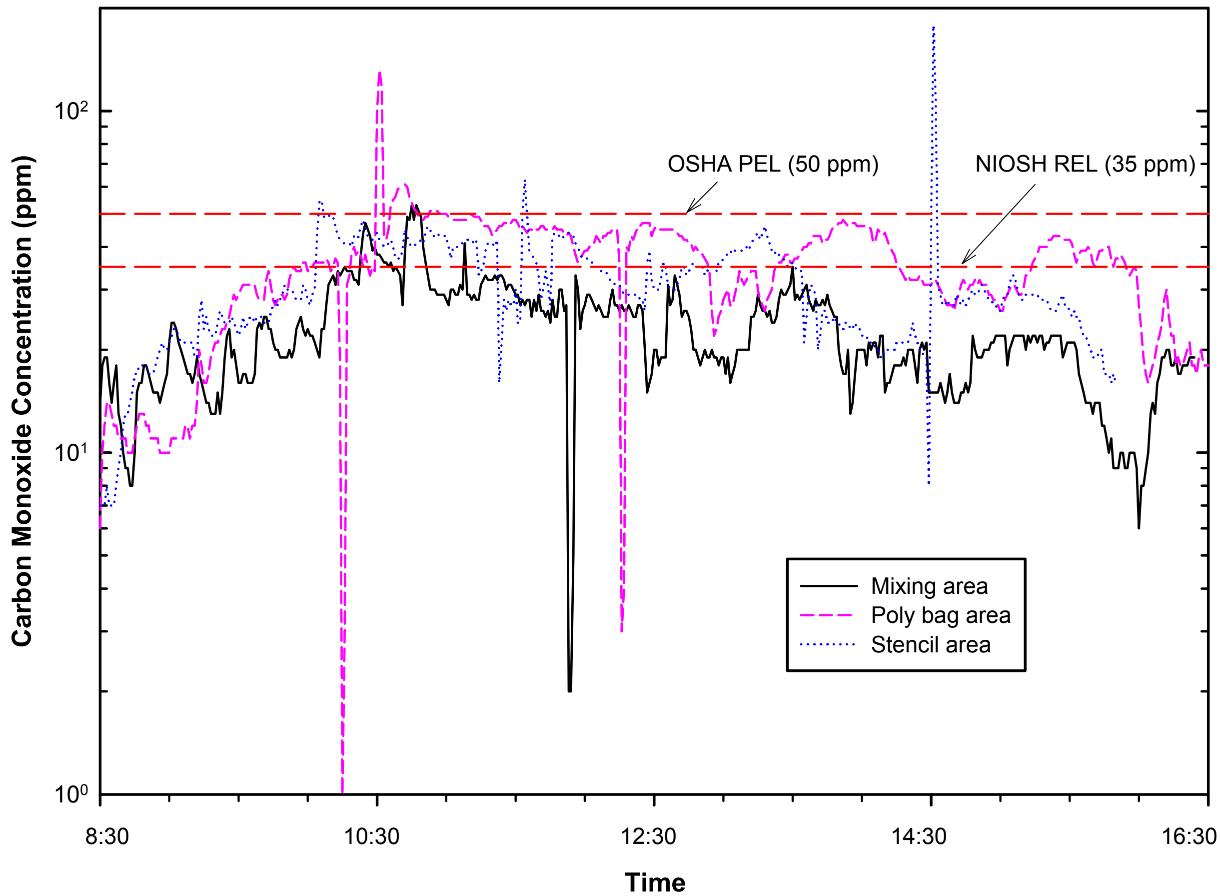
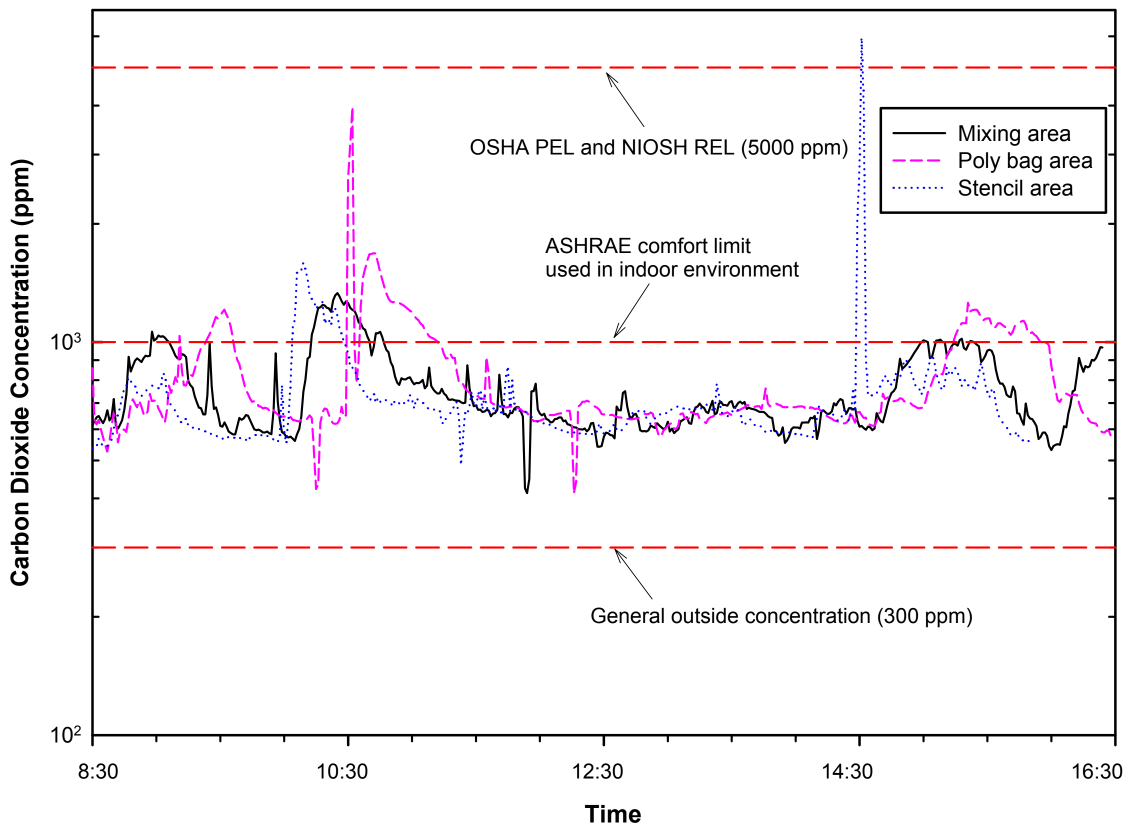


