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March 29, 2007
HETA 2007-0033
Interim Letter I

Mr. Jon Wellwood
Gold Coast Ingredients, Inc.
2429 Yates Avenue
Commerce, California 90040

Dear Mr. Wellwood:

The purpose of this letter is to convey a report on the progress of a National Institute for Occupational Safety and Health (NIOSH) Health Hazard Evaluation at the Gold Coast Ingredient, Inc. plant located in Commerce, California. NIOSH visited the plant from October 30, 2006 to November 1, 2006 to perform a medical survey consisting of an interview-administered questionnaire and spirometry (lung function) testing. We visited again on March 13-14, 2007 to perform follow-up spirometry and administer a paper questionnaire.

A copy of the interim report is enclosed. We recommend that you post the interim report in a prominent place accessible to the employees for a period of 30 calendar days.

We will continue to analyze the data from your plant and will be providing you with a final report in the future. If you have any questions or concerns, please feel free to contact me at (304) 285-5757.

Sincerely,

Rachel L. Bailey, D.O., M.P.H.
Lieutenant Commander
United States Public Health Service
Respiratory Disease Hazard Evaluation and
Technical Assistance Program
Field Studies Branch
Division of Respiratory Disease Studies

cc:
Kelly Howard
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**HETA 2007-0033**
**Interim Report**
**March 29, 2007**

## Introduction

On October 24, 2006, Gold Coast Ingredients, Inc. requested a Health Hazard Evaluation (HHE) for medical screening for occupational lung disease at their Commerce, California plant. The company was participating in a voluntary special emphasis program called the Flavoring Industry Safety and Health Evaluation Program (FISHEP). In 2006, this program was initiated by the California Department of Health Services (CDHS) and the California Division of Occupational Safety and Health (Cal/OSHA) to identify workers with flavoring-related lung disease such as bronchiolitis obliterans (BO) and institute preventive measures in the California flavoring industry. Under FISHEP, companies must report to CDHS the results of employee medical screening and worksite industrial hygiene assessments, and implement control measures recommended by Cal/OSHA.

## Background

Bronchiolitis obliterans (BO) is a rare life-threatening form of fixed obstructive lung disease that has previously been identified as an occupational hazard in microwave popcorn workers exposed to butter flavorings (1,2,3). In August 2004, the CDHS and the Cal/OSHA received the state's first report of a flavor manufacturing worker with BO. In April 2006, this was followed by a report of a second flavor manufacturing worker with BO at another California plant (http://www.dhs.ca.gov/ohb/flavoringcases.pdf). CDHS and Cal/OSHA are aware of at least eight cases of BO in California flavor manufacturing workers, and other possible cases are being evaluated. The flavor manufacturing workers were exposed to diacetyl, a chemical used in artificial butter and other flavorings. Exposure to diacetyl, either alone or in combination with other flavoring chemicals, has been shown to cause severe respiratory epithelial injury in animals (4,5).

## Process Description

The Gold Coast Ingredients plant manufactures and distributes liquid and powdered flavors to other companies for use in the production of many different products. The plant started making flavorings in the 1990s. Over 800 different flavoring products are produced using over 1000 chemical or natural ingredients. The plant consists of a liquid production room, powder production room, color room, walk-in cooler and freezer, two spray-drying areas, raw materials warehouse, finished products warehouse, laboratory, quality control, and offices.

During the medical survey in 2006, 47 employees worked at the plant, including 15 office workers, 12 production workers, 1 production manager, 11 quality control (QC) and laboratory workers, 5 warehouse workers, and 3 maintenance/custodial workers. The production workers used open containers to pour and measure flavor ingredients which were then transferred to open

tanks for liquid flavorings or to ribbon blenders for powdered flavorings. Computerized batch tickets were used to pull ingredients for the various flavors. The liquid production room was approximately 58 x 20 feet. The powder production room and two spray-drying areas were much smaller. The powder production area had five ribbon blenders (two large stationary, and three smaller mobile). There were three spray dryers (one large and one medium stationary spray dryer, and one mobile spray dryer).

**Methods**

From October 30, 2006 through November 1, 2006, two medical officers and a spirometry technician from the NIOSH conducted a medical survey consisting of an interviewer-administered, computerized questionnaire and spirometry testing. An initial walkthrough of the plant was done by both medical officers prior to starting the medical survey. All workers were invited to participate in the medical survey. After obtaining signed informed consents from participants, NIOSH staff administered a standardized questionnaire to collect information on symptoms, medical diagnoses, smoking history, work history, and work-related exposures. This questionnaire included questions from the American Thoracic Society standardized adult respiratory symptoms questionnaire and the Third National Health and Nutrition Examination Survey (NHANES III) (6,7), with additional questions on asthma symptoms (8) and questions on skin, upper respiratory, and mucus-membrane irritation or problems. A Cal/OSHA staff member assisted with Spanish translation during the questionnaire and spirometry testing.

