An evaluation of respiratory health at a flavoring manufacturing facility -- Kentucky

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Contents

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The cover photo is a close-up image of sorbent tubes, which are used by the HHE Program to measure airborne exposures. This photo is an artistic representation that may not be related to this Health Hazard Evaluation.

Highlights of this Evaluation

In October 2011, the National Institute for Occupational Safety and Health (NIOSH) received a confidential employee request for a health hazard evaluation at a flavorings manufacturing facility in Kentucky. The employees submitted the request because of concerns about exposure to flavoring chemicals including diacetyl and concerns about respiratory health. Diacetyl is a butter flavoring chemical that can cause lung disease. We visited the facility in November 2011 and conducted a medical survey at the facility in March 2012.

What NIOSH Did

- We collected air samples for volatile chemicals in multiple areas of the facility.
- We assessed local exhaust ventilation in the mini-bulk and liquid samples rooms.
- We collected and reviewed 735 reports of spirometry tests. These tests were conducted on employees from 2006-2011 by healthcare providers hired by the facility.
- In March 2012, we conducted a medical survey at the facility that included a questionnaire and breathing tests (spirometry and diffusing capacity).
- We considered survey participants who worked in production departments, who spent an hour or more per day in production areas, or who used flavoring ingredients as part of their jobs to have higher flavoring exposures than other survey participants.
- We considered survey participants who used cleaning products as part of their jobs to have higher cleaning product exposures than other survey participants.

What NIOSH Found

- The facility had many controls and practices in place to limit employees' exposure to flavoring chemicals.
- Some controls and practices had flaws that needed improvement.
- The facility's ventilation system appeared to function properly and was designed to keep air exhausted to the outside from re-entering the building through fresh air intakes.
- Production areas were kept under negative pressure by a general ventilation system that was separate from the ventilation to R&D and administration areas.
- There was no recirculation of air in either the production or R&D areas.
- We did not detect diacetyl and its substitute, 2,3-hexanedione, in any of air samples that we collected in the facility. We detected another diacetyl substitute, 2,3-pentanedione, in two air samples that we collected in the liquid samples room.
- The primary healthcare provider operated a mobile testing unit and conducted poor quality spirometry testing. The secondary healthcare provider was based at a medical clinic and conducted better quality spirometry testing, but had done few of the tests.
- Two former employees had been diagnosed with bronchiolitis obliterans, a lung disease

that can be caused by flavorings. In one case, we were able to review medical records that supported this diagnosis.

- Two employees had sought emergency care for respiratory symptoms following inhalation of fumes from diacetyl or a diacetyl substitute.
- Shortness of breath was more common among survey participants who had worked at the facility for 7 years.
- Asthma-like symptoms, nasal symptoms, sinusitis, cough, and phlegm were more common among participants in higher flavoring and/or cleaning product exposure groups.
- All work-related symptoms evaluated (breathing trouble, wheeze, nasal symptoms, sinusitis, eye symptoms, rash, and cough) were more common among participants in higher flavoring and/or cleaning product exposure groups.
- Breathing tests results showed lower lung function among participants who had worked at the facility for 7 years or more.
- Breathing test results showed lower lung function among participants in higher flavoring exposure groups, regardless of how long participants had worked at the facility.
- Work-related differences in lung function could not be explained by age, smoking, or work at another flavoring plant, and were seen even in analyses limited only to production employees.

What the Employer Can Do

- Continue to handle ingredients that contain the butter flavoring chemical diacetyl and its substitutes as respiratory toxins.
- Improve the design of exhaust hood enclosures over balances in the liquid compounding room to allow the front section to be fully closed when in use.
- When preparing flavoring recipes in the liquid compounding room, add diacetyl and other high priority chemicals last whenever possible, to minimize exposure time.
- Instruct employees to put on a respirator before adding diacetyl and other high priority chemicals and to wear the respirator until mixing is complete and the container is sealed.
- Ensure that respirators are always stored in a protective bag when not in use.
- Do not use open trash bins or uncapped drums for disposal of waste that may have residual flavoring material, as there is a risk of volatilization.
- When opening drums of chemicals in the mini-bulk area, keep drums as close to wall mounted ventilation slots as possible.
- Improve the design of slot hoods in the mini-bulk room for better capture efficiency.

- Always store and reseal chemicals using their original lids.
- Improve the design of local exhaust ventilation systems with articulating arms in the quality control laboratories to allow employees easier positioning of the system over their work areas.
- Develop a labeling system for small bottles/containers of flavors that are on the "Respirator Use Required List of Chemicals" but are too small to receive the warning stickers placed on larger containers.
- Include sanitation employees and all employees who spend time in production areas or use flavorings in the respiratory protection program.
- Conduct periodic spirometry testing on all employees who spend time in production areas or use flavorings.
- Ensure that the spirometry provider conducts high quality spirometry and monitors changes in lung function over time to identify employees with abnormal declines.
- Encourage employees to report new or ongoing respiratory symptoms to a designated individual at the facility.
- Consider work-related lung disease and re-evaluate the potential for exposure to respiratory hazards when new or ongoing respiratory symptoms or excessive declines in lung function occur in the workforce.

What Employees Can Do

- Use local exhaust ventilation systems as instructed by your employer.
- Follow your employer's rules about mandatory respiratory protection.
- Participate in spirometry testing offered by your employer.
- Report new or ongoing respiratory symptoms to your personal physician and to the designated individual at the facility.

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Abbreviations

ATS	American Thoracic Society
BMI	Body mass index
CI	Confidence interval
DLCO	Diffusing capacity of the lung for carbon monoxide
FEMA	Flavor and Extract Manufacturers Association
FEV_1	Forced expiratory volume in 1 second
FVC	forced vital capacity
LEV	local exhaust ventilation
MID	Meat inspection department
MSDS	Material safety data sheet
NIOSH	National Institute for Occupational Safety and Health
NHANES III	Third National Health and Nutrition Examination Survey
OSHA	Occupational Safety and Health Administration
ppb	Parts per billion
PPE	Personal protective equipment
ppm	Parts per million
PR	Prevalence Ratio
QA	Quality Assurance
R&D	Research and development
RTU	Roof top units
VOC	Volatile organic compound

The recommendations in this report are made on the basis of the findings at the workplace evaluated and may not be applicable to other workplaces.

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Summary

In October 2011, the National Institute for Occupational Safety and Health received a confidential employee request for a health hazard evaluation at a flavoring manufacturing facility in Kentucky. The request concerned exposure to chemicals including diacetyl, lack of respiratory protection and ventilation, and upper and lower respiratory problems including shortness of breath. Diacetyl is a butter flavoring chemical that can cause lung disease.

Prior to visiting the site, we interviewed employees, the health and safety manager, and the facility's spirometry provider by telephone and reviewed documents provided by the facility. From November 29 to December 1, 2011 we visited the facility. We toured the facility, interviewed managers, and conducted private interviews with employees representing the facility's departments. We conducted air sampling for volatile organic compounds using evacuated canisters and qualitatively assessed local exhaust ventilation. We collected and reviewed reports of spirometry tests. The spirometry testing often was not conducted according to international guidelines, so we could not reliably interpret the tests. From March 12 to 22, 2012, we conducted a medical survey at the facility consisting of an interviewer-administered questionnaire and lung function tests (spirometry and diffusing capacity).

Flavoring exposures at this facility appear to be better controlled than at other flavoring manufacturing facilities where employees developed lung disease. Nonetheless, employees who had worked at this facility longer or who were in higher flavoring exposure groups had more symptoms and lower lung function than other employees. While many controls are already in place to reduce exposure to flavoring chemicals, we noted potential opportunities for exposures during our site visit that can be addressed through enhanced engineering controls, modified work practices, and improved use of respiratory protection. Obtaining high quality spirometry will allow for monitoring of lung function over time and detection of declines that are greater than expected.

We found that the facility used thousands of chemicals, some of which are recognized respiratory toxins and most of which have unknown respiratory toxicity. The facility provided a list of chemicals for which respirator use is required during the preparation of flavor recipes. There were many controls in place to limit employees' exposure to these chemicals. However, we noted some opportunities for exposure to these chemicals, including: lack of labeling of respiratory hazards in some cases, inadequate local exhaust ventilation, early removal of respiratory protection, and disposal of flavoring waste into open containers. We did not detect diacetyl in any air samples. We detected a diacetyl substitute, 2,3-pentanedione, in two air samples taken in the liquid samples room.

Among current employees, some symptoms and diagnoses were more common than expected, while spirometric abnormalities were not in excess compared to U.S. adults. Most

participants with obstruction did not respond to bronchodilator, meaning they had fixed obstruction. Symptoms, work-related symptoms, lung function abnormalities, and average lung function values differed by work history characteristics. Employees with longer facility tenure, those who worked in production departments, those who spent more time in production areas, and those who used flavoring ingredients tended to have more symptoms, more work-related symptoms, more lung function abnormalities, and lower average lung function values than others. These differences could not be explained by age, smoking status, or employment at another flavoring plant, and persisted in analyses limited only to production employees, suggesting that they are a result of occupational exposures at the facility.

Introduction

In October 2011, the National Institute for Occupational Safety and Health (NIOSH) received a confidential employee request for a health hazard evaluation at a flavoring manufacturing facility in Kentucky. The request concerned exposure to chemicals including diacetyl, lack of respiratory protection and ventilation, and upper and lower respiratory problems including shortness of breath. Diacetyl is a butter flavoring chemical that has been associated with lung function abnormalities and obliterative bronchiolitis (also called bronchiolitis obliterans), a rare irreversible lung disease, in workers who make or use flavorings [NIOSH 2011a]. A diacetyl substitute, 2,3-pentanedione (also called acetyl propionyl), is chemically related to diacetyl and has been found to be a respiratory toxin in animal studies [Morgan et al. 2012; Hubbs et al. 2012]. Little is known about the toxicity of other diacetyl substitutes.

Process Description

The facility opened in 1998 and employs approximately 400 people over three shifts in the production of flavors, colors, and food and beverage ingredients used in the manufacture of consumer products. End products are in the form of liquids, powders, and pastes. The 196,000-square-foot facility comprises flavor and ingredient (savory, sweet, and beverage) and color production areas, research and development (R&D), pilot plant operations, shipping and receiving, warehouse, maintenance, utilities (waste water treatment and boilers), laboratories, and offices.

Production

Raw materials enter the facility via the shipping/receiving department and are initially processed in the quarantine room where quality assurance (QA) test samples are collected for analysis before the materials are sent to the raw materials storage area. When raw materials on the facility-designated "Respirator Use Required List of Chemicals" enter the facility, a label indicating the need for respiratory protection is placed onto the container.

In the liquid product areas, the liquid samples room prepares small sample containers of primarily sweet flavors for customers. The liquid compounding/mini-bulk area prepares batches of both sweet and savory flavors in up to 55-gallon containers. In other liquid product

area rooms, high volume production involves mixing in tanks and pouring into barrels and totes. The dairy room and the distillation room prepare a variety of liquid flavor distillates.

In the dry product area, the spray dry room prepares powder products by mixing a carrier with water in feed tanks heated by a gas burner. Flavors are then added to the mixture and pumped to the top of the spray dryer for processing. The final product is then screened before packaging in plastic-lined boxes. In the dry blend room, a ribbon blender is used to process powder seasonings which are then bagged and boxed.

In the culinary area, meat is inspected and weighed in the meat inspection department (MID), cooked in the kettle room, and dried in the vacuum drying room. After the moisture content of meat products is reduced, the resulting hard cake is milled to reduce its size for processing in a ribbon blender. The product is then sieved and loaded into plastic lined boxes.

The color department produces both liquid and powder colors in small batches on a relatively infrequent basis.

The beverage department produces flavors for the beverage industry. The department includes a beverage applications laboratory and a beverage pilot plant.

The QA department consists of several laboratories including a microbiology laboratory which conducts product testing and environmental sampling throughout the facility.

R&D units include taste testing (sensory), food group, flavor creation, technology and innovation, and colors laboratories where chefs and chemists work together to develop new products and evaluate finished consumer goods. After new products are developed, finished recipes are sent to either the beverage or culinary pilot plants for scale-up. In addition to preparing materials, creating samples, and internal testing, the pilot plants prepare small orders for customers. The sample department utilizes a small spray dryer for some preparations, and the culinary pilot plant includes a small vacuum dryer and a pressure cooker reactor.

Before materials are shipped to customers they are stored in the finished goods warehouse. Some finished materials are stored at an off-site cold storage area.

Maintenance personnel serving the facility work three shifts and repair equipment in their shop or in place in the production area. The maintenance shop has a forklift battery charging station with local exhaust ventilation (LEV). Also located on-site is a five member spill response team which receives Hazardous Waste Operations and Emergency Response training.

Production operations are supported by a variety of office-based departments such as business support, general administration, human resources, indirect plant administration, marketing, management information system , plant administration, regulatory/legal, safety and environmental, and sales.

Sanitation

The sanitation process is routinely conducted by trained sanitation personnel who follow standard operating procedures, with some departments having dedicated sanitation teams. The facility utilizes clean-in-place technology that allows cleaning chemicals and detergents to be pumped directly into the equipment being cleaned. The clean-in-place process begins in the cleaning chemical storage area where containers of chemicals are stored and dispensed into smaller containers for transfer to specific work areas. Various acidic and alkaline cleaning chemicals are used, including chlorinated cleaner, foamed cleaners, oven cleaners, and citrus-based cleaners.

