Medical Surveillance for Flavorings-Related Lung Disease Among Flavor Manufacturing Workers in California

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Background

A severe lung disease, bronchiolitis obliterans (BO), has been identified in food flavor manufacturing workers in California (1). The first case was diagnosed in 2004, and since that time additional cases have been found. An increased incidence of this disease was first identified in Missouri in 2000 among microwave popcorn workers exposed to flavoring ingredients (2). Subsequent investigation of the microwave popcorn industry by the National Institute for Occupational Safety and Health (NIOSH) has greatly enhanced our understanding of this disease and its association with flavoring exposures (3).

BO is a rare pulmonary disease characterized by fixed airways obstruction and fibrosis of the bronchioles. This lung disease has the potential to cause permanent impairment or death in affected workers and has been a growing concern among industry, workers and labor advocates, public health officials, medical providers, and government agencies. The available evidence demonstrates the association between diacetyl, a butter flavoring ingredient, and the development of fixed obstructive lung disease such as BO. Animal studies suggest that diacetyl is one cause of airway damage that can result in BO, but other flavoring chemicals may have the potential to cause BO or to contribute to airway damage (4). Chemicals now being used as substitutes for diacetyl are structurally related (e.g., diketones), but toxicity data is very limited or nonexistent. One common substitute, 2, 3-pentanedione, has been found to cause lung damage in rodents (5, 6). Since the original publication of these guidelines, further studies have linked diacetyl to lung disease in exposed workers, including among California flavor manufacturing workers (7, 8). NIOSH has issued a draft summary document and proposed recommended exposure limits for diacetyl and 2,3-pentanedione (9). A new Cal/OSHA occupational standard for diacetyl (8 CCR §5197) became effective on December 2, 2010 (10).

The focus of these medical guidelines is the recommended medical surveillance for flavor manufacturing workers exposed to diacetyl or its substitutes. However, it should be clearly noted that other ingredients may also contribute to the observed pulmonary injury, and that other workers exposed to flavoring ingredients outside of the flavor manufacturing industry, such as in food production, may also be at risk for developing similar lung disease.

Clinical Presentation

Flavorings-related fixed obstructive disease usually presents with a non-productive cough and the subsequent development of exertional shortness of breath, but some workers show no symptoms at all. These asymptomatic workers may only be identified by abnormal findings on screening spirometry. Onset of disease is usually gradual, but disease progression in a matter of months has been identified. Symptoms generally persist while away from work and are often attributed to other common conditions such as asthma, allergic rhinitis, acute or chronic bronchitis, chronic obstructive pulmonary disease (COPD), pneumonia, or other infectious processes. The gradual onset of disease and the persistence of symptoms when away from work make it difficult for both workers and clinicians to recognize this as a work-related condition.

Typical Findings on Examination and Diagnostic Testing

The **physical examination**, including lung auscultation, is typically normal. However, positive findings may include end-inspiratory crackles and wheezing (4). **Spirometry** reveals an airways obstruction which, upon the administration of a bronchodilator, does not reverse to normal. **Complete Pulmonary Function Tests** (PFTs) also demonstrate fixed airways obstruction, static lung volumes show air-trapping, and lung diffusing capacity for carbon monoxide (DLCO) is usually normal. **Chest X-Ray** is typically normal or may indicate hyperinflation. **High Resolution Computed Tomography Scanning (HRCT)** often shows heterogeneous air trapping on expiratory images, with cylindric bronchiectasis, and patchy ground glass opacities. A **lung biopsy** is not generally necessary and has some limitations for making the diagnosis of severe fixed obstructive lung disease, but may be performed by an evaluating pulmonary specialist with knowledge of flavorings-related fixed obstructive lung disease.

Medical Surveillance Program

A. Medical Oversight and Supervision

Medical surveillance should be under the supervision of a board-certified occupational medicine or pulmonary medicine physician. Upon request, the California Department of Public Health (CDPH) can provide assistance to companies in identifying suitable health care providers to meet their needs and the standards of the program. Optimal oversight includes administration, review, and interpretation of respiratory health questionnaires and spirometry results (including assessing spirometry quality). The physician will also need to communicate verbal and written results to employees and facilitate additional evaluations as necessary. Employers must be advised in writing of any workplace restrictions and the need for further medical or industrial hygiene evaluation.

Physician contact with workers during medical surveillance provides an opportunity to educate workers about the hazards, associated symptoms, and protective measures and practices related to flavorings exposure. If respirators are used, training, medical clearance for respirator use, and fit-testing should also be performed according to the Cal/OSHA respiratory protection standard. A worksite visit by the supervising physician to observe the work process and control measures can be useful and informative.