On the last day of the initial survey, November 1, 2006, another walkthrough was performed with two industrial hygienists from Cal/OSHA, and a closing meeting was completed with the company president, vice president of operations, general manager, production manager, and two Cal/OSHA industrial hygienists.

From March 13-14, 2007, one medical officer and one spirometry technician from NIOSH returned to the plant to conduct follow up spirometry testing. Workers completed a self-administered paper questionnaire (in English or Spanish) for CDHS and Cal/OSHA with assistance from NIOSH. These questionnaire results are not presented here. A Cal/OSHA employee assisted with Spanish translation during the questionnaire and spirometry testing. On the afternoon of March 13, 2007, NIOSH and CDHS medical officers did a walkthrough of the plant. On the last day, the NIOSH medical officer held a closing meeting with the company president and manager of operations.

Following ATS guidelines (9), spirometry testing was performed using a dry rolling-seal spirometer interfaced to a personal computer. Spirometry results were compared to reference values based on U.S. population data from NHANES III (10). Each participating worker's largest forced vital capacity (FVC) and forced expiratory volume in the first second of exhalation ($FEV_1$) were selected for analysis. Obstruction was defined as an $FEV_1$/FVC ratio and an $FEV_1$ below their respective lower limits of normal. Borderline obstruction was defined as a $FEV_1$/FVC ratio below the lower limit of normal with normal $FEV_1$ and FVC. Restriction was defined as an FVC below the lower limit of normal with normal $FEV_1$/FVC ratio. A mixed pattern (obstruction and restriction) was defined as an $FEV_1$/FVC ratio, $FEV_1$, and FVC all

below their respective lower limits of normal. Workers with evidence of airways obstruction were administered albuterol, a bronchodilator medication used to treat obstructive lung diseases such as asthma, and were then re-tested within 10 minutes to see if the obstruction was reversible. Reversible obstruction was defined as an improvement in the $FEV_1$ of at least 12% and at least 200 milliliters after administration of albuterol. Fixed obstruction was defined as airways obstruction in which neither the FVC nor $FEV_1$ increased by 12% or more and at least 200 milliliters after the administration of albuterol. Within two to four weeks after the spirometry test, each participant was mailed a report which explained their individual spirometry results and provided recommendations for follow-up of abnormalities. Spanish speakers were mailed reports in both Spanish and English.

**Data Analysis**

We combined laboratory workers and quality control workers for analysis and labeled them *laboratory/QC workers*. These workers often tended to go back and forth between the laboratory and quality control areas while performing their job duties. Workers from the office work areas were combined and labeled *office workers*. Warehouse workers, custodians, and the production manager who moved around the plant complex throughout the work day were combined into one category referred to as *warehouse/other*. Participants were placed in the *ever-production* category if they answered yes to "Do you or did you ever work in the production room?" and/or provided a work history that indicated they had worked in production. Participants were placed in the e*ver-laboratory/QC* category if they answered yes to "Do you or did you work in the lab?" and/or provided a work history that indicated they had worked in the laboratory or quality control area. The *flavoring-exposed* worker category was defined as workers who ever worked in production or who entered the production area on a daily basis as part of another job.

We calculated prevalences of symptoms and spirometry results for all workers and for workers in each of the above categories. We compared prevalence of airways obstruction by severity level to U.S. population prevalence from NHANES III (7) U.S. population data, stratified by age.

In addition, we calculated prevalence rate ratios for symptoms for all workers, ever-production workers, and never-production workers by dividing the observed prevalences by expected prevalences based on data from NHANES III (7), controlling for age (less than 50 years of age/equal or greater than 50 years of age), gender, smoking status (ever-smoked / never-smoked), and race. Statistically increased rates in the worker groups are indicated by 95% confidence intervals that exclude the value 1.0.

**Results**

***Walkthrough***

During the initial walkthrough of the plant, the NIOSH medical officers noted workers in the production areas wearing various respirators including full-face, half-face, and N-95 filtering facepiece respirators. Production workers wore the full-face and half-face respirators with NIOSH-certified organic vapor cartridges but not always with particulate filters. Some

production workers were not wearing respirators while co-workers performing the same tasks were wearing respirators. Pouring of liquid ingredients was observed in the corridor (pre-production area) outside of the liquid production area.