Assessment

To initiate the evaluation, we interviewed employees, the health and safety manager, and the facility's spirometry provider by telephone. We also reviewed documents provided to NIOSH prior to the site visit, including a facility map, a consultant's report of a 2008 industrial hygiene survey, the written respiratory protection program, and respirator training materials.

We visited the facility from November 29 to December 1, 2011. We toured the facility to understand processes, job tasks, controls in place to reduce exposures, and the use of personal protective equipment. We interviewed managers and conducted private interviews about work history and health concerns with employees representing the facility's departments. We collected additional documents including the facility's Occupational Safety and Health Administration (OSHA) Form 300 Logs of Work-related Injuries and Illnesses for 2006-2011, an employee roster, records pertaining to the hazard communication program, material safety data sheets (MSDSs) for butter flavor ingredients and products, MSDSs for cleaning products, and standard job descriptions. We asked the facility to provide information on the frequency of use of particular flavoring chemicals, including chemicals designated by the Flavor and Extract Manufacturers Association (FEMA) as "high priority" chemicals that may pose a respiratory hazard [FEMA 2012]. We also met with the spirometry provider to collect available spirometry records, which we reviewed using American Thoracic Society (ATS) standards [Miller et al. 2005]. Following our visit, we contacted a second healthcare provider used by the facility. From the second healthcare provider, we collected additional spirometry records as well as medical records pertaining to work-related illnesses.

During the same site visit, we conducted air sampling for volatile organic compounds (VOCs), including diacetyl, 2,3-pentanedione, and 2,3-hexanedione, at multiple locations in the facility. Thirteen area air samples were collected using evacuated canisters. The 450-milliliter canisters were equipped with either instantaneous grab sampling attachments (n=9) or capillary-based flow controllers (n=4). The air samples were analyzed for VOCs using a pre-concentrator/gas chromatograph/mass spectrometer system pursuant to a recently published method validation study [LeBouf et al. 2012] with the following modifications: 1) the pre-concentrator was a Model 7150 (Entech Instruments, Inc., Simi Valley, CA); 2) three additional analyte compounds, the alpha-diketones 2,3-butanedione (diacetyl), 2,3-pentanedione, and 2,3-hexanedione, were included; and 3) qualitatively-identified

compounds were compared to National Institute of Standards and Technology 2008 Mass Spectral Library and included in the analytical report if the quality factor was greater than 75%. At present, this canister method is partially validated and is being reviewed for incorporation into the NIOSH Manual of Analytical Methods.

We conducted a qualitative assessment of the local exhaust ventilation systems in the mini bulk and liquid samples rooms using smoke generating tubes to determine air flow and vapor capture patterns.

We also collected a tape sample from the return exhaust in the culinary laboratory for microscopic evaluation to determine if fungal material was present.

We conducted a medical survey at the facility from March 12 to 22, 2012. We invited all current employees to complete an interviewer-administered questionnaire and lung function tests (spirometry and measurement of diffusing capacity). Following the survey, we mailed reports to each participant at his or her home address. The reports explained individual lung function test results and provided recommendations for follow-up of abnormalities.

The questionnaire (Appendix A) included questions from the ATS adult respiratory questionnaire [Ferris 1978], the Third National Health and Nutrition Examination Survey (NHANES III) [DHHS 1996], and the European Community Respiratory Health Survey [Grassi et al. 2003]. Questions addressed respiratory and dermatological symptoms, asthma and other diagnoses, smoking history, work history and practices, and demographic information.

A NIOSH technician administered spirometry tests using a dry rolling-seal spirometer interfaced to a personal computer following ATS guidelines [Miller et al. 2005]. We compared spirometry results to reference values generated from NHANES III data [Hankinson et al. 1999]. Reference values were calculated on the basis of a participant's age, sex, height, and race. Each participant's largest forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) were selected for analysis. We classified participants as having airways obstruction if they had FEV_1 and a ratio of FEV_1/FVC below their respective lower limits of normal (5th percentiles) with a normal FVC. Participants with a low FEV_1/FVC ratio and normal FEV_1 were considered to have borderline obstruction. We defined restriction as a normal FEV_1/FVC ratio with FVC below the lower limit of normal. We classified participants with both FEV_1/FVC ratio and FVC below the lower limit of normal as having mixed obstructive and restrictive abnormalities.

Unless contraindicated, participants with any spirometric abnormality were administered a bronchodilator to determine reversibility, using four puffs of a beta-agonist (albuterol). In some cases, such as if a participant reported asthma, bronchodilator was offered despite normal spirometry. We defined reversibility as an increase in FEV_1 of at least 12% and 200 milliliter after bronchodilator administration [Pellegrino et al. 2005].

We measured the diffusing capacity of the lung for carbon monoxide (DLCO) using the

single breath technique with helium as the tracer gas following ATS guidelines [MacIntyre et al. 2005]. We compared the average of at least two DLCO values to reference values generated from a stratified random sample of a state population [Miller et al. 1983]. We defined DLCO below the lower limit of normal as low diffusing capacity. From the same test, we estimated total lung capacity using the calculated alveolar volume. We compared the alveolar volume to reference values [Miller et al. 1983] and defined low total lung capacity as alveolar volume below the lower limit of normal. Reference values were calculated on the basis of a participant's age, sex, and height.

Statistical Methods

We defined asthma-like symptoms as current use of asthma medicine and/or one or more of the following symptoms in the past 12 months: 1) wheezing or whistling in the chest, 2) awakening with a feeling of chest tightness, or 3) attack of asthma [Grassi et al. 2003]. We defined work-related symptoms as those that improved away from the facility.

We calculated prevalence ratios (PR) of symptoms, diagnoses, and spirometric abnormalities from comparisons with data obtained from the U.S. adult population from NHANES III [DHHS 1996] using indirect standardization for race (white, black, or Mexican-American), sex, age (17–39 years or ≥40 years), and cigarette smoking status (ever or never). For PRs of spirometric restriction, we also examined the effect of body mass index (BMI), as a high BMI can result in spirometric restriction even in the absence of lung disease. A PR above 1 indicates that the prevalence of the health problem is more common among participants than expected. A PR of 1 indicates that the health problem is as common among participants as expected. A PR below 1 indicates that the prevalence of the health problem is less common among participants than expected.

To explore potential associations between health problems and work, we examined questionnaire responses and lung function test results by work history characteristics using contingency tables and PRs (for binomial outcomes) and analysis of variance to compare means (for continuous outcomes). When these univariable analyses revealed significant associations, we used linear regression and generalized linear models to examine possible confounding by ever smoking (for all health outcomes) and age (for health outcomes based on questionnaire responses). We did not adjust for age for most of the health outcomes based on lung function test results, as these involve predicted values that already account for age (as well as sex, height, and, for spirometry, race). For analyses of the FEV_1/FVC ratio, which is calculated from raw (not predicted) values, we also adjusted for age.

Work history characteristics were categorized as follows: type of department (production vs. non-production); average amount of time spent daily in production areas (<1 hour vs. ≥1 hour); use of flavoring ingredients; use of cleaning products; or history of work at another flavoring plant. All work categories were defined on the basis of participants' self-reported work histories. We considered beverage, color, dairy, distillation room, dry blend, flavor creation, food group, liquids, maintenance, MID, QA, samples, sanitation, sensory, shipping/receiving, warehouse, spray dry, and technology innovation to be production departments.

We considered business support, general administration, human resources, indirect plant administration, marketing, management information system, plant administration, regulatory/legal, safety and environmental, and sales to be non-production departments. Use of flavoring ingredients was defined by the participant's response to the question: "As a [job title], do/did you sample, mix or pour flavoring ingredients?" Use of cleaning products was defined by the participant's response to the question "As a [job title], do/did you use cleaning products?" Employment with the same company at a prior location was considered to be work at another flavoring plant. In this report we present comparisons of current/not current and ever/never categories. We also examined comparisons of current/never and former/never categories, which had similar estimates.

We attempted to address the possible effect of unmeasured non-occupational factors that could influence lung function by examining the relationship between lung function and work history characteristics among the subgroup of survey participants who ever worked in a production department and, separately, the subgroup who never worked in a production department.

Statistical analyses were conducted using SAS software version 9.3 and JMP software version 10.0.1 (SAS Institute, Inc., Cary, NC). We considered two-sided $p \leq 0.05$ to be statistically significant.

Results

Summary of Prior Industrial Hygiene Evaluation

The facility provided us with a report concerning air sampling that was conducted by consultants in December 2008. The consultants focused their sampling on diacetyl and acetaldehyde exposures in the receiving area. They measured airborne levels of diacetyl during and after collection of liquid diacetyl aliquots in the quarantine room and airborne levels of acetaldehyde in the cold storage room.

During the collection of liquid diacetyl aliquots, an employee placed a container of product into position near a local exhaust hood and donned a full-faced respirator. The container was opened and 1.75 ounces of liquid diacetyl was taken using a pipette and suction bulb. The aliquot was transferred to a vial and sealed, the pipette was discarded into a lidded receptacle, and the container was sealed. The process involved two containers of diacetyl and took approximately two minutes per container.

Diacetyl air samples were collected on 2 silica gel tubes in series and analyzed using OSHA method PV 2118 [Shaw 2003]. Personal air samples were collected for 15-minutes during two separate procedures of liquid diacetyl sample collection. Diacetyl was not detected on either sample (the limit of detection was 0.095 parts per million [ppm]). Area air samples of varying lengths (15, 180, 210, and 420 minutes) were collected for diacetyl in the receiving department near the exhaust unit after the liquid diacetyl procedure was completed and after

the 15-minute personal air sampling events. None of the area air samples detected diacetyl, with limits of detection ranging from 0.030 to 0.095 ppm.

Acetaldehyde is not collected by pipette in the quarantine room like diacetyl. Instead, the sealed containers are delivered to the receiving department where they are labeled and sent to the cold storage room. Although no delivery of acetaldehyde occurred on the day of the survey, an area air sample was collected for 255 minutes in the cold storage room. Acetaldehyde was detected in this sample at a level of 0.143 ppm.

Summary of Employee Health Concerns

During telephone and in-person interviews, some employees expressed concerns about health problems that they attributed to workplace exposures. They described shortness of breath on exertion and at rest, cough, nasal congestion, postnasal drip, hoarseness, loss of sense of smell, sinus problems, eye irritation, and flu-like illness with fevers, chills, and aches. Some of these employees indicated that symptoms improved over the weekend, while others stated that symptoms did not improve over the weekend, but did improve over longer periods away from work. Some employees were concerned about exposure to flavoring chemicals and cited the following as possible contributors to exposure: potential cross-ventilation between production and non-production areas, insufficient fresh air brought in by the ventilation system, a lack of ventilation hoods in kitchen laboratories, a lack of respiratory protection in laboratories, a lack of guidance on when it was safe to remove a respirator after donning it for a respirator-required task, a lack of hazard labeling on some chemicals, and fumes from the use of open containers for disposal of refuse contaminated with volatile chemicals. Some employees were displeased with a lack of medical surveillance for non-production employees who use flavoring chemicals. In addition to concerns about flavoring chemical exposures, some employees also raised concerns about potential mold exposure from the ventilation system. Several employees noted that the safety culture at this facility was much better than at other companies where they previously had been employed. They indicated that the employer was responsive to health and safety concerns that were raised by employees.

We were informed that two former employees had been diagnosed with bronchiolitis obliterans. In one case, we were able to review medical records from a pulmonologist's consultation that supported this diagnosis. In the other case, we were unable to review medical records.

The facility contracted with a local hospital-based occupational health clinic for care for work-related illnesses and injuries. The clinic provided records for two encounters related to respiratory health since 2008. In the first encounter, an employee reported chest discomfort and cough with blood about 6 hours following exposure to diacetyl fumes. The employee noted that the blood he brought up smelled like the diacetyl fumes. Examination was unremarkable, and a chest radiograph and a pulmonary function test were interpreted as normal. He was diagnosed with an inhalational injury and instructed to avoid fumes for 72 hours. In the second encounter, an employee was seen in the clinic two days after an emergency room visit prompted by exposure to a diacetyl substitute chemical. Immediately

following the exposure he noted throat and lung irritation. He reported that the diacetyl substitute chemical required a respirator, but that this information was not marked on the chemical's container or on the work ticket. He was monitored in the emergency room and discharged to home. At the time of the clinic visit, he had no complaints and examination was unremarkable. He was diagnosed with toxic effects from fumes and informed that he could return to full duty.

Summary of Medical Surveillance Program

The primary spirometry provider offered hearing and lung function testing at the facility using a mobile testing unit. The owner served as the technician and had no formal spirometry training. She was aware of the availability of spirometry courses in her area, but did not consider such training worthwhile. She was unable to identify the model of spirometer she used or provide calibration records, although she stated that the spirometer was calibrated on an annual basis. She indicated that she and her medical consultant, a physician, considered a single expiratory effort sufficient in many cases, and she objected to the time required for multiple efforts. She had been conducting spirometry for this facility since approximately 2002, but provided records only for 2006-2011, as she had a practice of destroying records that were older than six years. She reported that she provided employers with written notification of her intention to destroy their employees' medical records before doing so. The health and safety manager for the flavoring manufacturing facility was unaware of this practice and indicated that he had not received notification to this effect.

Review of the available 546 spirometry records confirmed that the technician did not adhere to ATS guidelines [Miller et al. 2005]. In many cases, the tests used only one effort or two efforts that did not meet repeatability criteria. Flow-volume and volume-time curves were not consistently available, although they had been explicitly requested by NIOSH staff. Where curves could be examined, there was evidence of incomplete inhalation and poor initial blast, and some tests did not reach a volume-time plateau. Outdated reference equations were used. A high proportion of tests (27% in 2011) were interpreted as abnormal, but it was impossible to determine whether abnormal test results were due to abnormal lung function or poor test quality. We provided feedback to the technician, emphasizing the importance of daily calibration using a 3L syringe, acceptability criteria, repeatability criteria, and records retention. We encouraged her to enroll in a NIOSH-certified spirometry course and provided a reference poster on how to achieve valid spirometry results.