B. Which Workers to Include

All workers (including workers under contract) who regularly enter or work in areas where flavoring ingredients may be inhaled should participate in the medical surveillance program. This includes production workers, compounders, mixers, helpers, shipping/receiving workers, laboratory staff, quality control workers, and may also include non-production workers such as office staff who enter production or lab areas frequently as part of their usual duties. Special concern should be directed toward workers who are exposed to heated or powder flavorings. Workers who **previously** worked in or **frequently entered** the production areas should be tested with spirometry for a minimum of two rounds of surveillance six months apart.

C. Components of Surveillance Evaluation

The initial components of the evaluation may be administered by a licensed health care professional (i.e., physician assistant, nurse practitioner, or physician) and include the following:

- Respiratory symptom and work history questionnaire
- Spirometry

The respiratory health questionnaire should focus on demographic information, current respiratory symptoms (dyspnea with exertion, cough, wheeze), work duties, and details of chemical exposures; please see the sample questionnaires in English and Spanish in Appendix E. The need for additional evaluation or testing will be determined by the results of this initial assessment.

D. Frequency of Surveillance Evaluations: Pre-Placement, During Employment, and Employment Exit

Initially, **spirometry-based surveillance should be scheduled every six months**. **If a worker is determined to have flavorings-related lung disease, then all workers whose job tasks pose similar or greater exposures are recommended to undergo surveillance every**

three months. The decision to continue surveillance every three months or return to a six-month schedule will be determined by the surveillance physician based on factors of continued case incidence, knowledge of exposure risk and control, and clinical judgment.

Nevertheless, any individual worker who at any time reports newly developed shortness of breath, cough, wheezing, or other lower respiratory tract symptoms lasting more than three weeks should be promptly evaluated by the surveillance physician and be tested with spirometry.

A surveillance evaluation should be given to workers prior to the start of work and upon termination from their jobs. At the evaluation performed prior to assignment to work with flavorings (pre-placement), workers who indicate pre-existing lung disease of any kind in their questionnaire should be provided risk communication (see Appendix D: Diacetyl Hazard Alert) through their surveillance physician. The worker should be instructed to contact his/her primary care physician to determine the need for additional workplace precautions or accommodations. If a worker with pre-existing lung disease chooses to remain in a work setting where he/she is potentially exposed to flavoring chemicals, monitoring should continue in order to detect aggravation, exacerbation, or progression of disease. It may be difficult, however, to assess whether decline in lung function is attributable to the natural course of their pre-existing lung disease or is due to flavorings-related lung disease.

E. What Constitutes Acceptable Spirometry (See Appendices B and C)

Spirometry repeated over time is the cornerstone of the medical surveillance program. If performed properly, spirometry may detect early excessive lung function decline even before test results fall below the lower limit of normal (i.e., before a worker has lost so much lung function that he/she falls into the "abnormal" range for the test). Since advanced flavorings-related lung disease is typically irreversible, it is important to identify evidence of disease as early as possible. Spirometry results will serve as the basis for further medical evaluation and workplace intervention; therefore, it is critical that spirometry results are valid and repeatable (i.e., high quality is essential). Detailed information on how to ensure high quality spirometry is provided in Appendices B and C. Providers of spirometry testing and spirometry technicians need to be aware of the standards for equipment specifications, technician competency, and testing procedures.

Maximum forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) should be obtained from a minimum of three acceptable trials using a properly calibrated spirometer and following American Thoracic Society (ATS) guidelines for standardization of spirometry (11). The maximum FVC and FEV_1 need not be from the same maneuver.

If spirometry software allows a choice of reference values, National Health and Nutrition Examination Survey III (NHANES III) reference values (12) should be used, as recommended by

ATS. If NHANES III reference values are not available, then Crapo et al (1981; may be referred to as ITS) values should be used (13).

Spirometry should be postponed for one hour after smoking, use of a bronchodilator, or after a heavy meal. If the worker is using a bronchodilator, the name of the medication and time of the last dose should be recorded on the spirometry report. For workers with acute illnesses lasting shorter than three weeks, testing should be postponed for three days if the worker simply feels ill or postponed for three weeks if the worker has had a severe respiratory illness or ear infection. Spirometry testing should be postponed for at least six weeks if the worker has had eye, ear, chest, or abdominal surgery and does have not a surgeon's release statement.