Management stated its policy was to require respirator use when acetoin, acetaldehyde, diacetyl, acetic acid, and benzaldehyde were used. Management stated that qualitative fit testing was done with isoamyl acetate (banana oil). No quantitative fit testing had been done.

During the walkthrough on November 1, 2006, production had ceased for the day. All of the workers performing cleaning activities in the production areas wore half-face or full-face respirators with organic vapor cartridges. Some had particulate filters, as well.

During the walkthrough on March 13, 2007, no production activities were occurring. All workers in the production rooms were wearing full-face respirators with organic vapor cartridges, and some had particulate filters. All the current production workers, except for one worker and the production manager, had been quantitatively fit tested for a Survivair Opti-Fit full-face respirator. Mention of company names or products does not constitute endorsement by NIOSH.

***Medical Survey***

*Participation and Demographics*

October-November 2006: Out of 47 workers employed at the plant, 41 (87%) participated in the medical survey (Table 1). Among participants, 61% were Hispanic, 24% Caucasian, 12% Asian, and 2% African American. Sixty-eight percent were male; the mean age was 38 years (range: 19-68); median age of production workers was 35 years; median age for all other workers was 36 years. The median tenure for production workers was 1.3 years; the median tenure for all other workers was 1.9 years. Twenty-seven (66%) participants were never-smokers; 2 (17%) production workers were current or former smokers; 12 (41%) other workers were current or former smokers.

March 2007: Out of 46 workers employed at the plant, 37 (80%) participated in the medical survey. Thirty-four participants participated for the second time, and 3 participants participated for the first time.

*Work History*

October-November 2006: Among the 41 participants, four workers reported previously working for other flavoring companies in the past.

Fourteen workers reported current or past work in the production room. Of these workers, 13 reported working four to eight hours (or more) per day in the production room. All reported mixing or pouring flavoring chemicals. Four reported handling diacetyl on a daily basis; 3 reported handling diacetyl two to three times per week; 2 two to three times per month, and 1

worker handled diacetyl less than once a month. Five reported using respirator or dust masks all the time when in the production room, and 9 reported wearing a respirator some of the time. Among the 12 current production workers, 4 reported using respirators or masks all the time, and 8 reported wearing respirators or masks some of the time.
Fourteen workers reported current or past work in the laboratory/QC. Thirteen of these workers reported they mixed or poured flavoring chemicals, including diacetyl. Four reported handling diacetyl on a daily basis; 4 reported handling diacetyl two to three times per week; 4 reported handling diacetyl two to three times a month, and 1 reported handling diacetyl less than once a month. Among the 11 current laboratory/QC workers, 6 reported wearing a respirator or mask some or all of the time.

Among the 23 current production and laboratory/QC workers, 18 reported using respirators or masks and 1 reported being respirator fit tested (qualitatively).

Twenty-six workers reported that they entered the production room regularly as part of another job. Fourteen reported entering the production room on a daily basis, 9 reported two to three times a week, 1 reported two to three times a month, and two reported entering the production room less than once a month.

*Worker Symptoms*

The percentage of workers reporting post-hire onset of eye and nasal irritation was high in all work areas (Table 1). Among all workers, 46% and 66% reported post-hire nasal and eye symptoms, respectively. Office workers (69%) and warehouse/other workers (60%) were the most likely to report post-hire nasal irritation. Over 80% of current laboratory/QC workers and more than 90% of current production workers reported post-hire eye symptoms. Chemicals reported by the workers to cause both eye and nasal irritation included diacetyl, acetaldehyde, benzaldehyde, acetoin, and capsicum.

Seventeen workers (41%) reported that chemicals in the plant made them cough or feel short of breath. These included diacetyl, acetaldehyde, benzaldehyde, acetoin, and capsicum. Some workers did not know the names of the chemicals, or could not determine which chemicals specifically bothered them.

Skin problems were most common in production workers (25%), followed by warehouse/other workers (20%) (Table 1).

Table 2 shows worker symptoms, medical conditions, and spirometry (lung function) results by work history of ever/never production workers, ever/never flavoring exposed workers, and ever/never laboratory/QC workers. A persistent cough and shortness of breath when hurrying on level ground or walking up a slight hill were present in 7% of ever-production workers and 4%-7%, respectively, of never-production workers. Persist trouble breathing in the last 12 months was found in 7% of ever-production workers and not found in any never-production workers.