The secondary spirometry provider was the occupational health clinic that also provided care to the facility's employees for work-related illnesses and injuries. Employees who were not available on the day that the mobile testing unit visited the facility or who had abnormalities deemed by the primary provider to require follow-up were sent to the secondary provider. We reviewed 189 spirometry records conducted from 2006-2011. The reports showed the flow-volume and volume-time curves, and indicated the number of efforts performed and the prediction equations being used. Three or more efforts were routinely performed, reflecting an understanding of the importance of obtaining repeatable measurements. More recent tests were conducted using the updated ATS effort protocol [Miller et al. 2005], and values were

compared to predicted values generated from NHANES III.

Close to half of the secondary provider's spirometry tests met ATS criteria for acceptability and repeatability. Other tests had one or more quality issues. These included no plateau, test length less than six seconds, FEV_1 and/or FVC not repeatable, poor effort, poor peak flow, and excessive extrapolated volume. In addition, some tests that were interpreted as showing obstruction had evidence of extra breaths, which tend to falsely increase FVC and decrease the ratio. Most of the reports we reviewed did not provide information on calibration checks. We provided feedback to the responsible physician, emphasizing the high quality of some of the tests we reviewed and ways that quality could be further improved for the remainder.

Summary of Respiratory Protection Program

Most production employees are in a Respiratory Protection Program that includes medical evaluation (questionnaire and spirometry), fit testing for full-face respirators, and training that notes the chemicals that require respiratory protection. Employees in the Respiratory Protection Program undergo annual medical evaluation consisting of self-administered questionnaire and spirometry. Employees in the beverage pilot plant, R&D, and the laboratories are not in the respiratory protection program.

Production employees are required to wear full-face respirators and weigh under a hood when handling materials on the facility-designated "Respirator Use Required List of Chemicals," which included both diacetyl and the diacetyl substitute 2,3-pentanedione. When raw materials on the list enter the facility through the quarantine room of the shipping/receiving department, a label indicating the need for respiratory protection is placed onto containers of chemicals on the list. In addition to labels on the containers, chemicals on the list are identified in each product recipe displayed on the computer workstations in the product preparation rooms. When employees preparing a recipe come to an ingredient that requires the use of respiratory protection, they are required to don their full-face respirator and inform other employees in the room that they need to vacate the room until the task is complete. Also, a warning light is activated and barricade tape is put in place to prevent workers from entering the area.

NIOSH Evaluation

Workplace Observations

The facility uses thousands of flavoring chemicals, some of which are on the FEMA "high priority" list [FEMA 2012] (Table 1). We found the facility clean and organized. We observed employees in the production area wearing facility uniforms, hair covers, beard covers (if applicable), and personal protective equipment (PPE) such as hearing and eye protection, bump caps, and steel toe shoes with non-skid soles. Full-face respirators were being used by production employees handling materials on the facility-designated "Respirator Use Required List of Chemicals."

In the liquid compounding room, we noted opportunities for potential exposure to chemicals on the "Respirator Use Required List of Chemicals" during the preparation of flavor recipes. We observed that when an employee was preparing a recipe containing a chemical on the list that, although the employee donned a full-face respirator when adding the listed chemical to the mixture, the employee took the respirator off immediately after its addition, rather than after the entire recipe was completed. Also, preparation of flavor recipes was conducted on a balance placed under an exhaust hood enclosure that appeared to be improperly designed. The front section of the enclosure lid could not be fully closed during use and still allow a workers hands into the enclosure, which could allow vapors to escape. Another potential for exposure was that after completion of the recipe preparation, the employee discarded used pipettes into an un-lidded receptacle. We also observed that when not in use, the employee's respirator was next to the work station open to the air, rather than being stored in a protective bag to prevent contamination.

We detected strong odors of flavorings in the mini-bulk compounding room during our visit. We used smoke tubes to qualitatively assess the room's wall-mounted LEV and found them to be inadequate when the container of material being prepared was not placed within a foot of the LEV. Also in the mini-bulk area, we observed that containers of opened chemicals were stored with loosely covered plastic sheeting rather than being resealed with their original lid. This method of storage was also likely contributing to the strong odor of chemicals in the room.

We observed in the QA laboratories, the articulating arm LEV units were difficult for employees to reach and place in position over a work area. Thus, these LEV units were ineffective in lowering potential exposures. We observed that used pipettes were being discarded into un-lidded containers. In addition, the balance exhaust hood enclosures could not be fully closed during weighing. We also observed that a used 55-gallon drum was being used as a waste disposal receptacle for all liquid waste material used in the QA laboratory but was not sealed after use thus allowing chemical to volatilize into the room.

We discussed the above observations with the safety manager at the time of the survey.

We observed that diacetyl was stored in the combustible liquid cooler located in the material storage department. It was reported that diacetyl was used more in the past and in some recipes substitutes such as acetoin and 2,3-pentanedione were being used.

We observed in several production and laboratory areas where small containers (less than 50 ml) of flavors are used, the containers did not have a label indicating the need for respiratory protection, which presents a risk of potential respiratory hazard.

Outgoing products containing >1% acetaldehyde or diacetyl were labeled with a warning that "this flavor may pose an inhalation hazard." These labels were not affixed to outgoing products that contained 2,3-pentanedione, nor did the corresponding MSDSs note a potential respiratory hazard.

Ventilation System Overview

LEV hoods were located throughout the production and laboratory areas. They consisted of elephant trunk (snorkel), bench-top, side wall-mounted, laboratory reach-in and walk-in, and over cooktop hoods.

Roof top units (RTU) 1-6 provided heating, ventilating, and air-conditioning needs of the production areas without recirculation, primarily to provide make-up air. Production rooms were kept at negative pressure, mostly via the high volume pulled through LEV hoods, with respect to hallways (also called transfers) to keep air from migrating from source rooms. RTU 7-10 served the administration and R&D areas of the building. Most of the administration area air was recirculated, but there is minimal recirculation in the R&D areas because of the high volume of air pulled out through the LEV hoods. RTU 11 provided heating, ventilating, and air-conditioning needs of the computer area of the building and recirculated a major portion of the air.

Exhaust fans A, B, C, and AP pulled air out of the building through the production area LEV hoods. Two of them passed the air through media bed packing and water spray scrubbers for odor removal. Exhaust fan E, which served the hoods in the R&D area, also scrubbed the air. RTU 1-10 were all located at the same elevation on the production area roof. RTU 11 was on the administration area roof about 20 feet higher than the production roof. Exhaust fan E was also on the roof with RTU 11, but its stack exhausted 20 feet above the RTU 11 outside air intake. Exhaust fan E was positioned about 40 feet south of RTU 11 and east of all other RTUs for the facility, thus taking advantage of the prevailing westerly winds to prevent entrainment of exhaust air into air intakes. Exhaust fans A, B, C, and AP had 11-foot stacks and were located together on the spray dry roof that was 22 feet higher than the main production roof holding most of the RTUs. These stacks were positioned at least 75 feet from the nearest RTU and northeast, north, or northwest of any of the RTUs, taking advantage of the mostly-westerly winds.

NIOSH Air Sampling

We were not aware of diacetyl use at the time of sampling. Diacetyl and 2,3-hexanedione were not detected in any air samples taken in the plant (Table 2). 2,3-pentanedione was detected in two air samples taken in the liquid compounding room. The detection limits ranged from 1.4 to 2.9 parts per billion (ppb) for diacetyl, 1.5 to 3.2 ppb for 2,3-pentanedione, and 1.7 to 3.6 ppb for 2,3-hexanedione.

Of the two air samples that detected 2,3-pentanedione in the liquid compounding room, sample 523 was an instantaneous sample taken near the trash can that an employee was using to dispose of used pipettes while making a flavoring recipe and resulted in a level of 47 ppb. The other sample that detected 2,3-pentanedione in the liquid compounding room, 545, was collected for 187 minutes while the sampling canister was placed on a work table approximately in the center of the room. During the sampling period, several employees were preparing recipes, which included fruit and cheese flavors. The resulting 2,3-pentanedione level was 26 ppb.

Ethanol, acetone, isopropyl alcohol, and chloroform were detected in the canister samples at concentrations less than 1 ppm and well below any occupational exposure guidelines. Limonene was detected in 11 samples.

The tape sample from the return exhaust in the culinary laboratory did not show evidence of fungal spores.

Medical Survey

Due to the poor quality of the primary provider's spirometry, the limited number of tests conducted by the secondary provider, and the exclusion of many employees from annual spirometry testing, we were unable to make a determination about the respiratory health of the workforce using existing records. We therefore conducted a medical survey.

A total of 367 (93%) of 393 current employees participated in the medical survey. All participants completed the questionnaire. Most participants also had spirometry testing (n=357) and measurement of diffusing capacity (n=347). All spirometry tests and 325 (94%) of the diffusing capacity tests were interpretable and included in our analyses. Table 3 shows participants' demographic characteristics, and Table 4 shows participants' work history characteristics.

Although the work history characteristics tended to identify distinct subgroups of participants, overlap among these groups was evident. Nearly all participants who reported ever working ≥ 1 hour daily in production areas (95%), ever using flavorings (97%), or ever using cleaning products (93%) also reported ever working in a production department. Majorities of participants who reported ever working in a production department also reported ever working ≥ 1 hour daily in production areas (59%), ever using flavorings (70%), or ever using cleaning products (76%); similar patterns were observed in other cross-tabulations of work history characteristics.

Participants who reported ever working in a production department had significantly higher proportions of males (69% versus 39%) and ever smokers (48% versus 26%), and a lower mean age (41.6 years versus 43.6 years) than participants who reported never working in a production department. Both groups had similar mean tenure at the facility (7.9 years versus 7.3 years). Similar patterns were observed for the other work history characteristics.

Table 5 shows participants' responses to questions about respiratory protection and local exhaust ventilation. Twenty-eight percent of participants reported using respiratory protection in their current job, most commonly disposable N95 filtering-facepiece respirators and full face respirators. The majority of those who reported using respiratory protection indicated that they had been fit-tested for the device. The most common reason for using respiratory protection was that it was required. Other reasons for using respiratory protection included dust, when using powders, and to clean up spills. Thirty-six percent of participants reported using local exhaust ventilation in their current job. Most of these participants indicated a reason for using local exhaust ventilation other than those listed in Table 5. These other reasons included dust, when using powders, when using raw materials,

for compounding, when using particular chemicals such as acetaldehyde, ammonia, and acetic acid, and when dumping flavors; in addition, many participants reported that the local exhaust ventilation was always or usually on, regardless of task.

Table 6 displays participants' responses to questions on symptoms and diagnoses. These symptoms and diagnoses were generally more common (up to twice as prevalent) among the subgroup of participants with abnormal spirometry. The most commonly reported symptoms among all participants were nasal, sinus, and eye symptoms, which were reported by 44% to 47% of participants. The most commonly reported chest symptoms were wheeze and shortness of breath, which were each reported by 22% of participants. Twenty-eight percent of participants reported asthma-like symptoms.

The prevalence of work-related symptoms ranged from 3% to 15% of participants. Participants reported a variety of exposures at work that caused or aggravated their symptoms (Table 7). Some participants noted that sinus symptoms were worse in the mini-bulk room and the spray dry area, and during quality control activities that involve smelling the products. The MID room was reported as contributing to cough.

In addition, 86 (23%) participants reported an exposure at the facility that had affected their breathing (not shown). These reported exposures included powders, dust, liquids, fumes, perfumes, fragrances, seasonings, alcohol, acetic acid, acetaldehyde, benzaldehyde, citric acid, diacetyl, diacetyl substitute, aspartame sweetener, capsicum or capsaicin, dimethyl sulfide, cinnamon, garlic oil, ginger, grape seed extract, horseradish oil, maltodextrin, mustard oil, pepper, jalapeno pepper, a silicon dioxide preparation, a sulfur compound, trimethylene, terpenes, caustic solutions used to clean and sanitize the pasteurizers, a chemical used for fogging a room to eradicate bacteria, propane powered floor buffers, a floor epoxy, and other chemicals and ingredients. Some participants noted breathing difficulties in the mini-bulk room that they could not attribute to a particular chemical or ingredient.

Twelve percent of all participants reported that they had ever been diagnosed with asthma, and 8% reported that they still had asthma. Among participants with abnormal spirometry, 20% reported ever receiving a diagnosis of asthma and 10% reported current asthma. Responses to additional questions on diagnoses for all participants were as follows: 15 (4%) reported heart disease, 10 (3%) reported chronic bronchitis, 2 reported chronic obstructive pulmonary disease, and 1 reported bronchiolitis obliterans. No participant reported a diagnosis of emphysema, hypersensitivity pneumonitis, or chemical pneumonitis.

Compared to the U.S. adult population, participants were significantly more likely to report wheeze in the last 12 months, sinusitis or sinus problems in the last 12 months, bringing up phlegm on most days for three consecutive months or more during the year, a diagnosis of hay fever, a diagnosis of asthma, and current asthma (Table 8). Participants were significantly less likely to report nasal symptoms. These patterns were consistent in analyses of subgroups of participants defined by work history characteristics (ever worked in a production department, ever worked ≥ 1 hour daily in production areas, ever used flavorings, or ever used cleaning products).