Figure 9. Real-time monitoring of CO_2 at three work areas, Agrilink plant, November 6, 2002.



APPENDIX A

Medical Questionnaire

Interviewer: __________

Interview Date: __ __ / __ __ / __ __ __ __
(Month) (Day) (Year)

Section I: Identification and Demographic Information

Name:____________________________ ______________________ ____
(Last name) (First name) (MI)

Address:____
(Number, Street, and/or Rural Route)

_________________________ _____ ___________
(City) (State) (Zip Code)

Home Telephone Number: (   ) _______ - __________

If you were to move, is there someone who would know how to contact you?

Name:____________________________ ______________________ ____
(Last name) (First name) (MI)

Relationship to you:____________________

Address:____
(Number, Street, and/or Rural Route)

_________________________ _____ ___________
(City) (State) (Zip Code)

Telephone Number: (   ) _______ - __________

~~~~~~

1. Date of Birth: __ __ / __ __ / __ __ __ __
(Month) (Day) (Year)

2. Sex: 1. ____ Male 2. ____ Female

3. Race:
1. ___ White
2. ___ African-American or Black
3. ___ Asian
4. ___ American Indian or Alaska Native
5. ___ Native Hawaiian or Other Pacific Islander
6. ___ Other (*specify below)*
~~~~~~

Section II: Health Information

I'm going to ask you some questions about your health. The answer to many of these questions will be "Yes" or "No." If you are in doubt about whether to answer "Yes" or "No," then please answer "No."