Prevalence rate ratios are shown in the Appendix for all workers, ever-production workers, and

never-production workers for selected respiratory symptoms and conditions in comparison with NHANES III data (10). The populations of 36 non-Asian workers, 22 never-production workers, and 14 ever-production workers were small and none of the rate ratios were statistically significant, although increased prevalence ratios for production workers existed for shortness of breath on exertion, chronic chough, and physician-diagnosed bronchitis.

*Spirometry Results*

October-November 2006

Two (Employees A and B) of fourteen participants who had ever worked in the production room were found to have abnormal spirometry that was not reversible with bronchodilator. Employee A had borderline obstruction (normal $FEV_1$ and FVC but decreased $FEV_1$/FVC ratio). Employee B had severe fixed obstruction ($FEV_1$ of 17.9 percent predicted and a $FEV_1$/FVC ratio of 37.4%). Both workers had liquid and powder production experience. Employee B had worked as a flavoring compounder and developed shortness of breath and cough one to four years, respectively, after beginning employment. He never smoked and had no history of asthma. During his first year of employment, he did not wear respiratory protection. For the next four years, he wore an N-95 filtering facepiece respirator some of the time; he then began to wear a full-face piece respirator some of the time. For the first six years, he worked exclusively in powder production which involved adding liquid flavoring mixtures to large quantities of powder and monitoring the blending and packaging operations. Because of his respiratory symptoms, he was moved to liquid flavoring production where he worked for about five years. When he was no longer able to do the work and wear a respirator, he was transferred to a nonproduction job. At the time of our survey, he reported a chronic cough and the need to stop for breath after walking about 100 yards or a few minutes on level ground. In 2005, spirometry showed severe obstructive lung disease ($FEV_1$ of 20% predicted and $FEV_1$/FVC ratio of 47% without bronchodilator response). A lung specialist diagnosed bronchiectasis of unknown etiology based on high-resolution chest computerized tomography scan. The worker was hospitalized on two occasions due to exacerbation of his lung condition.

We found one worker with mild restriction who currently works in the laboratory/QC.

March 2007

Among the 34 workers tested a second time, one asymptomatic production worker had a more than one liter (25%) drop in $FEV_1$. This worker who previously had borderline airways obstruction now has mild fixed airways obstruction (Table 3). Among 3 newly hired workers who were tested for the first time, one worker was identified with borderline airways obstruction.

Combined October/November 2006 and March 2007 Surveys

Forty-four workers completed at least one survey. The results from the most recent spirometry test showed one worker with mild airways obstruction and one worker with severe airways obstruction. Among workers less than 50 years of age, the prevalence of severe airways obstruction was 2.7% (1/37) compared to the expected prevalence of 0.1% based on NHANES III data (Table 4).

## Discussion

We found 2 workers with production work history that had fixed airways obstruction. The very severe case was not previously able to wear a respirator and had been transferred to a job with less exposure to flavoring chemicals. Such cases are sentinels of risk to co-workers. The second case evolved during FISHEP participation and demonstrates the importance of: 1) mandatory use of appropriate fit-tested respirators with both organic vapor/acid gas cartridges and particulate filters; and 2) implementation of engineering controls to lower exposure in plants with cases of fixed airways obstruction. This second case had an extreme drop in lung function into the abnormal range within a 4.5 month period of time and without symptoms.

In this facility, current production workers did not have an excess of chest symptoms compared to other workers, although the two cases developed during production work. When sick workers transfer to less physically demanding work or leave employment altogether, the remaining workers can look "healthier" in comparison to the rest of the workforce. This effect is common in cross-sectional studies and such findings should not be interpreted as an absence of risk in production workers. In this facility, the sickest employee transferred out of production, and thereby contributed his/her symptoms to a nonproduction employee grouping in Table 1. Considering the results of both spirometry surveys, the two cases of fixed obstruction arising in production employment are consistent with flavoring exposure being associated with risk.

Whether restrictive abnormalities are related to flavoring exposures remains unclear. No flavoring-exposed workforce studied to date has had a statistically significant excess of restrictive spirometry. However, individual cases with restriction have occurred in the microwave popcorn industry without explanation or alternate diagnosis (11,12). Longitudinal follow-up may clarify whether cases of restriction are coincidental, a stage of flavoring-related abnormalities, or a less common response to flavoring exposure. Similarly, longitudinal follow-up may establish whether borderline obstruction seen in two workers in production indicates higher risk of progression to fixed airways obstruction of bronchiolitis obliterans syndrome.

## Recommendations

Many of the following recommendations were provided to you in a letter dated February 7, 2007 from Kevin H. Dunn of NIOSH (13).