Table 9 shows unadjusted PRs for symptom comparisons among subgroups of survey participants defined by current work history characteristics. Compared to survey participants with < 7 years tenure at the facility, participants with ≥ 7 years tenure had significantly higher prevalence of shortness of breath. Compared to survey participants who did not currently work in a production department, participants who did currently work in a production department had significantly higher prevalence of usual cough and higher prevalence of usual phlegm. Excluding departments with fewer than 10 participants, production departments (current or ever) with higher prevalence of usual cough were dry blend, flavor creation, food group, liquids, maintenance, samples, warehouse, and technology and innovation. Excluding departments with fewer than 10 participants, production departments (current or ever) with higher prevalence of usual phlegm were dry blend, flavor creation, food group, liquids, maintenance, QA, samples, warehouse, and technology and innovation.

Table 9 also shows that compared to survey participants who currently spent < 1 hour daily in production areas, participants who currently spent ≥ 1 hour daily in production areas had significantly higher prevalence of asthma-like symptoms, usual cough, and phlegm; for these symptoms, PRs were significantly elevated for ever spending ≥ 1 hour daily in production areas as well (not shown). Compared to survey participants who did not currently use flavorings, participants who did currently use flavorings had significantly higher prevalence of nasal symptoms, sinusitis, and phlegm. Compared to participants who did not currently use cleaning products, participants who currently used cleaning products had significantly higher prevalence of nasal symptoms, sinusitis, rash, and phlegm. In addition, compared to participants who never used cleaning products, participants who ever used cleaning products at the plant had significantly higher prevalence of wheeze and asthma-like symptoms (not shown). There were no associations between symptoms and history of work at another flavoring plant (not shown). As indicated in Table 9, for nasal symptoms, sinusitis, rash, shortness of breath and phlegm, these associations were significant in models adjusted for smoking status. The association between tenure and shortness of breath remained significant when adjusted for both smoking status and participant age.

Table 10 shows unadjusted PRs for work-related symptom comparisons among subgroups of survey participants defined by current work history characteristics. There was no significant association between work-related symptoms and tenure at the facility (of note, work-relatedness of shortness of breath was not assessed by the questionnaire). Compared to survey participants who did not currently work in a production department, participants who did currently work in a production department had higher prevalence of all work-related symptoms; differences were statistically significant for work-related nasal symptoms, work-related sinusitis, and work-related eye symptoms. In addition, prevalence of work-related eye symptoms was significantly higher in participants who ever worked in a production department, compared to participants who never worked in a production department (not shown). All participants reporting work-related rash were in the ever production department category (not shown).

Excluding departments with fewer than 10 participants, production departments (current or ever) with higher prevalence of work-related breathing trouble were dry blend, food group,

liquids, and warehouse. Excluding departments with fewer than 10 participants, production departments (current or ever) with higher prevalence of work-related wheeze were dry blend, flavor creation, food group, liquids, samples, shipping/receiving, and warehouse. Excluding departments with fewer than 10 participants, production departments (current or ever) with higher prevalence of work-related nasal symptoms were flavor creation, liquids, samples, and technology and innovation. Excluding departments with fewer than 10 participants, production departments (current or ever) with higher prevalence of work-related sinusitis were dry blend, flavor creation, food group, liquids, samples, and warehouse. Excluding departments with fewer than 10 participants, production departments (current or ever) with higher prevalence of work-related eye symptoms were dry blend, flavor creation, food group, liquids, samples, shipping/receiving, warehouse, and technology and innovation. Excluding departments with fewer than 10 participants, production departments (current or ever) with higher prevalence of work-related rash were dry blend, food group, liquids, MID, and technology and innovation. Excluding departments with fewer than 10 participants, production departments (current or ever) with higher prevalence of work-related usual cough were dry blend, flavor creation, food group, liquids, shipping/receiving, warehouse, and technology and innovation.

Table 10 also shows that compared to survey participants who currently spent < 1 hour daily in production areas, participants who currently spent ≥ 1 hour daily in production areas had significantly higher prevalence of all work-related symptoms but eye symptoms. For some of these work-related symptoms (work-related breathing trouble, sinusitis, and rash), PRs also were significantly elevated for participants who reported ever spending ≥ 1 hour daily in production areas (not shown). Compared to survey participants who did not currently use flavorings, participants who did currently use flavorings had significantly higher prevalence of all work-related symptoms except rash. For all work-related symptoms but rash and usual cough, PRs were significantly elevated for ever using flavorings as well (not shown). Compared to participants who did not currently use cleaning products, participants who did currently use cleaning products had significantly higher prevalence of work-related wheeze, work-related nasal symptoms, and work-related sinusitis; for these same work-related symptoms except wheeze, PRs were significantly elevated for ever using cleaning products as well (not shown). There were no associations between work-related symptoms and history of work at another flavoring plant. As indicated in Table 10, for most work-related symptoms, the associations were significant in models adjusted for smoking status.

The results of the lung function tests are displayed in Table 11. Thirty (8.4%) participants who had spirometry testing had an abnormal result. An additional 18 (5.0%) had borderline obstruction. The mean percent predicted values for FEV_1 (99%) and FVC (101%) were normal. Bronchodilator was administered to 36 participants, including 12 (4%) of those with normal baseline spirometry and 24 (80%) of those with abnormal spirometry. None of the participants with normal baseline spirometry responded to bronchodilator with a significant increase in FEV_1. Four (17%) of the participants with abnormal baseline spirometry responded to bronchodilator with a significant increase in FEV_1. The majority (67%) of participants with obstruction or a mixed pattern (which may represent obstruction) had a fixed abnormality. Among participants who had diffusing capacity testing, 15 (4.6%) had a

low diffusing capacity and 24 (7.4%) had low total lung capacity. Most (73%) participants with low diffusing capacity had normal spirometry; 1 had obstruction, 2 had restriction, and 1 had a mixed pattern on spirometry. In addition, 2 participants with low diffusing capacity had borderline obstruction. Most (67%) participants with low total lung capacity had normal spirometry; 8 (33%) had restriction on spirometry.

Compared to the U.S. adult population, the prevalence of obstruction on spirometry among participants was as common as expected (Table 12). Participants had a significantly lower than expected prevalence of restriction on spirometry. When comparisons were adjusted for BMI, the PR for restriction was 0.5 (95% CI 0.3-0.8). These patterns were consistent in analyses of subgroups of participants defined by work history characteristics (ever worked in a production department, ever worked ≥ 1 hour daily in production areas, ever used flavorings, or ever used cleaning products).

Table 13 shows PRs for lung function abnormalities among subgroups of survey participants defined by current work history characteristics. There was no significant association between these lung function abnormalities and tenure at the facility. When borderline obstruction was included in "any spirometric abnormality," participants with ≥ 7 years tenure had significantly higher prevalence of any spirometric abnormality than participants with < 7 years tenure at the facility (PR=1.8; 95% CI 1.0-3.1) (not shown); this association remained significant with adjustment for smoking status. Compared to survey participants who did not currently work in a production department, participants who did currently work in a production department had higher prevalence of all lung function abnormalities, although the differences did not reach statistical significance. These patterns were also observed in comparisons of participants who ever worked in a production department with participants who never worked in a production department (not shown). All participants with restriction on spirometry fell in the ever worked in a production department category (not shown). When borderline obstruction was included in "any spirometric abnormality," participants who ever worked in a production department had significantly higher prevalence of any spirometric abnormality than participants who never worked in a production department (PR 2.6; 95% CI 1.0-7.1) (not shown). Excluding departments with fewer than 10 spirometry tests, production departments (current or ever) with higher prevalence of any abnormal spirometry were dry blend, liquids, maintenance, MID, samples, and shipping/receiving, and warehouse. Excluding departments with fewer than 10 diffusing capacity tests, production departments (current or ever) with higher prevalence of low diffusing capacity were food group, samples, technology and innovation, and warehouse; production departments (current or ever) with higher prevalence of low total lung capacity were dry blend, food group, maintenance, QA, regulatory/legal, and technology and innovation.

Table 13 also shows that compared to survey participants who currently spent < 1 hour daily in production areas, participants who currently spent ≥ 1 hour daily in production areas had higher prevalence of all lung function abnormalities; the difference was statistically significant for any spirometric abnormality and for low diffusing capacity. These patterns were also observed in comparisons of participants who ever spent ≥ 1 hour daily in production areas with participants who never spent ≥ 1 hour daily in production areas (not shown);

the difference was statistically significant for restriction (PR 4.0; 95% CI 1.1-14) and any abnormal spirometry (PR 3.3; 95% CI 1.4-7.4). Elevated PRs were also seen for some lung function abnormalities and use of current flavorings and current use of cleaning products, although the differences did not reach statistical significance. Furthermore, elevated PRs were observed for all lung function abnormalities and ever use of current flavorings and ever use of cleaning products (not shown); the difference was statistically significant for low diffusing capacity and ever used cleaning products (PR 7.7; 95% CI 1.0-58). When borderline obstruction was included in "any spirometric abnormality," participants who ever used flavorings had significantly higher prevalence of any spirometric abnormality than participants who never used flavorings (PR 1.9; 95% CI 1.0-3.5). There were no associations between lung function abnormalities and history of work at another flavoring plant. The observed associations between lung function abnormalities and ever work history characteristics remained significant in models that adjusted for smoking status.

Table 14 shows the mean values of lung function parameters by current work history characteristics. Compared to survey participants with < 7 years tenure at the facility, participants with ≥ 7 years tenure had significantly lower mean values of all lung function parameters. Compared to survey participants who did not currently work in a production department, participants who currently worked in a production department had lower mean values of spirometric parameters, although the differences were not statistically significant. Similar patterns were noted for ever working in a production department (not shown); the difference in mean values of percent predicted FVC between participants who ever worked in a production department (100.6%) and participants who did not ever work in a production department (103.8%) was statistically significant. Compared to survey participants who currently spent < 1 hour daily in production areas, participants who currently spent ≥ 1 hour daily in production areas also had significantly lower mean values of all spirometric parameters. Similar patterns were observed for ever spending ≥ 1 hour daily in production areas; differences for mean percent predicted FEV_1 and mean percent predicted FVC were statistically significant (not shown). Currently using flavoring ingredients and ever using flavoring ingredients (not shown) were also associated with lower mean values of spirometric parameters for most comparisons, but these differences were not statistically significant. Currently using cleaning products was not associated with differences in mean values of lung function parameters. There were no associations between mean values of lung function parameters and history of work at another flavoring plant.

The observed associations between lung function parameters and current work history characteristics (Table 14) or ever work history (not shown) remained significant in models that adjusted for smoking status in all but one instance. Furthermore, associations remained significant in models that included both tenure and other work history characteristics, with the exception of the association between mean percent predicted FVC and ever worked in a production department (p=0.01 for tenure; p=0.08 for ever worked in a production department).

Tables 15 and 16 show the PRs for lung function abnormalities and the mean values of lung function parameters by current work history characteristics for the subgroup who ever

worked in a production department. The elevated PRs for lung function abnormalities that we observed for all survey participants (Table 13) were evident among participants who ever worked in a production department (Table 15). Similarly, the differences in mean values of lung function parameters by current work history characteristics that we observed for all survey participants (Table 14) were also evident among participants who ever worked in a production department (Table 16), and in most cases were statistically significant. We noted similar patterns in mean values of lung function parameters in analyses limited to the subgroup of survey participants who never worked in a production department, but these analyses were limited by small sample sizes (64–69 participants total and 5–26 participants in the smaller arm, depending on the analysis). It was not possible to examine patterns in prevalence of lung function abnormalities in analyses limited to the subgroup of survey participants who never worked in a production department, as there were so few lung function abnormalities (0–2, depending on the abnormality) in this subgroup.

Discussion

We responded to a health hazard evaluation request from employees at a flavoring manufacturing facility who expressed concerns about exposure to flavoring chemicals and respiratory health. Our evaluation included a tour of the facility, air sampling for selected flavoring chemicals and other VOCs, and a medical survey of the workforce.

The facility uses thousands of flavoring chemicals, including diacetyl and the diacetyl substitutes 2,3-pentanedione and 2,3-hexanedione. Diacetyl is a butter flavoring chemical with four carbons; 2,3-pentanedione has the same structure but 5 carbons, while 2,3-hexanedione has the same structure but 6 carbons. Occupational exposure to diacetyl can cause obliterative bronchiolitis (also known as bronchiolitis obliterans), a rare lung disease in which the lung's small airways become scarred, leading to breathlessness [NIOSH 2011a]. Studies of laboratory animals exposed to the diacetyl substitute 2,3-pentanedione indicate that it is also toxic to the respiratory system [Morgan et al. 2012; Hubbs et al. 2012]. Little is known about the toxicity of other diacetyl substitutes including 2,3-hexanedione, or the long-term respiratory toxicity of other flavoring chemicals.