4. During the last 12 months, have you had any trouble with your breathing? 1.____Yes 2. ____No

IF YES:

a) Which of the following statements best describes your breathing?
1. ___ I only rarely have trouble with my breathing
2. ___ I have regular trouble with my breathing but it always gets completely better
3. ___ My breathing is never quite right

5. Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill? 1. ___ Yes 2. ___ No

IF YES:

a) Do you get short of breath walking with people of your own age on level ground? 1. ___ Yes 2. ___ No

b) Do you ever have to stop for breath when walking at your own pace on level ground? 1. ___ Yes 2. ___ No

c) Do you ever have to stop for breath after walking about 100 yards (or after a few minutes) on level ground? 1. ___ Yes 2. ___ No

d) In what month and year did this breathlessness start? __ __ / __ __ __ __
(Month) (Year)

6. Do you usually have a cough? (*Count cough with first smoke or on first going out-of-doors. Exclude clearing of throat.*) 1. ___ Yes 2. ___ No

IF YES:

a) Do you usually cough on most days for 3 consecutive months or more during the year? 1. ___ Yes 2. ___ No

b) In what month and year did this cough begin? __ __ / __ __ __ __ (Month) (Year)

c) When you are away from this plant on days off or on vacation, is this cough:
1. ___ Better
2. ___ The same
3. ___ Worse
4. ___ N/A

7. Have you ever had wheezing or whistling in your chest? 1. ___ Yes 2. ___ No

IF YES:

a) Have you had this wheezing or whistling when you did *not* have a cold? 1. ___ Yes 2. ___ No

b) In what month and year did this wheezing or whistling begin? __ __ / __ __ __ __ (Month) (Year)

c) When you are away from this plant on days off or on vacation, is this wheezing or whistling
1. ___ Better
2. ___ The same
3. ___ Worse
4. ___ N/A

d) During the last 12 months, have you had this wheezing or whistling in your chest when you did *not* have a cold? 1. ___ Yes 2. ___ No

8. Have you ever had to change your job, job duties, or work area at this plant because of breathing difficulties? 1. ___ Yes 2. ___ No

IF YES:

a) What month and year did you change your job, job duties, or work area? __ __ / __ __ __ __ (Month) (Year)

b) What was your job, job duties, and/or work area before the change?

Describe: ______________________________

c) How did your job, job duties, and/or work area differ after the change?

Describe: ______________________________

d) Were your breathing problems after the change: 1. ___ Better 2. ___ The Same 3. ___ Worse

9a. While working at this plant, have you had fever or chills once a month or more often? 1. ___ Yes 2. ___ No

9b. While working at this plant, have you had night-sweats once a month or more often? 1. ___ Yes 2. ___ No

10. While working at this plant, have you had unusual tiredness or fatigue that lasted more than a few days or occurred frequently? 1. ___ Yes 2. ___ No

11. Since you began working at this plant, have you ever had attacks of bronchitis? 1. ___ Yes 2. ___ No

IF YES:

a) Was it confirmed by a doctor? 1. ___ Yes 2. ___ No

b) While working at this plant, how many times have you had bronchitis? ______ Times

12. Have you ever had chronic bronchitis? 1. ___ Yes 2. ___ No

IF YES:

a)	Was it confirmed by a doctor?	1. ___ Yes 2. ___ No
b)	How old were you when it began?	______ Years old

13. Since you began working at this plant have you ever had pneumonia? (*Include bronchopneumonia*) 1. ___ Yes 2. ___ No

14. Have you ever had asthma? 1. ___ Yes 2. ___ No

IF YES:

a)	How old were you when it began?	______ Years old
b)	Was it confirmed by a doctor?	1. ___ Yes 2. ___ No
c)	Do you still have it?	1. ___ Yes 2. ___ No

15. Have you ever had a pneumothorax (collapsed lung)? 1. ___ Yes 2. ___ No

16. Since working at this plant, have you had symptoms of nasal irritation such as a stuffy or blocked nose, an itchy nose, a stinging or burning nose, or a runny nose? (*apart from a cold)* 1. ___ Yes 2. ___ No

IF YES:

a)	Is there an exposure at work that causes or aggravates these nose symptoms?	1. ___ Yes 2. ___ No
IF Yes:		
b)	Describe exposure(s): ____	

17. Since working at this plant, have you had any symptoms of eye irritation such as : watering or tearing eyes, red or burning eyes, itching eyes, dry eyes? 1. ___ Yes 2. ___ No

IF YES:

a) Is there an exposure at work that causes or aggravates these eye symptoms? 1. ___ Yes 2. ___ No

IF Yes:
b) Describe exposure(s): ____

18. Since working at this plant, have you developed any new skin rash or skin problems? 1. ___ Yes 2. ___ No

Section III. Work Information

I'm now going to ask you questions about your work history at this plant.