### 1. Engineering Controls:

a. Ensure that exhaust hoods in the laboratory and quality control room meet the California Code of Regulations, Title 8 CCR, Section 5154.1 (http://www.dir.ca.gov/Title8/5154_1.html).

b. Install local exhaust systems in work areas where chemicals are poured, weighed, or mixed. Use design criteria as outlined in American Conference of Governmental Industrial Hygienists (ACGIH) Industrial Ventilation - A Manual of Recommended Practice (14).

c. Obtain engineering consultation to identify processes that could be effectively isolated or

otherwise contained.

**2. Work Practices:**

a. Keep containers of flavorings and ingredients sealed when not in use. Keep empty flavoring containers sealed because they may contain residual flavorings. If these containers are to be washed, the worker or workers doing this should wear NIOSH-certified full-face respirators with organic vapor/acid gas cartridges and particulate filters (this is the minimum level of respiratory protection recommended).

b. Utilize cold water washes and cold storage of chemicals when feasible.

c. Promptly clean spills and leaks to minimize emissions of chemical vapors. Be sure to wear appropriate personal protective equipment including respirators.

**3. Skin and Eye Protection:** Enforce the use of chemical-resistant gloves and tight-fitting goggles by workers with potential skin and eye exposure to flavorings or their chemical ingredients.

**4. Respiratory Protection:**

a. Implement a formal Respiratory Protection Program that adheres to the requirements of the OSHA Respiratory Protection Standard (29 CFR 1910.134). This standard requires a written program, training of workers, medical evaluation, fit testing, and a program administrator. Details on the Respiratory Protection Standard and how a company can set up a respiratory protection program are available on the OSHA website (www.osha.gov).

b. Fit testing should use an approved quantitative method.

c. Replace respirator cartridges per manufacturer's recommendations.

d. Designate a trained employee or supervisor with responsibility to run the program and evaluate its effectiveness. Make sure that the responsible person's training or experience is appropriated to the level of complexity of the program.

e. Require mandatory respirator use (and fit testing) for all production workers and other employees that enter the production rooms (and spray-drying areas).

f. Restrict access to production rooms and spray-drying areas to only employees that need to be there and have been properly fit-tested with respirators.

g. Ensure that workers understand how and when to wear a respirator, the nature of the respiratory hazard associated with flavoring chemicals, and that a respirator must be used 100% of the time during the production operation. Workers who have not been fit-tested for an appropriate respirator should not enter the production rooms.

h. Ensure that workers perform positive and negative fit checks every time they put on their respirator.

i. A NIOSH-certified full-face respirator with organic vapor/acid gas cartridges and particulate filters is the minimum level of respiratory protection recommended. A loose-fitting powered air-purifying respirator (PAPR) with organic vapor/acid gas cartridges and particulate filters is an option for increased worker comfort and does not require fit testing.

**5. Medical Surveillance:**

a. Perform a baseline or preplacement spirometry test on all laboratory and production workers, as well as any other workers who enter the production area. Have a physician evaluate workers who have pre-existing lung disease or abnormal spirometry to determine the risk of progression of their lung disease from work exposures. The physician should also assess their possible increased vulnerability with respect to lung function impairment to any effects of work exposures. It is important that the spirometry test be performed by a healthcare provider who can assure high quality tests in order to compare results over time to determine whether lung function is remaining stable. This healthcare provider should provide documentation that the spirometry technician has attended a NIOSH-certified spirometry course, and that routine calibrations of their spirometer are performed as recommended by the American Thoracic Society. The provider should follow ATS guidelines for performance of high-quality spirometry.

b. Perform spirometry tests every 3 months on all production and laboratory workers until engineering controls are implemented and evaluated. This will identify any workers with falling lung function who should receive more intense monitoring, education on health effects of exposures, and/or removal from further exposure. In the near term, workers with $FEV_1$ falls of about 10% to 15% (depending on spirometry quality) from baseline should be medically evaluated.

c. Encourage workers to report respiratory symptoms such as persistent cough, shortness of breath, and wheezing to their supervisors, company-contracted physician, and personal physician. Workers should provide their personal physician with copies of information sheets (see 6.b., below) when reporting problems.

d. Workers with abnormal spirometry should be medically evaluated. Refer any symptomatic workers and any workers with abnormal or declining spirometry results meeting the above criteria for further medical evaluation. This evaluation should establish the likelihood of compensable work-related lung disease, and identify measures to prevent further injury or progression, including respiratory protection and relocation or exposure cessation.