Prior evaluations at other flavoring manufacturing facilities demonstrated high diacetyl exposures and lack of effective engineering controls and respiratory protection programs [NIOSH 2007; NIOSH 2008; Martyny et al. 2008]. At 16 flavoring manufacturing facilities evaluated by an academic group, diacetyl concentrations in air were as high as 60 ppm, with an average of 1.8 ppm [Martyny et al. 2008]. At a flavoring manufacturing facility evaluated by NIOSH, the company provided air sampling results that documented diacetyl exposures as high as 10 ppm [NIOSH 2011b]. NIOSH has proposed a recommended exposure level of 5 ppb, which is hundreds to thousands of times lower than these values [NIOSH 2011a]. In contrast to prior evaluations at other flavoring manufacturers, this facility did not have documented high diacetyl exposures and had many safeguards in place to reduce exposures to flavoring chemicals, including ventilation, work practices, and respiratory protection. Past sampling conducted by the facility's consultants while diacetyl was used did not detect

diacetyl in the air. Our own sampling did not detect diacetyl, which was not in use at the time. The facility's general ventilation system was notable for a design that minimized the re-entrainment of exhaust air by locating the roof mounted exhaust stacks well above any intakes. The stacks were also designed to force the exhausted air upwards away from the building. Furthermore, separate ventilation was provided for the production areas, which received 100% fresh air and were kept under negative pressure. The facility used multiple means to communicate respiratory hazard information to employees, including signs, labels on containers, and warning incorporated into recipes. An additional proactive safeguard was to include 2,3-pentanedione (acetyl propionyl) on the "Respirator Use Required List of Chemicals."

Although flavoring exposures at this facility appear to be better controlled than at other flavoring manufacturing facilities, the facility reported using amounts of diacetyl substitutes that put it in the same higher health risk category as California flavoring manufacturing facilities that used larger amounts of diacetyl annually [Kreiss et al. 2012]. Therefore, ongoing efforts to control flavoring exposures are warranted. We found several areas where improvements could be made. Some employees may be exposed to flavoring chemicals for which the facility requires respiratory protection because small bottles or containers lack hazard labeling. In addition, we noted problems with the design and/or placement of LEV that reduced the effectiveness of these controls. We also observed early removal of respiratory protection that could lead to hazardous exposures. It is important to note that once a hazardous chemical has been added to a mixture, it still has the potential to volatilize into the breathing zone of the employee. Thus, a mixture containing a hazardous chemical should be considered hazardous as well. Similarly, a hazardous chemical in waste still has the potential to volatilize into the breathing zone of the employee. Thus, waste containing a hazardous chemical also should be considered hazardous. Our detection of 2,3-pentanedione at a concentration of 47 ppb near an un-lidded trash receptacle highlights the potential for exposure to flavoring chemicals from disposed waste. NIOSH has proposed a short-term (15-minute) exposure limit of 31 ppb for 2,3-pentanedione [NIOSH 2011a]. Additionally, although 2,3-pentanedione was on the "Respirator Use Required List of Chemicals," the instructions stated that respirator use was required, but similar chemicals, such as diacetyl, stated that respirator use was required and the chemical should be weighed under a hood. The instructions for handling 2,3-pentanedione should also include the warning to weigh material under a hood.

We found evidence that obliterative bronchiolitis had occurred in the facility's workforce in the past. To determine the burden of respiratory disease in the current workforce, we offered a medical evaluation to all current employees. Obliterative bronchiolitis traditionally has been described as an obstructive lung disease. Symptoms may include cough, shortness of breath, and wheeze, with lung function tests showing obstruction on spirometry. Low diffusing capacity may be present, particularly with severe disease. However, some patients with obliterative bronchiolitis on lung biopsy have been found to have normal or restrictive spirometry and normal diffusing capacity [King et al. 2011]. Prior evaluations at other flavoring manufacturing facilities have documented a variety of lung function abnormalities, including obstruction [Kim et al. 2010], restriction [NIOSH 2011b], and increased declines

in lung function over time [Kreiss et al. 2012]. In addition, given the diversity of potential exposures in the facility, we considered the possibility that other adverse health outcomes involving the respiratory tract, mucous membranes, and skin were possible. Thus, in designing the medical survey and conducting analyses of the data, we did not focus exclusively on obstructive lung disease.

The employer was fully supportive of the medical survey, publicizing it among the workforce, providing ample time for participation during the workday, and making available to us multiple offices and conference rooms at the facility over the course of the two-week survey. Indeed, the high participation rate (93%) reflects the interest and commitment of both employees and the employer to the evaluation. This high participation rate is important because it means that the results of the medical survey are likely to accurately reflect the experiences of all current employees at the facility. With lower participation, it would be difficult to know whether the results applied to all current employees, or were skewed because only certain types of employees (for instance, those with symptoms, those who worked in a particular department, or those with longer tenure) participated.

We began by examining responses to questions about symptoms and diagnoses. When we compared the workforce to the U.S. adult population, we found that some respiratory symptoms (wheeze, sinus symptoms, usual phlegm) and self-reported diagnoses (hay fever, asthma) were more common than expected. We also made comparisons within the workforce. We found that some respiratory symptoms (asthma-like symptoms, nasal symptoms, sinusitis, shortness of breath, usual cough, and usual phlegm) were more common among participants who might have had higher flavoring chemical exposures than among those who might have had lower flavoring chemical exposures, based on facility tenure, department, time spent in production areas, or self-reported use of flavoring ingredients. Work-related symptoms (those that tend to improve away from the facility) were even more strongly associated with work history characteristics that suggest higher flavoring chemical exposures. Some symptoms and work-related symptoms were more common among participants who reported using cleaning products at work than among participants who reported not using cleaning products at work. Taken together, these findings suggest that exposures at the facility contributed to an excess burden of self-reported respiratory problems in the workforce.

We next considered the lung function test results, starting with category (normal/abnormal). Abnormal test results have values below the predicted values. Overall, obstructive spirometric abnormalities were no more common than expected and spirometric restriction was actually less common than expected. However, comparisons within the workforce demonstrated that the rates of abnormal spirometry and abnormal diffusing capacity differed among groups defined by work history characteristics. Obstruction, restriction, a combined category that included any spirometric abnormality, and abnormally low diffusing capacity were generally more common among participants with longer tenure, those who worked in production departments, those who spent more time in production areas, and those who used flavoring ingredients; differences were statistically significant for time spent in production areas in some cases and not explained by smoking status or work at another flavoring plant. Since

lung function test interpretations take into account a person's age, sex, height, and, for spirometry, race, the observed differences cannot be explained by these factors either.

We also examined lung function test results by average values. When all participants were considered together as a group, average lung function values were normal. However, comparisons within the workforce demonstrated that average lung function values differed among groups defined by work history characteristics. Average lung function values tended to be lower among participants with longer tenure, those who worked in production departments, those who spent more time in production areas, and those who used flavoring ingredients. For tenure and time spent in production areas, the differences were statistically significant and could not be explained by smoking status or work at another flavoring plant. Again, because the average lung function values take into account a person's age, sex, height, and, for spirometry, race, these factors also cannot explain the observed differences.

Lung function varies over a person's lifespan, with growth in childhood and adolescence, a plateau during young adulthood, and decline beginning in later adulthood [Jackson et al. 2004]. Lower than expected lung function may therefore be related to low lung function at birth, decreased growth of lung function during youth, a shortened plateau phase during early adult life, or an increased decline in lung function in later adult life [Prescott and Vestbo 1999]. Our findings of lower lung function related to work history characteristics are consistent with workplace exposures' contributing to increased declines in lung function in the current workforce, as was observed in California flavoring manufacturing employees [Kreiss et al. 2012]. While some of the declines may have been severe enough to lead to lung function abnormalities, most were not, resulting in rates of lung function abnormalities that were no more common (or even lower) than expected.

An alternative explanation is that the observed differences in lung function by work history characteristics are related to non-occupational factors that tend to differ between production employees and non-production employees. Indeed, there is evidence of socioeconomic differences in lung function, with lower socioeconomic status being associated with lower lung function [Prescott and Vestbo 1999; Jackson et al. 2004; Van Sickle et al. 2011]. The cause is likely multifactorial, including prenatal exposures, more frequent lower respiratory tract illness in childhood, housing conditions, air pollution, environmental (second-hand) tobacco smoke, diet, and other lifestyle factors including smoking [Prescott and Vestbo 1999]. As noted above, we assessed smoking status and demonstrated that the differences were not explained by smoking. However, other potentially explanatory non-occupational factors were not assessed. If the relationships between work history characteristics and lung function were confounded by some unmeasured non-occupational factor, then we would not expect to see differences in lung function by work history characteristics when analyses were limited to production employees only or to non-production employees only. Instead, in these subgroup analyses, the relationships between work history characteristics and lung function persisted. In other words, even among only those participants who had ever worked in a production department (who would be expected to be more similar than the workforce as a whole in terms of social and environmental factors affecting lung function), lung function was lower among participants with longer tenure, those who spent more time in production areas,

and those who used flavoring ingredients. These findings support the conclusion that the uneven distributions of lung function abnormalities and average lung function values in this workforce were related to occupational exposures, rather than non-occupational factors.

There are several limitations to address. First, because our medical survey was a one-time evaluation, it was not possible to demonstrate patterns of lung function change over time. Nonetheless, our findings are most consistent with increased declines in serial lung function among subgroups defined by work history characteristics, for the reasons described above. Due to the complexity of the workplace environment, with thousands of potential exposures and great variability in exposures on a day-to-day basis, using air measurements to estimate exposures or create exposure groups was not practical. Instead, we focused on the work history characteristics that arguably better integrate exposure information across chemicals and time than would time-limited sampling data. Yet each work history characteristic was undoubtedly subject to some misclassification. For instance, some jobs within production departments were primarily administrative; production area was not explicitly defined in the questionnaire; use of flavoring ingredients and cleaning chemicals did not incorporate frequency or type, which may have varied. As such, the consistency and strength of the associations with tenure, which is less subject to misclassification (and confounding by non-occupational factors), is very important. We conducted the survey in the early spring during allergy season, which may have affected our estimates of symptom prevalence. However, spirometry showed mostly fixed obstruction, not consistent with an allergic response, and diffusing capacity would not be expected to be affected by seasonal allergies. Finally, we were made aware of two former employees who left employment due to lung disease, and it is possible that others may have left employment due to respiratory illness. Thus, the current workforce included in the survey may have been healthier than the entire cohort of people who had been employed at this facility [Li and Sung 1999]. The absence of former employees in our survey may have obscured relationships between exposure and health outcomes that an evaluation of both current and former employees would have found. Nonetheless, even among relatively healthy current employees, the impact of exposure on health was evident.

Conclusions

The facility uses thousands of chemicals, some of which are recognized respiratory toxins and most of which have unknown respiratory toxicity. Among current employees, some symptoms and diagnoses were more common than expected, while spirometric abnormalities were not in excess. Symptoms, work-related symptoms, lung function abnormalities, and average lung function values differed by work history characteristics. Employees with longer facility tenure, those who worked in production departments, those who spent more time in production areas, and those who used flavoring ingredients tended to have more symptoms, more work-related symptoms, more lung function abnormalities, and lower average lung function values than others. These differences could not be explained by smoking status or employment at another flavoring plant, and persisted in analyses limited only to production employees, suggesting that they reflect outcomes of occupational exposures at the facility. While many controls are already in place to reduce exposure to flavoring chemicals, we noted

potential opportunities for exposures during our site visit that can be addressed through enhanced engineering controls, modified work practices, and improved use of respiratory protection.

Recommendations

Based on our findings, we recommend the actions listed below to create a more healthful workplace.

Elimination and Substitution

Elimination and substitution of a toxic/hazardous process material have traditionally been highly effective means for reducing hazards. However, these may not be feasible approaches in this facility, given the limited toxicological information available. Substitution for diacetyl is particularly challenging, as little is known about the health effects of substitute flavorings. Available information on the diacetyl substitute 2,3-pentanedione indicates that it has similar toxicity to diacetyl, which raises concerns that other substitutes with similar chemical structure may also be respiratory toxins.

1. Until more is known about the safety of diacetyl substitutes, continue to handle ingredients that contain these butter flavoring chemicals as respiratory toxins.

Engineering Controls

Engineering controls reduce exposures to employees by removing the hazard from the process or placing a barrier between the hazard and the employee. Engineering controls can be effective at protecting employees without placing primary responsibility of implementation on the employee.

1. Improve the design of local exhaust ventilation systems with articulating arms in the QA laboratory.
2. Improve the design of wall-mounted ventilation hoods in the mini-bulk area for more effective capture of vapors.
3. Improve the design of hoods over weigh stations in the liquid compounding room.
4. Improve the design of slot hoods in the mini bulk room.
5. Conduct period air sampling as a way to determine the efficacy of engineering controls.

Administrative Controls

Administrative controls are management-dictated work practices and policies to reduce or prevent exposures to workplace hazards. The effectiveness of administrative changes in work practices for controlling workplace hazards is dependent on management commitment

and employee acceptance. Regular monitoring and reinforcement is necessary to ensure that control policies and procedures are not circumvented in the name of convenience or production.

1. To reduce volatilization of flavorings, keep containers tightly closed when not in use.
2. To reduce volatilization of flavorings, do not use open trash bins or uncapped containers for disposal of waste that may have residual flavoring material.
3. When compounding flavoring recipes, add diacetyl and other high priority chemicals last, if possible, to minimize exposure time.
4. Ensure that employees don a respirator prior to the addition of diacetyl and other high priority chemicals and wear the respirator until mixing is complete and the container is sealed.

Personal Protective Equipment

PPE is the least effective means for controlling employee exposures. Proper use of PPE requires a comprehensive program, and calls for a high level of employee involvement and commitment to be effective. The use of PPE requires the choice of the appropriate equipment to reduce the hazard and the development of supporting programs such as training, change-out schedules, and medical assessment if needed. PPE should not be relied upon as the sole method for limiting employee exposures. Rather, PPE should be used until engineering and administrative controls can be demonstrated to be effective in limiting exposures to acceptable levels.