19.

a) Have you ever worked as a mixer, even for as little as one day? 1. ___Yes 2.___No

IF YES:

i) How long have you worked (or did you work) as a mixer?
______ Years ______ Months ______ Days

ii) How many hours per day do you (or did you) spend in the mixing area?
_____ Hours

b) Have you ever spent time within 20 feet of the mixing tanks or nurse tanks? 1.___Yes 2.___No

c) Have you ever worked in quality control (popping bags in microwave ovens to check the product)? 1.___Yes 2.___No

d) Have you ever worked cleaning out the mixing tanks? 1.___Yes 2.___No

20. What is your usual work shift?

7:00am - 5:30pm Mon - Thurs. _____
7:00am - 3:30pm Mon - Fri. _____
3:30pm - 2:00am Mon - Thurs. _____
5:30pm - 2:00am Mon - Fri. _____

21. How many hours per day do you currently spend:

a) on the production floor? _________
b) in the quality control area? _________
c) in the warehouse? _________
d) in the lunchroom? _________
e) outdoors or processing room? _________
f) in the main office area? _________

22. Have you ever been exposed to a spill or unusual chemical release at work? 1. ___ Yes 2. ___ No

IF YES:

a)	Did you have any symptoms from it?	1. ___ Yes 2. ___ No
IF YES:		
b)	What were your symptoms?	
	____	

I'm now going to ask you some questions about all the jobs that you have had while at this plant. We will start with your current job and work back through time. T

	Job Title	Start Month/Year	End Month/Year	Major Work Areas	Comments
A					
B					
C					
D					
E					
F					
G					
H					
I					
J					
K					
L					

23. Have you ever:

a) Worked in mining? 1. ___ Yes 2. ___ No *IF YES:* _____ Years

b) Worked in farming? 1. ___ Yes 2. ___ No *IF YES:* _____ Years

c) Worked in chemical manufacturing like explosives, dyes, lacquers, and celluloid? 1. ___ Yes 2. ___ No *IF YES:* _____ Years

d) Been exposed to fire smoke? *(Do not count campfires, stoves.)* 1. ___ Yes 2. ___ No *IF YES:* _____ Years

e) Been exposed to irritant gases like chlorine, sulfur dioxide, ammonia, and phosgene? 1. ___ Yes 2. ___ No *IF YES:* _____ Years

f) Been exposed to mineral dusts including coal, silica, and talc? 1. ___ Yes 2. ___ No *IF YES:* _____ Years

g) Been exposed to grain dusts? 1. ___ Yes 2. ___ No *IF YES:* _____ Years

h) Been exposed to oxides of nitrogen including silo gas? 1. ___ Yes 2. ___ No *IF YES:* _____ Years

i) Been exposed to asbestos? 1. ___ Yes 2. ___ No *IF YES:* _____ Years

j) Been exposed to any chemical or substance that affected your breathing? 1. ___ Yes 2. ___ No

IF YES TO QUESTION j:

k) *Describe exposure:*

____

____

Section IV: Tobacco Use Information

I'm now going to ask you a few questions about tobacco use.

24. Have you ever smoked cigarettes? 1. ___ Yes 2. ___ No
(*NO if less than 20 packs of cigarettes in a lifetime or less than 1 cigarette a day for 1 year.*)

IF YES:

a) How old were you when you first started smoking regularly? ______ Years old

b) Over the entire time that you have smoked, what is the average number of cigarettes that you smoked per day? ______ Cigarettes/day

c) Do you still smoke cigarettes? 1. ___ Yes 2. ___ No

IF NO:

d) How old were you when you stopped smoking regularly? ______ Years old

Thank you for participating in this survey!

APPENDIX B

Evaluation Criteria

To assess the hazards posed by workplace exposures, NIOSH investigators use a variety of environmental evaluation criteria. These criteria suggest exposure levels to which most workers may be exposed for a working lifetime without experiencing adverse health effects. However, because of wide variation in individual susceptibility, some workers may experience occupational illness even if exposures are maintained below these limits. The evaluation criteria do not take into account individual hypersensitivity, pre-existing medical conditions, or possible interactions with other work place agents, medications being taken by the worker, or environmental conditions.