**6. Hazard Communication:**

a. Employee education should comply with Occupational Safety and Health Administration

(OSHA) Hazard Communication Standard, 29 CFR 1910.1200 and/or the applicable Cal/OSHA standard (Title 8 CCR, Section 5194 at http://www.dir.ca.gov/title8/5194.html) when applicable.

b. Worker information sheets in both English and Spanish are available at CDHS's website, http://www.dhs.ca.gov/ohb/flavorings.htm and NIOSH's website, http://www.cdc.gov/niosh/topics/flavorings/.

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13. Dunn KH. Letter of February 7, 2007, from K. Dunn, Division of Applied Research and Technology, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Department of Health and Human Services, to Jon Wellwood, Gold Coast Ingredients, Incorporated, Commerce, California, 2007.

14. ACGIH. Industrial Ventilation: A Manual of Recommended Practice, 25th ed. 2004; Cincinnati, Ohio, 2004

**Table 1. Prevalence of symptoms and medical conditions by current work area for 41 current workers, October-November 2006.**

| Health Outcome | Production (N=12) | Laboratory/ QC (N=11) | Warehouse/ Other* (N=5) | Office (N=13) |
|---|---|---|---|---|
| Trouble breathing in last 12 months[1] | 0 | 2 (18%) | 2 (40%) | 3 (23%) |
| -Always resolves[2] | 0 | 0 | 0 | 1 (8%) |
| -Persists[3] | 0 | 0 | 1 (20%) | 0 |
| Shortness of breath on exertion (hurrying or walking up hill)[4] | 2 (17%) | 0 | 2 (40%) | 4 (31%) |
| Shortness of breath on exertion (walking with people of same age)[5] | 0 | 0 | 2 (40%) | 1 (8%) |
| Chronic cough[6] | 0 | 0 | 1 (20%) | 1 (8%) |
| Wheeze[7] | 0 | 1 (9%) | 1 (20%) | 1 (8%) |
| Asthma-like symptoms[8] | | | | |
| -1 or more yes responses | 1 (8%) | 4 (36%) | 3 (60%) | 3 (23%) |
| -3 or more yes responses | 0 | 1 (9%) | 3 (60%) | 1 (8%) |
| Acute bronchitis[9] | 0 | 1 (9%) | 2 (40%) | 2 (15%) |
| Diagnosed chronic bronchitis[10] | 0 | 1 (9%) | 2 (40%) | 0 |
| Pneumonia[11] | 0 | 0 | 1 (20%) | 1 (8%) |
| Diagnosed asthma[12] | 0 | 2 (18%) | 2 (40%) | 0 |
| Post-hire nasal irritation[13] | 2 (17%) | 5 (45%) | 3 (60%) | 9 (69%) |
| Post-hire eye irritation[14] | 11 (92%) | 9 (82%) | 2 (40%) | 5 (38%) |
| Post-hire skin rash[15] | 3 (25%) | 2 (18%) | 1 (20%) | 2 (15%) |

[1] During the last 12 months, have you had any trouble with your breathing?
[2] I have regular trouble with my breathing but it always gets completely better?
[3] My breathing is never quite right?
[4] Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?
[5] Do you get short of breath walking with people of your own age on level ground?
[6] Do you usually cough on most days for 3 consecutive months or more during the year?
[7] During the last 12 months, have you had this wheezing or whistling in your chest when you did not have a cold?
[8] If you run, or climb stairs fast do you ever cough? If you run, or climb stairs fast do you ever wheeze? If you run, or climb stairs fast do you ever get tight in the chest? Is your sleep ever broken by difficulty breathing? Do you ever wake up in the morning with wheeze? Do you ever wake up in the morning with difficulty breathing? Do you ever wheeze if you are in a smoky room? Do you ever wheeze if you are in a very dusty place?
[9] Since you began working at this plant, have you ever had attacks of bronchitis?
[10] Have you ever had chronic bronchitis (confirmed by a doctor)?
[11] Since you began working at this plant have you ever had pneumonia?
[12] Have you ever had asthma (confirmed by a doctor)?
[13] Since working at this plant, have you had symptoms of nasal irritation such as a stuffy or blocked nose, an itchy nose, a stinging or burning nose, or a runny nose (apart from a cold)?
[14] Since working at this plant, have you had any symptoms of eye irritation such as: watering or tearing eyes, red or burning eyes, itching eyes, dry eyes?
[15] Since working at this plant, have you developed any new skin rash or skin problems?