1. Given the observed increased burden of respiratory symptoms and lung function abnormalities in potentially flavoring-exposed employees, include all employees who spend time in production areas or use flavorings in the respiratory protection program.
2. Given the increased burden of respiratory symptoms among employees who used cleaning products, include sanitation employees in the respiratory protection program.
3. Respirators should always be stored in their original protective bag when not in use. It is important for respirators to be stored properly to protect them from damage, contamination, dust, sunlight, extreme temperatures, excessive moisture, and damaging chemicals. Respirators should never be left hanging on a machine, lying on a workbench, or tossed into a toolbox or a drawer.

Medical Surveillance

Monitoring of spirometry results over time can identify clusters of employees with declines in lung function parameters that are greater than expected with normal aging. This information can be used to evaluate the effectiveness of current controls in place and prioritize the introduction of new controls. Spirometry quality is crucial to this effort: without high quality spirometry, it is impossible to know if year-to-year variations in values are real or reflect imprecise measurements.

1. Ensure that the spirometry provider conducts high quality spirometry testing. Multiple resources are available to assist. The OSHA/NIOSH Infosheet in Appendix B includes a checklist for employers detailing critical elements of spirometry testing that should be considered for inclusion in contracts with providers. OSHA's Best Practices document [OSHA 2013] may also be useful.
2. Ensure that the spirometry provider conducts longitudinal assessment of spirometry values to monitor changes in lung function over time. A general rule of thumb is that an annual decline in FEV_1 of greater than 10% is excessive and should prompt further evaluation [Wang 2006]. More specifically, Spirometry Longitudinal Data Analysis software is a visual and quantitative tool intended to assist the healthcare provider in monitoring and interpreting computerized longitudinal spirometry data for individuals as well as for a group. Spirometry Longitudinal Data Analysis software can be downloaded for free from the NIOSH website (http://www.cdc.gov/niosh/topics/spirometry/ spirola.html).
3. Encourage employees to report new or ongoing respiratory symptoms to a designated individual at the facility.
4. The occurrence of new or ongoing respiratory symptoms or excessive declines in lung function in the workforce should prompt consideration of work-related lung disease and re-evaluation of the potential for exposure to respiratory hazards.

Hazard Communication

1. Develop a labeling system for small bottles/containers of flavors that are on the "Respirator Use Required List of Chemicals" but are too small to receive the warning stickers placed on larger containers.
2. For outgoing products, improve hazard communication about potential respiratory toxicity by labeling products that contain diacetyl substitutes the same way products that contain diacetyl are labeled.
3. For outgoing products' MSDS, incorporate information about potential respiratory toxicity for products that contain diacetyl substitutes.

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Tables

Table 1. FEMA high priority flavoring chemicals in use at the facility, November 2011.

Chemical Name
Acetaldehyde
Acetic Acid
Acetoin
Benzaldehyde
Butyric Acid
Diacetyl (2,3 butanedione)
Formic Acid
Furfural
2,3-hexanedione
Isobutyraldehyde
Isobutyric acid
Methyl Mercaptan
Methyl Sulfide
2,3-pentanedione
2-pentenal
Phosphoric acid
Propionaldehyde
Propionic acid
Trimethylamine
Valeraldehyde

FEMA=Flavor and Extract Manufacturers' Association

Table 2. Results of NIOSH air sampling using evacuated canisters.

Location	Outside (up wind of plant)	Liquid Samples Room (center of room on table)	Liquid Samples Room (near used pipet trash can)	Mini Bulk (liquid compounding)	Mini Bulk (liquid compounding)	Receiving (quarantine room)	Raw materials lab	MID (Culinary kettle room)	MID (Culinary tote hose down room)	MID (Culinary vacuum drying room)	Finished Products laboratory	Dairy room	Sweet pilot plant (spray dry room)	Undiluted LOD (ppb)*	Undiluted LOQ (ppb)*	Maximum calibration point
Sample ID	**538**	**545**	**523**	**533**	**525**	**514**	**540**	**515**	**532**	**531**	**537**	**518**	**519**	--	--	--
Sample period	instant	187	instant	181	instant	186	instant	instant	instant	instant	instant	183	instant	--	--	--
2,3-butanedione (diacetyl)	--	--	--	--	--	--	--	--	--	--	--	--	--	**0.9**	**2.9**	**21**
2,3-pentanedione	--	26	47	--	--	--	--	--	--	--	--	--	--	**1.0**	**3.4**	**21**
2,3-hexanedione	--	--	--	--	--	--	--	--	--	--	--	--	--	**1.1**	**3.5**	**20**
Ethanol	(2.7)	7,100	8,500	21,000	40,000	520	400	82	46	52	200	24	54	**1.0**	**3.4**	**21**
Acetone	--	(2.8)	--	8	--	110	38	17	9.7	(3.7)	160	(3.4)	--	**1.6**	**5.5**	**21**
Isopropanol	4.4	--	--	--	--	--	7.1	--	(3.1)	(2.6)	22	(1.7)	--	**1.1**	**3.6**	**21**
Hexane	--	--	--	--	--	--	(2.4)	--	--	--	--	--	--	**0.9**	**2.9**	**21**
Chloroform	--	--	--	--	--	--	--	--	11.5	4.7	--	--	--	**0.9**	**3.0**	**21**
Alpha-pinene	--	56	110	--	--	--	--	--	--	--	--	--	--	**1.3**	**4.4**	**20**
Limonene	--	450	360	46	60	7.8	8.2	6.2	(3.5)	5.3	6.4	1,100	1,100	**1.5**	**5.2**	**21**
Dilution factor	1.53	3.13	1.51	3.23	1.51	3.20	1.52	1.51	1.50	1.50	1.51	3.24	1.51	--	--	--

LOD=limit of detection; LOQ=Limit of Quantification; -- =Not detected at the LOD; () = value is between LOD and LOQ

Notes: All results in ppb. Results greater than the max calibration point were subsequently analyzed with smaller aliquots or dilution. No recovery correction was performed. No interferences with qualitatively identified compounds. One field blank had results below the limit of detection for all analytes. A second field blank had results below the limit of detection for all analytes except isopropanol (detected at 1.2 ppb).

*LODs and LOQs shown in table are for samples without dilution; actual limit for each sample compound after dilution can be calculated by multiplying undiluted limit by dilution factor.

Table 3. Demographic characteristics of medical survey participants (N=367)

Characteristic	Value
Age, years, mean (range)	42 (20-71)
Male, n (%)	231 (63)
Race, n (%)	
White	334 (91)
Black	23 (6)
Other	10 (3)
Smoking status, n (%)	
Current	70 (19)
Former	91 (25)
Never	206 (56)

Table 4. Work history characteristics of medical survey participants (N=367)

Characteristic	Value
Tenure, years, median (range)*	7 (<1-14)
Work in production department	
Current	269 (73)
Ever	293 (80)
Spend ≥1 hour in production daily, n (%)	
Current	138 (38)
Ever	182 (50)
Use flavoring ingredients, n (%)	
Current	165 (45)
Ever	212 (58)
Worked at another flavoring plant, n (%)*	82 (22)
Use cleaning products, n (%)	
Current	211 (57)
Ever	240 (65)

*Tenure at the current facility, which opened in 1998. Employment with the same company at a prior location was considered to be work at another flavoring plant.

Table 5. Practices related to respiratory protection and local exhaust ventilation in current job among medical survey participants (N=367)

Practice	n/N (%)
Use respiratory protection	101/367 (28)
Type of respiratory protection used	
Dust mask	11/101 (11)
N95 filtering-facepiece respirator	75/101 (74)
Half-face respirator	1/101 (1)
Full-face respirator	67/101 (66)
Had fit test for device	72/101 (71)
When respiratory protection used	
When handling hazardous chemical	13/101 (13)
Due to odor	13/101 (13)
Due to irritation	16/101 (16)
When required or instructed to use	58/101 (57)
Other	52/101 (51)
Use local exhaust ventilation*	132/367 (36)
When local exhaust ventilation used	
When handling hazardous chemical	9/132 (7)
Due to odor	11/132 (8)
Due to irritation	2/132 (2)
When required or instructed to use	17/132 (13)
Other	115/132 (87)

*Such as fume hoods, snorkels, Nederman arms, and wall slot vents

Table 6. Symptoms and self-reported diagnoses of medical survey participants (N=367)

Symptom or diagnosis*	n (%)
Breathing trouble	75 (20)
Work-related breathing trouble	25 (7)
Wheeze	82 (22)
Work-related wheeze	20 (5)
Asthma-like symptoms†	101 (28)
Nasal symptoms	164 (45)
Work-related nasal symptoms	55 (15)
Sinusitis	174 (47)
Work-related sinusitis	43 (12)
Eye symptoms	161 (44)
Work-related eye symptoms	30 (8)
Rash	59 (16)
Work-related rash	14 (4)
Shortness of breath‡	81 (22)
Usual cough	45 (12)
Work-related usual cough	12 (3)
Usual phlegm	56 (15)
Hay fever or nasal allergies diagnosis	115 (31)
Asthma diagnosis	
Ever	44 (12)
Current	28 (8)

*Work-related symptoms were defined as symptoms that improved away from the facility.†Asthma-like symptoms were defined as current use of asthma medicine and/or one or more of the following symptoms in the past 12 months: wheezing or whistling in the chest, awakening with a feeling of chest tightness, or attack of asthma.
‡Shortness of breath when hurrying on level ground or walking up a slight hill

Table 7. Workplace exposures reported to contribute to symptoms of medical survey participants (N=367)*

	Work-related Symptom					
Exposure	Nasal	Sinusitis	Eye	Rash	Wheeze	Cough
Acetaldehyde				X	X	
Acetic acid						X
Acetoin					X	X
Alcohols		X	X		X	X
Benzaldehyde					X	X
Boxes				X		
Caffeine					X	
Capsaicin			X			X
Capsicum	X		X		X	
Carrier used in spray dry flavors					X	
Chlorinated soaps	X			X		
Cinnamon					X	
Citric acid						X
Computer monitors			X			
Diacetyl		X			X	
Dry air				X		
Dust	X	X	X		X	X
Ethyl acetate					X	
Fragrances		X				
Frequent hand-washing				X		
Garlic		X				
Gloves				X		
Hot sauce						X
Lab coats				X		
Liquids		X	X	X	X	X
Maltodextrin					X	
Maple			X			
Odors	X					
Onion			X			
Perfumes		X			X	
Powders	X	X	X	X	X	X
Silicon dioxide prep	X					
Stevia			X			
Sucrose						X
Ventilation in lab area					X	
Wing flavor						X

*X indicates that at least one participant reported that the exposure caused or aggravated the symptom.
Some of the chemicals in this table are on the facility's "Respirator Use Required List of Chemicals."

Table 8. Adjusted* comparisons of symptoms and self-reported diagnoses among medical survey participants to U.S. adult population (NHANES III) (N=365)

Symptom or Diagnosis	Observed (n)	Expected (n)	PR	95% CI
Wheeze	82	58.1	**1.4**	**1.1-1.8**
Nasal symptoms	163	207.3	**0.8**	**0.7-0.9**
Sinus symptoms	172	136.0	**1.3**	**1.1-1.5**
Eye symptoms	161	147.1	1.1	0.9-1.3
Shortness of breath	81	65.9	1.2	1.0-1.5
Usual cough	26	28.1	0.9	0.6-1.4
Usual phlegm	56	25.5	**2.2**	**1.7-2.8**
Hay fever, ever	114	49.9	**2.3**	**1.9-2.7**
Asthma, ever	44	28.4	**1.5**	**1.2-2.1**
Asthma, current	28	17.7	**1.6**	**1.1-2.3**
Chronic bronchitis, ever	10	18.4	0.5	0.3-1.0

Statistically significant prevalence ratios and confidence intervals are in bold.
*Adjusted for race, sex, age, and smoking status.