The primary sources of evaluation criteria for the workplace are: NIOSH Criteria Documents and Recommended Exposure Limits (RELs)[1], the Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELs)[2], and the American Conference of Governmental Industrial Hygienists (ACGIH®) Threshold Limit Values (TLVs®).[3] The objective of these criteria for chemical agents is to establish levels of inhalation exposure to which the vast majority of workers may be exposed without experiencing adverse health effects.

Occupational health criteria are established based on the available scientific information provided by industrial experience, animal or human experimental data, or epidemiologic studies. Differences between the NIOSH RELs, OSHA PELs, and ACGIH® TLVs® may exist because of different philosophies and interpretations of technical information. It should be noted that RELs and TLVs are guidelines, whereas PELs are standards which are legally enforceable. OSHA PELs are required to take into account the technical and economical feasibility of controlling exposures in various industries where the agents are present. The NIOSH RELs are primarily based upon the prevention of occupational disease without assessing the economic feasibility of the affected industries and as such tend to be conservative. A Court of Appeals decision vacated the OSHA 1989 Air Contaminants Standard in *AFL-CIO v OSHA,* 965F.2d 962 (11th cir., 1992); and OSHA is now enforcing the previous 1971 standards (listed as Transitional Limits in 29 CFR 1910.1000, Table Z-1-A). However, some states which have OSHA-approved State Plans continue to enforce the more protective 1989 limits. NIOSH encourages employers to use the 1989 limits or the RELs, whichever are lower.

Evaluation criteria for chemical substances are usually based on the average personal breathing zone exposure to the airborne substance over an entire 8- to 10-hour workday, expressed as a time-weighted average (TWA). Personal exposures are usually expressed in parts per million (ppm), milligrams per cubic meter (mg/m^3), or micrograms per cubic meter ($\mu g/m^3$). To supplement the 8-hour TWA where there are recognized adverse effects from short-term exposures, some substances have a short-term exposure limit (STEL) for 15-minute peak periods; or a ceiling limit, which is not to be exceeded at any time. Additionally, some chemicals have a "skin" notation to indicate that the substance may be absorbed through direct contact of the material with the skin and mucous membranes.

It is important to note that not all workers will be protected from adverse health effects if their exposures are maintained below these occupational health exposure criteria. A small percentage may experience adverse health effects because of individual susceptibility, a pre-existing medical condition, previous exposures, and/or hypersensitivity (allergy). In addition, some hazardous substances may act in combination with other work place exposures, or with medications or personal habits of the worker (such as smoking, etc.) to produce health effects even if the occupational exposures are controlled to the limit set by the evaluation criterion. These combined effects are often not considered by the chemical specific evaluation criteria. Furthermore, many substances are appreciably absorbed by direct contact with the skin and thus potentially increase the overall exposure and biologic response beyond that expected from inhalation alone. Finally, evaluation criteria may change over time as new information on the toxic effects of an agent become available. Because of these reasons, it is prudent for an employer to maintain worker exposures well below established occupational health criteria.

Diacetyl, Acetoin, and 2-Nonanone

The ketones, diacetyl, acetoin, and 2-nonanone are predominant components of artificial butter flavorings and are extremely irritating to skin, eyes, mucous membranes and the respiratory tract. Currently, there are no NIOSH, OSHA, or ACGIH® occupational exposure standards or guidelines for them.

Acetaldehyde

Acetaldehyde is a colorless liquid used as a flavoring agent and adjuvant. When ingested or inhaled it can irritate the eye, nose, and throat. The Food and Drug administration regulates it as a direct food additive and a synthetic flavoring substance. The OSHA PEL is 200 ppm (8-hour TWA). Acetaldehyde is considered a potential occupational carcinogen by the U.S. Environmental Protection Agency (EPA), the International Agency for Research on Cancer (IARC), and NIOSH. For this reason NIOSH recommends that occupational exposure levels of acetaldehyde be kept at the Lowest Feasible Concentration (LFC). ACGIH® has a ceiling limit of 25 ppm.