**Table 2. Prevalence of symptoms, medical conditions, and lung function abnormalities by work history for 41 current workers, October-November, 2006**

| Health Outcome | Ever-Production (N=14) | Never-Production (N=27) | Flavoring-Exposed† (N=27) | Not Flavoring-Exposed (N=14) | Ever-Laboratory/QC (N=15) | Never-Laboratory/QC (N=26) |
|---|---|---|---|---|---|---|
| Trouble breathing in last 12 months[1] | 1 (7%) | 6 (22%) | 2 (7%) | 5 (36%) | 3 (20%) | 4 (15%) |
| -Always resolves[2] | 0 | 1 (4%) | 0 | 1 (7%) | 1 (7%) | 0 |
| -Persists[3] | 1 (7%) | 0 | 1 (4%) | 0 | 0 | 1 (4%) |
| Shortness of breath on exertion (hurrying or walking up hill)[4] | 3 (21%) | 5 (18%) | 5 (19%) | 3 (21%) | 1 (7%) | 7 (27%) |
| Shortness of breath on exertion (compared with people of same age)[5] | 1 (7%) | 2 (7%) | 3 (11%) | 0 | 0 | 3 (12%) |
| Chronic cough[6] | 1 (7% ) | 1 (4%) | 1 (4%) | 1 (7%) | 1 (7%) | 2 (8%) |
| Wheeze[7] | 0 | 3 (11%) | 2 (7%) | 1 (7%) | 2 (13%) | 1 (4%) |
| Asthma-like symptoms[8] | | | | | | |
| -1 or more yes responses | 2 (14%) | 9 (33%) | 7 (26%) | 4 (29%) | 6 (40%) | 5 (19%) |
| -3 or more yes responses | 1 (7% ) | 4 (15%) | 4 (15%) | 1 (7%) | 2 (13%) | 3 (12%) |
| Acute bronchitis[9] | 1 (7%) | 4 (15%) | 3 (11%) | 2 (14%) | 2 (13%) | 3 (12%) |
| Diagnosed chronic bronchitis[10] | 1 (7%) | 2 (7%) | 3 (11%) | 0 | 1 (7%) | 2 (8%) |
| Pneumonia[11] | 1 (7% ) | 1 (4%) | 1 (11%) | 1 (7%) | 1 (7% ) | 1 (4%) |
| Diagnosed asthma[12] | 0 | 4 (15%) | 2 (7%) | 2 (14%) | 2 (13%) | 2 (8%) |
| Post-hire nasal irritation[13] | 3 (21%) | 16 (59%) | 11 (41%) | 8 (57%) | 8 (53%) | 11(42%) |
| Post-hire eye irritation[14] | 13 (93%) | 15 (55%) | 17 (63%) | 10 (71%) | 10 (67%) | 17(65%) |
| Post-hire skin rash[15] | 3 (21%) | 5 (18%) | 6 (22%) | 2 (14%) | 2 (13%) | 6 (23%) |
| Obstruction or mixed pattern on spirometry | 1 (7%) | 0 | 1 (4%) | 0 | 0 | 1 (4%) |
| Borderline obstruction | 1 (7%) | 0 | 1 (4%) | 0 | 0 | 1 (4%) |
| Restriction on spirometry | 0 | 1 (4%) | 0 | 1 (7%) | 1 (7%) | 0 |

1-15: See Table 1 for symptom questions.
†Workers having entered the production work area on a daily basis as part of a non-production job or with a history of ever working in production.

**Table 3. Longitudinal changes in $FEV_1$ and newly identified airways obstruction for 34 workers who had a second spirometry test during period March 13-14, 2007**

| Decline in $FEV_1$ | Number of workers | Percent change in $FEV_1$ | Number with newly identified airways obstruction |
|---|---|---|---|
| No decline | 9 | +0.8% to +15.6% | 0 |
| < 100 ml decline | 13 | -0.3% to -3.1% | 0 |
| ≥ 100 ml to <200 ml decline | 7 | -3.2% to -4.3% | 0 |
| ≥ 200 ml to <300 ml decline | 4 | -4.9% to -7.7% | 0 |
| ≥ 300 ml to <1000 ml decline | 0 | 0 | 0 |
| > 1000 ml decline | 1 | -25.4% | 1 |