Table 9. Prevalence ratios of symptoms among medical survey participants by current work history characteristics (N=367)

	Work history characteristic Prevalence ratio (95% CI)				
Symptom	Tenure ≥7 years	Production department	Spend ≥1 hr in production daily	Use flavoring ingredients	Use cleaning products
Breathing trouble	0.9 (0.6-1.4)	1.2 (0.7-1.9)	1.3 (0.9-2.0)	1.4 (0.9-2.1)	1.3 (0.9-2.0)
Wheeze	1.1 (0.7-1.6)	1.4 (0.9-2.3)	1.4 (0.9-2.0)	1.2 (0.8-1.8)	1.4 (0.9-2.1)
Asthma-like symptoms	0.9 (0.6-1.2)	1.4 (0.9-2.1)	**1.6 (1.1-2.2)***	1.2 (0.9-1.7)	1.4 (1.0-2.0)
Nasal symptoms	1.0 (0.8-1.2)	1.2 (0.9-1.5)	1.2 (0.9-1.5)	**1.3 (1.0-1.6)***	**1.3 (1.0-1.7)***
Sinusitis	1.1 (0.9-1.3)	1.1 (0.9-1.5)	1.2 (1.0-1.5)	**1.3 (1.1-1.6)***	**1.3 (1.0-1.6)***
Eye symptoms	1.2 (0.9-1.5)	0.9 (0.7-1.2)	1.0 (0.8-1.3)	1.1 (0.8-1.3)	1.2 (0.9-1.5)
Rash	1.5 (1.0-2.5)	1.1 (0.6-1.8)	1.1 (0.7-1.8)	1.3 (0.8-2.0)	**1.8 (1.1-3.1)***
Shortness of breath	**1.9 (1.3-2.9)***	1.3 (0.8-2.0)	1.0 (0.7-1.5)	1.3 (0.9-1.8)	1.3 (0.9-2.0)
Usual cough	0.8 (0.5-1.5)	**2.9 (1.2-7.2)***	**2.3 (1.3-3.9)***	1.5 (0.9-2.7)	1.8 (1.0-3.4)
Usual phlegm	1.0 (0.6-1.6)	1.9 (1.0-3.7)	**2.4 (1.5-3.9)***	**1.9 (1.2-3.1)***	**1.8 (1.1-3.2)***

hr=hour
For each prevalence ratio, comparison is of the prevalence of the symptom among the subgroup of participants who met the work history characteristic and prevalence of the symptom among the subgroup of participants who did not meet the work history characteristic. Statistically significant prevalence ratios and confidence intervals are in bold.
*Association was significant in model adjusted for smoking status (ever/never) and age·

Table 10. Prevalence ratios of work-related symptoms among medical survey participants by current work history characteristics (N=367)

	Work history characteristic Prevalence ratio (95% CI)				
Symptom	Tenure ≥7 years	Production department	Spend ≥1 hr in production daily	Use flavoring ingredients	Use cleaning products
WR breathing trouble	0.7 (0.3-1.5)	2.7 (0.8-8.7)	**3.5 (1.6-8.0)***	**3.1 (1.3-7.4)***	1.9 (0.8-4.4)
WR wheeze	0.9 (0.4-2.0)	3.3 (0.8-14)	**2.5 (1.0-5.9)***	**2.9 (1.1-7.3)***	**3.0 (1.0-8.7)***
WR nasal symptoms	0.8 (0.5-1.3)	**2.1 (1.0-4.4)**	**1.9 (1.1-3.0)***	**2.7 (1.6-4.7)***	**2.6 (1.4-4.9)***
WR sinusitis	1.2 (0.7-2.1)	**2.8 (1.1-6.8)***	**2.5 (1.4-4.5)***	**2.8 (1.5-5.2)***	**3.8 (1.7-8.3)***
WR eye symptoms	1.2 (0.6-2.4)	**5.1 (1.2-21)***	1.9 (1.0-3.8)	**2.4 (1.2-5.1)***	2.0 (0.9-4.4)
WR rash	0.6 (0.2-1.7)	†	**9.9 (2.3-44)***	3.1 (1.0-9.6)	9.6 (1.3-73)
WR usual cough	1.1 (0.3-3.2)	4.0 (0.5-31)	**3.3 (1.0-11)**	**6.1 (1.4-28)***	3.7 (0.8-17)

hr=hour; WR=work-related
For each prevalence ratio, comparison is of the prevalence of the symptom among the subgroup of participants who had the work history characteristic and prevalence of the symptom among the subgroup of participants who did not have the work history characteristic. Statistically significant prevalence ratios and confidence intervals are in bold.
*Association was significant in model adjusted for smoking status (ever/never) and age.
†Prevalence ratio could not be calculated, as all participants reporting work-related rash were in the current production department category.

Table 11. Results of lung function tests of medical survey participants

Spirometry (N=357)	
Obstruction, n (%)	13 (4)
Restriction, n (%)	15 (4)
Mixed, n (%)	2 (1)
Any abnormality, n (%)*	30 (8)
FEV1% predicted, mean (range)	99 (50-139)
FVC % predicted, mean (range)	101 (59-132)
FEV1/FVC %, mean (range)	79 (44-96)
Bronchodilator	
FEV1 response, overall, n/N (%)	4/36 (11)
FEV1 response, baseline normal, n/N (%)	0/12
FEV1 response, baseline obstruction, n/N (%)	2/10 (20)
FEV1 response, baseline restriction, n/N (%)	0/12
FEV1 response, baseline mixed, n/N (%)	2/2 (100)
FEV1 response, baseline any abnormality, n/N (%)	4/24 (17)
Diffusing capacity (N=325)	
Low diffusing capacity, n (%)	15 (5)
Low total lung capacity, n (%)	24 (7)
Diffusing capacity % predicted, mean (range)	95 (40-134)
Total lung capacity % predicted, mean (range)	92 (63-118)

*Any abnormality includes obstruction, restriction, and mixed pattern. An additional 18 participants had borderline obstruction.

Table 12. Adjusted* comparisons of spirometric abnormalities among medical survey participants to U.S. adult population (NHANES III)

Abnormality	Observed (n)	Expected (n)	PR	95% CI
Obstruction	13	12.6	1.0	0.6-1.8
Obstruction including mixed	15	18.7	0.8	0.5-1.3
Restriction	15	25.4	**0.6**	**0.4-1.0**

Statistically significant prevalence ratios and confidence intervals are in bold.
*Adjusted for race, sex, age, and smoking status.

Table 13. Prevalence ratios of lung function abnormalities by current work history characteristics for all participants (N=357 for spirometry, N=325 for diffusing capacity and total lung capacity)

	Work history characteristic Prevalence ratio (95% CI)				
Abnormality	Tenure ≥7 years	Production department	Spend ≥1 hr in production daily	Use flavoring ingredients	Use cleaning products
Obstruction	1.2 (0.4-3.6)	1.9 (0.4-8.5)	2.6 (0.9-7.7)	1.9 (0.6-5.7)	1.1 (0.4-3.4)
Restriction	2.1 (0.7-6.1)	4.9 (0.6-37)	1.8 (0.7-4.9)	1.0 (0.4-2.8)	0.8 (0.3-2.2)
Any spirom abnormality	1.8 (0.9-3.7)	2.3 (0.8-6.3)	**2.4 (1.2-4.8)***	1.6 (0.8-3.1)	1.1 (0.5-2.2)
Low diffusing capacity	2.2 (0.8-6.3)	5.0 (0.7-37)	**3.2 (1.1-9.3)***	1.9 (0.7-5.2)	3.0 (0.9-10)
Low total lung capacity	1.1 (0.5-2.4)	1.3 (0.5-3.5)	1.4 (0.6-3.0)	0.8 (0.3-1.7)	1.0 (0.5-2.3)

hr=hour; spirom=spirometric
For each prevalence ratio, comparison is of the prevalence of the abnormality among the subgroup of participants who had the work history characteristic and the prevalence of the abnormality among the subgroup of participants who did not have the work history characteristic. Statistically significant prevalence ratios and confidence intervals are in bold.
*Association was significant in model adjusted for smoking status (ever/never).

Table 14. Mean values of lung function parameters of medical survey participants by current work history characteristics (N=357 for spirometry, N=325 for diffusing capacity and total lung capacity)

	Work history characteristic Mean value with; mean value without				
Parameter	Tenure ≥7 years	Production department	Spend ≥1 hr in production daily	Use flavoring ingredients	Use cleaning products
FEV1 % pred	**97.4; 101.5***	98.9; 101.0	**96.6; 101.3***	98.7; 100.1	99.7; 99.1
FVC % pred	**99.8; 102.5***	100.8; 102.5	**98.9; 102.6***	100.6; 101.8	101.3; 101.2
FEV1/FVC	**77.3; 80.3*†**	78.8; 79.1	**77.9; 79.5**	79.0; 78.8	79.4; 78.2
Diffusing cap % pred	**93.0; 97.0***	94.9; 95.6	95.5; 94.9	94.7; 95.4	94.6; 95.8

hr=hour; % pred=percent predicted; cap= capacity
For each cell, first value is the mean for the subgroup of participants with the work history characteristic and the second value is the mean for the subgroup of participants without the work history characteristic. Statistically significantly different means are in bold.
*Association was significant in model adjusted for smoking status (ever/never).
†Association was not significant in model adjusted for both smoking status and age.

Table 15. Prevalence ratios of lung function abnormalities by current work history characteristics for the subgroup who ever worked in a production department (N=288 for spirometry, N=261 for diffusing capacity and total lung capacity)

	Work history characteristic Prevalence ratio (95% CI)			
Abnormality	Tenure ≥7 years	Spend ≥1 hr in production daily	Use flavoring ingredients	Use cleaning products
Obstruction	1.7 (0.5-5.6)	3.2 (0.9-12)	2.2 (0.6-8.1)	1.3 (0.4-4.8)
Restriction	1.9 (0.7-5.5)	1.4 (0.5-3.7)	0.7 (0.3-1.9)	0.6 (0.2-1.5)
Any abnl spirometry	2.0 (0.9-4.3)	**2.2 (1.0-4.6)***	1.3 (0.6-2.6)	0.9 (0.4-1.8)
Low diffusing capacity	1.8 (0.6-5.3)	**3.1 (1.0-9.6)***	1.2 (0.4-3.3)	3.0 (0.7-13)
Low total lung capacity	1.2 (0.5-2.7)	1.2 (0.6-2.7)	0.6 (0.3-1.4)	0.9 (0.4-2.0)

abnl=abnormal
For each prevalence ratio, comparison is of the prevalence of the abnormality among the subgroup of participants with the work history characteristic and the prevalence of the abnormality among the subgroup of participants without the work history characteristic. Statistically significant prevalence ratios and confidence intervals are in bold.
*Association was significant in model adjusted for smoking status (ever/never).

Table 16. Mean values of lung function parameters by current work history characteristics for the subgroup who ever worked in a production department (N=288 for spirometry, N=261 for diffusing capacity and total lung capacity)

	Work history characteristic Mean value with; mean value without			
Parameter	Tenure ≥7 years	Spend ≥1 hr in production daily	Use flavoring ingredients	Use cleaning products
FEV1 % pred	**96.8; 101.0***	**96.6; 100.7***	98.9; 98.8	99.4; 97.8
FVC % pred	99.5; 101.8	**99.0; 101.9***	100.6; 100.6	100.9; 100.1
FEV1/FVC	**77.0; 80.6*†**	**77.9; 79.6**	79.1; 78.4	79.3; 77.8
Diffusing cap % pred	**93.2; 96.8***	95.2; 94.8	94.9; 95.1	94.5; 95.9
total lung cap % pred	**90.5; 93.3***	91.9; 91.9	91.9; 92.0	91.9; 91.9

% pred=percent predicted; hr=hour
For each cell, first value is the mean for the subgroup of participants with the work history characteristic and the second value is the mean for the subgroup of participants without the work history characteristic. Statistically significantly different means are in bold.
*Association was significant in model adjusted for smoking status (ever/never).
†Association was not significant in model adjusted for both smoking status and age.

Appendix A: Medical Survey Questionnaire

ID:_____

HETA 2012 – 0012

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

Section I: Identification and Demographic Information

Name:_____ _____ ____
(Last Name) (First Name) (M.I.)

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

_____ _____ _____
(City) (State) (Zip Code)

Primary Telephone Number: (____) - ____ - _____ [ ] Home [ ] Cell

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

Name:_____ _____ ____
(Last Name) (First Name) (M.I.)

Relationship to you:_____

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

_____ _____ _____
(City) (State) (Zip Code)

Contact Telephone Number: (____) - ____ - _____

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

2. Sex: 1. ____ Male 0. ____Female

3. Are you Spanish, Hispanic or Latino? 1. ____ Yes 0. ____No

4. Select <u>one or more</u> of the following categories to describe your race:
   1.___ American Indian or Alaska Native
   2.___ Asian
   3.___ African-American or Black
   4.___ Native Hawaiian or Other Pacific Islander
   5.___ White

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."

5. During the last 12 months, have you had any trouble with your breathing? 1.____ Yes 0. ____ No

IF YES:

5.1. 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

5.2. When you are away from this plant on days off or on vacation, are these breathing symptoms

1.___ Same
2.___ Worse
3.___ Better

(Asthma)

6. Have you had wheezing or whistling in your chest at any time in the last 12 months? 1.____ Yes 0. ____ No

IF YES:

6.1. When you are away from this plant on days off or on vacation, is this wheezing or whistling

1.___ Same
2.___ Worse
3.___ Better

6.2. Is there an exposure at work that causes or aggravates this wheezing or whistling? 1.____ Yes 0. ____ No

IF YES:

6.2.1. Describe exposure(s):_____

7. Have you woken up with a feeling of tightness in your chest at any time in the last 12 months? 1.____ Yes 0. ____ No

8. Have you been woken by an attack of shortness of breath at any time in the last 12 months? 1.____ Yes 0. ____ No

9. Have you had an attack of asthma in the last 12 months? 1.____ Yes 0. ____ No

10. Are you currently taking any medicine (including inhalers, aerosols or tablets) for asthma? 1.____ Yes 0. ____ No

(Respiratory, Eye and Dermal Irritation)

11. In the last 12 months, apart from a cold, has your nose been stuffy, blocked, itchy, stinging, burning, or runny?) 1.____ Yes 0. ____ No

IF YES:

11.1. When you are away from this plant on days off or on vacation, are these nose symptoms
1.___ Same
2.___ Worse
3.___ Better

11.2. Is there an exposure at work that causes or aggravates these nose symptoms? 1.____ Yes 0. ____ No

IF YES:

11.2.1. Describe exposure(s):_____

12. In the last 12 months, have you had sinusitis or sinus problems? 1.____ Yes 0. ____ No

IF YES:

12.1. When you are away from this plant on days off or on vacation, are these sinus symptoms
1.___ Same
2.___ Worse
3.___ Better

12.2. Is there an exposure at work that causes or aggravates these sinus symptoms? 1.____ Yes 0. ____ No

IF YES:

12.2.1. Describe exposure(s):_____

13. In the last 12 months, have your eyes been watery or tearing, red, burning, itching or dry? 1.____ Yes 0. ____ No

IF YES:

13.1. When you are away from this plant on days off or on vacation, are these eye symptoms
1.___ Same
2.___ Worse
3.___ Better

13.2. Is there an exposure at work that causes or aggravates these eye symptoms? 1.____ Yes 0. ____ No

IF YES:

13.2.1. Describe exposure(s):_____

14. In the last 12 months, have you had any skin rash or skin problems? 1.____ Yes 0. ____ No

IF YES:

14.1. When you are away from this plant on days off or on vacation, are these skin symptoms
1.___ Same
2.___ Worse
3.___ Better

14.2. Is there an exposure at work that causes or aggravates these skin problems? 1.____ Yes 0. ____ No

IF YES:

14.2.1. Describe exposure(s):_____

(Obstructive disease)

15. Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill? 1.____ Yes 0. ____ No

15.1. In what month and year did this shortness of breath begin? __ __ / __ __ __ __
(Month) (Year)

16. Do you usually have a cough? 1.____ Yes 0. ____ No
(Count cough with first smoke or on first going out-of-doors. Exclude clearing of throat.)