Acetic Acid

Acetic acid is a colorless liquid with a strong vinegar-like odor. It is used in making dyes, drugs, plastics, food additives, and insecticides. The OSHA PEL is 10 ppm (8-hour TWA). NIOSH has an REL of 10 ppm (10-hour TWA) and a ceiling limit of 15 ppm. ACGIH® also has a TLV® of 10 ppm (8-hour TWA) and a ceiling limit of 15 ppm.

Volatile Organic Compounds

Volatile organic compounds describe a large class of chemicals which are organic (i.e., containing carbon) and have a sufficiently high vapor pressure to allow some of the compound to exist in the gaseous state at room temperature. These compounds are emitted in varying concentrations from numerous indoor sources and chemicals including, but not limited to, carpeting, fabrics, adhesives, solvents, paints, cleaners, waxes, cigarettes, combustion sources, and the flavorings used in the production of microwave popcorn.

Studies have measured wide ranges of VOC concentrations in indoor air as well as differences in the mixtures of chemicals which are present. Research also suggests that the irritant potency of these VOC mixtures can vary. The use of this total VOC (TVOC) indicator, however, has never been standardized and neither NIOSH nor OSHA currently have specific exposure criteria for VOC mixtures.

Particulates, Not Otherwise Classified

Often the chemical composition of the airborne particulate does not have an established occupational health exposure criterion. It has been the convention to apply a generic exposure criterion in such cases. Formerly referred to as nuisance dust, the preferred terminology for the non-specific particulate is now *"particulates, not otherwise classified (n.o.c.)* (ACGIH® TLV®)*,"* or *"particulates, not otherwise regulated" (n.o.r.)* (OSHA PEL).

The OSHA PEL for total particulate, n.o.r., is 15.0 mg/m^3 and 5.0 mg/m^3 for the respirable fraction, determined as 8-hour averages. The ACGIH® recommended TLV® for exposure to a particulate, n.o.c., is 10.0 mg/m^3 (total dust, 8-hour TWA). These are generic criteria for airborne dusts which do not produce significant organic disease or toxic effect when exposures are kept under reasonable control. These criteria are not appropriate for dusts that have a biologic effect and may not be appropriate for evaluating general particulate matter in microwave popcorn packaging facilities.

Carbon Monoxide

Carbon monoxide (CO) is a colorless, odorless, tasteless gas which can be a product of the incomplete combustion of organic compounds. CO combines with hemoglobin and interferes with the oxygen carrying capacity of blood. Symptoms include headache, drowsiness, dizziness, nausea, vomiting, collapse, myocardial ischemia, and death. The OSHA PEL for carbon monoxide is 50 ppm (8-hour TWA). The NIOSH REL for carbon monoxide is 35 ppm (10-hour TWA). NIOSH also recommends a ceiling limit of 200 ppm. The ACGIH® TLV® for carbon monoxide is 25 ppm (8-hour TWA).

Carbon Dioxide

Carbon dioxide (CO_2) is a normal constituent of exhaled breath and a product of combustion. High concentrations of CO_2, a colorless, odorless gas which displaces oxygen, can cause death. Lower concentrations can cause symptoms such as headache, sweating, rapid breathing, and increased heart rate.

Indoor CO_2 concentrations in office settings are normally 300 to 350 ppm higher than the generally constant ambient (outdoor) CO_2 concentration. Carbon dioxide concentration is used as an indicator of the adequacy of outside air supplied to occupied areas. When indoor CO_2 concentrations exceed 1000 ppm in areas where the only known source is exhaled breath, inadequate ventilation is suspected. Elevated CO_2 concentrations suggest that other indoor contaminants may also be increased. It is important to note that CO_2 is not an effective indicator of ventilation adequacy if the ventilated area is not occupied at its usual level.

The OSHA PEL (8-hour TWA), ACGIH® TLV® (8-hour TWA), and NIOSH REL (10-hour TWA) is 5,000 ppm for carbon dioxide.

References

1. NIOSH [2003]. Pocket guide to chemical hazards. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) publication No.97-140.

2. CFR [1997]. 29 CFR 1910.1000 Code of Federal Regulations. Washington, DC: U.S. Government Printing Office, Office of the Federal Register.

3. ACGIH [2003]. 2003 TLVs® and BEIs®; threshold limit values for chemical substances and physical agents. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

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