**Table 4. Prevalence (percent) of airways obstruction on most recent spirometry test by age and severity and NHANES III prevalences**

| Severity grade of airways obstruction | $FEV_1$ % predicted | Age 17-49 (n=37) | Age 50-69 (n=7) | Total (N=44) |
|---|---|---|---|---|
| Mild | 65% to lower limit of normal | 1 (2.7%) *[2.7%]* | 0 (0%) *[5.0%]* | 1 (2.3%) *[3.3%]* |
| Moderate | 40% to 64% | 0 (0%) *[0.7%]* | 0 (0%) *[4.4%]* | 0 (0%) *[1.7%]* |
| Severe | < 40% | 1 (2.7%) *[0.1%]* | 0 (0%) *[1.8%]* | 1 (2.3%) *[0.5%]* |
| Total | Less than lower limit of normal | 2 (5.4%) *[3.5%]* | 0 (0%) *[11.3%]* | 2 (4.5%) *[5.5%]* |

## APPENDIX

**Table A. Prevalence ratios of observed to expected number of all workers with selected respiratory symptoms and conditions based on NHANES III data, adjusted for gender, race, age, and smoking categories.**

| Symptom/Condition | N* | Observed Number | Expected Number | Prevalence Ratio | CI† |
|---|---|---|---|---|---|
| Shortness of breath on exertion[1] | 36 | 8 | 5.7 | 1.4 | 0.7 – 2.8 |
| Chronic cough[2] | 36 | 2 | 2.1 | 1.0 | 0.3 – 3.5 |
| Wheeze[3] | 36 | 5 | 4.6 | 1.1 | 0.5 – 2.6 |
| Ever diagnosed with chronic bronchitis[4] | 36 | 3 | 1.2 | 2.5 | 0.9 – 7.5 |
| Ever diagnosed with asthma[5] | 36 | 3 | 1.9 | 1.6 | 0.5 – 4.6 |

* Total number of workers with demographic characteristics comparable to NHANES III data. Five Asians excluded due to no reference rates for Asians.
† CI=95% confidence interval
[1] Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?
[2]Do you usually cough on most days for 3 consecutive months or more during the year?
[3] During the 12 months, have you had this wheezing or whistling in your chest when you did not have a cold?
[4] Have you ever had chronic bronchitis (confirmed by a doctor)?
[5]Have you ever had asthma (confirmed by a doctor)?

**Table B. Prevalence ratios of observed to expected number of ever-production workers with selected respiratory symptoms and conditions based on NHANES III data, adjusted for gender, race, age, and smoking categories.**

| Symptom/Condition | N* | Observed Number | Expected Number | Prevalence Ratio | CI† |
|---|---|---|---|---|---|
| Shortness of breath on exertion[1] | 14 | 3 | 1.4 | 2.1 | 0.7 – 6.2 |
| Chronic cough[2] | 14 | 1 | 0.6 | 1.7 | 0.3 – 9.1 |
| Wheeze[3] | 14 | 0 | 1.4 | - | - |
| Ever diagnosed with chronic bronchitis[4] | 14 | 1 | 0.3 | 3.3 | 0.6 – 17.7 |
| Ever diagnosed with asthma[5] | 14 | 0 | 0.6 | - | - |

* Total number of workers
† CI=95% confidence interval
[1] Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?
[2]Do you usually cough on most days for 3 consecutive months or more during the year?
[3] During the 12 months, have you had this wheezing or whistling in your chest when you did not have a cold?
[4] Have you ever had chronic bronchitis (confirmed by a doctor)?
[5]Have you ever had asthma (confirmed by a doctor)?

**Table C. Prevalence ratios of observed to expected number of never-production workers with selected respiratory symptoms and conditions based on NHANES III data, adjusted for gender, race, age, and smoking categories.**

| Symptom/Condition | N* | Observed Number | Expected Number | Prevalence Ratio | CI† |
|---|---|---|---|---|---|
| Shortness of breath on exertion[1] | 22 | 5 | 4.3 | 1.2 | 0.5 – 2.7 |
| Chronic cough[2] | 22 | 1 | 1.4 | 0.7 | 0.1 – 3.9 |
| Wheeze[3] | 22 | 5 | 3.2 | 1.6 | 0.7 – 3.6 |
| Ever diagnosed with chronic bronchitis[4] | 22 | 2 | 0.8 | 2.5 | 0.6 – 8.6 |
| Ever diagnosed with asthma[5] | 22 | 3 | 1.3 | 2.3 | 0.8 – 6.6 |

* Total number of workers with demographic characteristics comparable to NHANES III data. Five Asians excluded due to no reference rates for Asians.

† CI=95% confidence interval

[1] Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?

[2] Do you usually cough on most days for 3 consecutive months or more during the year?

[3] During the 12 months, have you had this wheezing or whistling in your chest when you did not have a cold?

[4] Have you ever had chronic bronchitis (confirmed by a doctor)?

[5] Have you ever had asthma (confirmed by a doctor)?