IF YES:

16.1. Do you usually cough on most days for **3 consecutive months** or more during the year? 1.____ Yes 0. ____ No

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

16.3. When you are away from this plant on days off or on vacation, is your cough
1.___ Same
2.___ Worse
3.___ Better

16.4. Is there an exposure at work that causes or aggravates this cough? 1.____ Yes 0. ____ No

IF YES:

16.4.1. Describe exposure(s):_____

17. Do you bring up phlegm on most days for 3 consecutive months or more during the year? 1.____ Yes 0. ____ No

18. Have you ever had to change your job, job duties, or work area at this plant because of breathing difficulties? 1.____ Yes 0. ____ No

IF YES:

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

18.2. What was your job, job duties or work area?
Describe:_____

18.3. How did your job, job duties, and/or work area differ after the change:
Describe:_____

18.4. Were your breathing problems after the change:

1.___ Same
2.___ Worse
3.___ Better

19. Have you **ever** been exposed to any chemical or substance while working at this plant that affected your breathing? 1.____ Yes 0. ____ No

IF YES:

19.1. Describe exposure(s):_____

20. Have you **ever** been told by a physician or other health professional that you had any of the following conditions?

Conditions	Told by a physician you had?	Month and Year of first diagnosis?
1. Hay fever or nasal allergies	1. Yes ___ 0.No ___	
2. Heart disease	1. Yes ___ 0.No ___	
3. Chronic bronchitis	1. Yes ___ 0.No ___	
4. Emphysema	1. Yes ___ 0.No ___	
5. Chronic obstructive pulmonary disease (COPD)	1. Yes ___ 0.No ___	
6. Hypersensitivity pneumonitis	1. Yes ___ 0.No ___	
7. Chemical pneumonitis	1. Yes ___ 0.No ___	
8. Bronchiolitis obliterans	1. Yes ___ 0.No ___	
9. Asthma	1. Yes ___ 0.No ___	
9.1. **IF YES:** Do you still have asthma?	1. Yes ___ 0.No ___	

21. Have you **ever** been told by a physician or other health professional that you had any other respiratory condition?

IF YES:

21.1. What was it? _____

21.2. In what month and year were you first told you had this respiratory condition?

__ __ / __ __ __ __
(Month) (Year)

Section III. Work Information
I'm now going to ask you to list all of the jobs that you have had while working at this plant.
We will start with your current job and work back through time.
[*NOTE: facility opened in late 1997 and was fully operational in Jan 1998*]

Job Number	Department	Major Work Area	Job Title	Start Date (MM/YYYY)	End Date (MM/YYYY)	Avg. Hours/Week Worked
	Drop Down menus populated with lists	Drop Down menus populated with lists				

I am now going to ask you questions about all the jobs that you have had while working at this plant. 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."

ASK THE FOLLOWING ABOUT EACH JOB:

As a [job title], ……..

How many hours do/did you spend in the production area on an average day? ____ # hours

Do/did you sample, mix or pour flavoring ingredients? 1. ___Yes 0. ___No

IF YES:
Do/did you ever heat the flavoring ingredients? 1. ___Yes 0. ___No

Do/did you work mostly with:
1. ___ liquids
2. ___ powders
3. ___ both

Do/did you use cleaning products? 1. ___Yes 0. ___No

IF YES:
How often do/did you use cleaning products?
1. ___ Daily
2. ___ Weekly
3. ___ Monthly
4. ___ Less than monthly

CURRENT JOB ONLY:

Do you wear a respirator or dust mask? 1. ___Yes 0. ___No

IF YES:
Which type of respirator or mask do you wear:
[*NOTE: Show photos; check all that apply*]
1. ___ Dust mask
2. ___ Disposable respirator ("N95")
3. ___ Half-face respirator
4. ___ Full-face respirator
5. ___ Other

Describe other:_____

Were you fit tested for this device? 1. ___Yes 0. ___No

When do you wear the respirator or dust mask?
[*NOTE: check all that apply*]

1. ___ handling hazardous chemical
2. ___ because of odor
3. ___ because of irritation
4. ___ when required/instructed to
5. ___ Other

Describe: _____

Do you use fume hoods, snorkels, Nederman arms, wall slot vents or other local exhaust ventilation in your immediate work area? 1. ___Yes 0. ___No

IF YES:

When do you use local exhaust ventilation?
[*NOTE: check all that apply*]

1. ___ handling hazardous chemical
2. ___ because of odor
3. ___ because of irritation
4. ___ when required/instructed to
5. ___ Other

Describe: _____

Have you ever been exposed to an unusual chemical spill or release in this plant? 1.___ Yes 0.___ No

IF YES:

What was the chemical?	What was the date of the spill or release? (mm/yyyy)	Did you have any symptoms from it?	If Yes, What were your symptoms?
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	

Have you ever worked at any other flavoring plants? 1. ___Yes 0. ___No

[NOTE: Include other jobs with this company or its predecessors prior to the opening of this facility]

IF YES:

Job	Plant Name	Start Date (mm / yyyy)	End Date (mm / yyyy)	Job Title	Job Description
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					

Section IV: Tobacco Use Information

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

Have you ever smoked cigarettes? 1. ___ Yes 0. ___ 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 you smoked per day? _____ Cigarettes/day

c) Do you still smoke cigarettes? 1. ___ Yes 0. ___ No

IF NO:

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

Thank you for participating in this survey!

Appendix B: OSHA-NIOSH Infosheet

OSHA·NIOSH INFOSHEET

Maximize Your Spirometry Screening and Surveillance Resources

Spirometry is a common type of pulmonary function test (PFT) that measures how well a person can move air in and out of their lungs. In occupational settings, spirometry can be used to establish a baseline before assigning a worker to job tasks that are physically demanding, that require use of a respirator, or that may expose the worker to respiratory hazards. It is also used to track lung function over time and to evaluate workers who experience signs or symptoms of respiratory disease.

The Need for Spirometry Testing

Spirometry testing is required for some workers by OSHA standards. Accurate spirometry testing, interpretation, and follow-up are critical to effective screening and surveillance of workers exposed to respiratory hazards. Technically poor spirometry is of little value to the purchaser of these services and may provide misleading information.

Technician Training

Spirometry technicians should have a valid certificate from a National Institute for Occupational Safety and Health (NIOSH)-approved course or an equivalent training course. For more information go to: www.cdc.gov/niosh/topics/spirometry/training.html.

Spirometry Equipment

The spirometry equipment and software used in such testing should be validated by independent laboratory testing documented by the manufacturer and should comply with the most recent American Thoracic Society/European Respiratory Society standards. Spirometry results should be computerized and the computer file kept by the healthcare provider. Spirometry technicians should check the calibration of the spirometer before use each day and keep calibration records as long as the related health records are retained. The spirometry technician and the healthcare professional are responsible for reviewing the spirometry results, checking validation criteria, and informing the employer of any equipment malfunctions.

Frequency of Testing

Periodic spirometry tests must be performed in accord with OSHA standards. For occupational exposures to substances for which no OSHA standard applies, periodic spirometry is usually recommended, although such testing can be done more or less frequently to evaluate changes in lung function over time. Testing less frequently than every 3 years is not recommended. The frequency of testing should be determined by the applicable OSHA standard or, where no standard applies, by the specific hazard to which workers are being exposed.

Screening and Surveillance

Periodic spirometry screening of individual workers can detect breathing problems or significant changes in lung function at an early stage so that hazardous workplace exposures can be identified and eliminated to prevent or reduce occupational lung disease. Equally important, surveillance can detect changes in lung function over time among groups of workers with similar exposures and thus help to recognize serious health effects in the workplace at a time when individual results may not be severe or noticeable. Employers should consider periodically reviewing grouped data from worksite exposure assessments with a healthcare professional and should be alert for any significant changes in grouped results. Reviewing grouped data may help identify occupational exposures and assist in reducing or eliminating any hazards identified. Additional resources on monitoring spirometry data over time in individuals or groups of workers can be found at: www.cdc.gov/niosh/topics/spirometry/spirola.html.

The healthcare professional should analyze baseline and periodic spirometry test results and explain all results to the worker. The healthcare professional should determine when a spirometry test result indicates that the worker needs further medical evaluation. Finally, the healthcare professional should notify the employer if there are any concerns about occupational exposures while maintaining the confidentiality of worker health information.

Checklist for Employers

Critical elements of spirometry testing that maximize your company's resources and should be considered for inclusion in required contracts include:

Technicians and Clinical Healthcare Professionals
☐ Technicians who perform testing should have successfully completed a National Institute for Occupational Safety and Health (NIOSH)-approved course, or equivalent, within the past 5 years. *A certificate should be available for you to inspect.*
☐ The program should be supervised by a healthcare professional knowledgeable about spirometry accuracy and test validity. *Documentation of the professional's spirometry update training should be available.*
Spirometry Equipment
☐ A letter from the spirometer manufacturer indicating successful validation testing of the spirometer, following current American Thoracic Society/ European Respiratory Society standards, should be available for review.
☐ The spirometer's calibration is checked by the technician each day of use. *Records of daily spirometer calibration checks should be maintained and available for review.*
Interpretation of Results
☐ Worker's results are compared to normal values. *The report should specify the source of the normal or predicted values. If the testing satisfies a regulatory requirement, then the appropriate predicted values must be used.*
☐ Current worker's results are compared to his or her previous baseline values, if available. This is the preferred method of evaluating change over time.
Reporting of Results
☐ The healthcare professional reports the results to the worker indicating how the worker's results compared to the normal range and whether changes over time require further medical evaluation.

Resources

For more information about spirometry screening, surveillance, and training visit OSHA online at www.osha.gov/SLTC/medicalsurveillance/index.html and www.osha.gov/Publications/osha3162.pdf (*Screening and Surveillance: A Guide to OSHA Standards*) and NIOSH online at: www.cdc.gov/niosh/topics/spirometry/default.html. Other helpful references that present the American College of Occupational and Environmental Medicine's position on Occupational Spirometry are: Townsend, MC. ACOEM position statement. Spirometry in the occupational setting. American College of Occupational and Environmental Medicine. J Occup Environ Med. 2000 Mar;42(3):228-45. and Townsend, MC. ACOEM Position Statement Spirometry in the Occupational Health Setting–2010 Update at: www.acoem.org/uploadedFiles/Policies_And_Position_Statements/ACOEM%20Spirometry%20Statement.pdf.

OSHA Publications

OSHA has an extensive publications program. For a listing of free items, visit OSHA's website at www.osha.gov/pls/publications/pubindex.list or contact the OSHA Publications Office, U.S. Department of Labor, 200 Constitution Avenue, N.W., N-3101, Washington, DC 20210. Telephone (202) 693-1888 or fax to (202) 693-2498.

Contacting OSHA

To report an emergency, file a complaint or seek OSHA advice, assistance or products, call (800) 321-OSHA or contact your nearest OSHA regional, area, or State Plan office; TTY: 1-877-889-5627.

Contacting NIOSH

To receive documents or more information about occupational safety and health topics, please contact NIOSH: 1-800-CDC-INFO (1-800-232-4636); TYY: 1-888-232-6348; e-mail: cdcinfo@cdc.gov or visit the NIOSH web site at www.cdc.gov/niosh.

This guidance document is not an OSHA standard or regulation but contains recommendations that are advisory in nature and intended to assist employers in providing a safe and healthful workplace. The mention of any non-governmental organization or link to its web site in this guidance does not constitute an endorsement by NIOSH or OSHA of that organization, its products or services or web site.

For more complete information:

OSHA® Occupational Safety and Health Administration
www.osha.gov
(800) 321-OSHA

CDC Workplace Safety and Health
NIOSH National Institute for Occupational Safety and Health
www.cdc.gov/niosh
(800) 232-4636

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Keywords: North American Industry Classification System 325199 (Flavoring materials manufacturing), respiratory, flavorings, diacetyl, 2,3-pentanedione, lung function, bronchiolitis

NIOSH Health Hazard Program Description

The Health Hazard Evaluation Program investigates possible health hazards in the workplace under the authority of the Occupational Safety and Health Act of 1970 (29 U.S.C. 669(a)(6)) or the Federal Mine Safety and Health Act of 1977 (30 U.S.C. 951(a)(11)). The Health Hazard Evaluation Program also provides, upon request, technical assistance to federal, state, and local agencies to investigate occupational health hazards and to prevent occupational injury and disease. Regulations guiding the Program can be found in Title 42, Code of Federal Regulations, Part 85; Requests for Health Hazard Evaluations (42 CFR 85).

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Availability of Report

Copies of this report have been sent to employee and employer representatives, the Kentucky Department for Public Health, and the OSHA Regional Office. This report is not copyrighted and may be freely reproduced.

This report is available at http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0012-3192.pdf.

All other HHE Reports may be found at http://www2a.cdc.gov/hhe/search.asp

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