The physician's role in establishing and maintaining a spirometry quality program is essential and can be aided by understanding testing acceptability and repeatability criteria. These quality scoring criteria, based on at least three acceptable trials, are provided in Appendix C. **Spirometry tests with a quality score of C or D should be repeated.**

F. Case Confirmation and Management

After a review of the questionnaire and spirometry results, the physician is expected to identify and respond to abnormalities on screening spirometry.

We recommend using the **FEV_1/FVC ratio alone** to define cross-sectional normal versus obstructive results on spirometry**.** We also recommend using the **lower limit of normal (LLN) criterion, FEV_1/FVC < LLN as determined by NHANES LLN values,** to define obstruction rather than a < 70% predicted criterion (14). This approach will increase the sensitivity of surveillance testing. **A worker with this finding should be referred for complete PFTs.**

Obstructive abnormalities can also be characterized longitudinally by detecting an excessive decline in FEV_1. This **excessive decline in FEV_1 is a decline in the most current FEV_1 that is greater than 15% below the worker's previous best FEV_1. A worker with an excessive decline in FEV_1, even if within the normal range, should have spirometry repeated within one month** to confirm that the decline was not due to a viral respiratory infection or other acute respiratory illness. **If the decline is confirmed, then complete PFTs should be performed.**

It is not clear whether a restrictive pattern on spirometry represents lung disease related to flavorings exposure. We recommend following the algorithm in Figure 1 and advising the worker to undergo complete PFTs to determine if restriction is truly present or is an artifact due to obesity, airtrapping, or effort. If true restrictive lung abnormalities are confirmed with static lung volume measurements (low total lung capacity), we recommend a high resolution computed tomography scan and pulmonary consultation.

In summary, if a worker demonstrates **any** abnormal spirometry pattern (obstructive, restrictive, or a significant decline in FEV_1), we recommend referring the patient to a pulmonary function lab to obtain complete PFTs. The primary purpose of complete PFTs is to determine the fixed or reversible characteristics of these obstructive defects following the administration of bronchodilators. Other common PFT findings that are consistent with flavorings-related lung disease are found in Table 1.

Alternatively, the worker may be referred to a pulmonary specialist for this testing and follow-up. If the worker is referred to a pulmonary specialist, we recommend one with knowledge of flavorings-related fixed obstructive lung disease. It is the responsibility of the occupational medicine provider to provide the specialist with necessary medical records and information on the risk of flavorings-related lung disease. **Due to the potential seriousness of this disease process, we recommend that the provider identify a pulmonary specialist and pulmonary function laboratory prior to the discovery of suspected or confirmed cases.**

If upon completion of PFTs the following conditions are present:

- Fixed obstruction,
- OR post-hire onset of non-fixed obstruction (i.e., asthma),
- OR pre-hire asthma with worsening control and symptoms (i.e., dyspnea, wheeze, or cough).

referral for a **high resolution computed tomography scan (HRCT) with both inspiratory and expiratory views** is recommended**.** See Table 1 for common findings consistent with BO that are seen on HRCT.

Table 1

Common Findings for Flavorings-Related Lung Disease on Further Pulmonary Evaluation

Static lung volumes by whole body plethysmography or by helium dilution:	**Residual volume increased (increased RV/TLC with normal Total Lung Capacity)**
Diffusing capacity for carbon monoxide (DLCO):	**Usually normal, may be decreased in advanced disease (Reduced in emphysema)**
High resolution CT scan of the chest:	
1 mm inspiratory sections every 2 cm **1 mm expiratory sections every 4 cm**	**Heterogeneous air trapping during expiration** **Cylindric bronchiectasis** **Bronchial wall thickening** **Patchy ground glass opacities** **Mosaic pattern of attenuation**

HRCT has proved to be a useful tool in diagnosing BO with reasonable confidence, but the sensitivity for early disease has not been clearly defined. We recommend that a worker with both fixed obstructive airways defect and an HRCT demonstrating patterns consistent with

BO in a setting of probable flavorings exposure should be considered a case of flavorings-related lung disease.

However, classification status of workers with reversible obstructive airways defect and a suggestive HRCT is indeterminate. Severe asthma and BO have similar findings on HRCT (15); therefore, this group may either represent severe asthmatics or may evolve into BO cases.

Workers with either fixed or reversible obstructive defects and normal HRCTs may represent a group with early flavorings-related lung disease and therefore should be considered suspect cases. This group should be monitored for further progression toward BO and receive further evaluation to exclude other explanations for their condition. Although fixed obstructive pattern is a major characteristic of flavorings-related lung disease, occupational asthma or other lung conditions may also develop due to flavorings exposure and therefore should not be missed. See the algorithm in Figure 1 and definitions in Table 2 (Section H of this document).

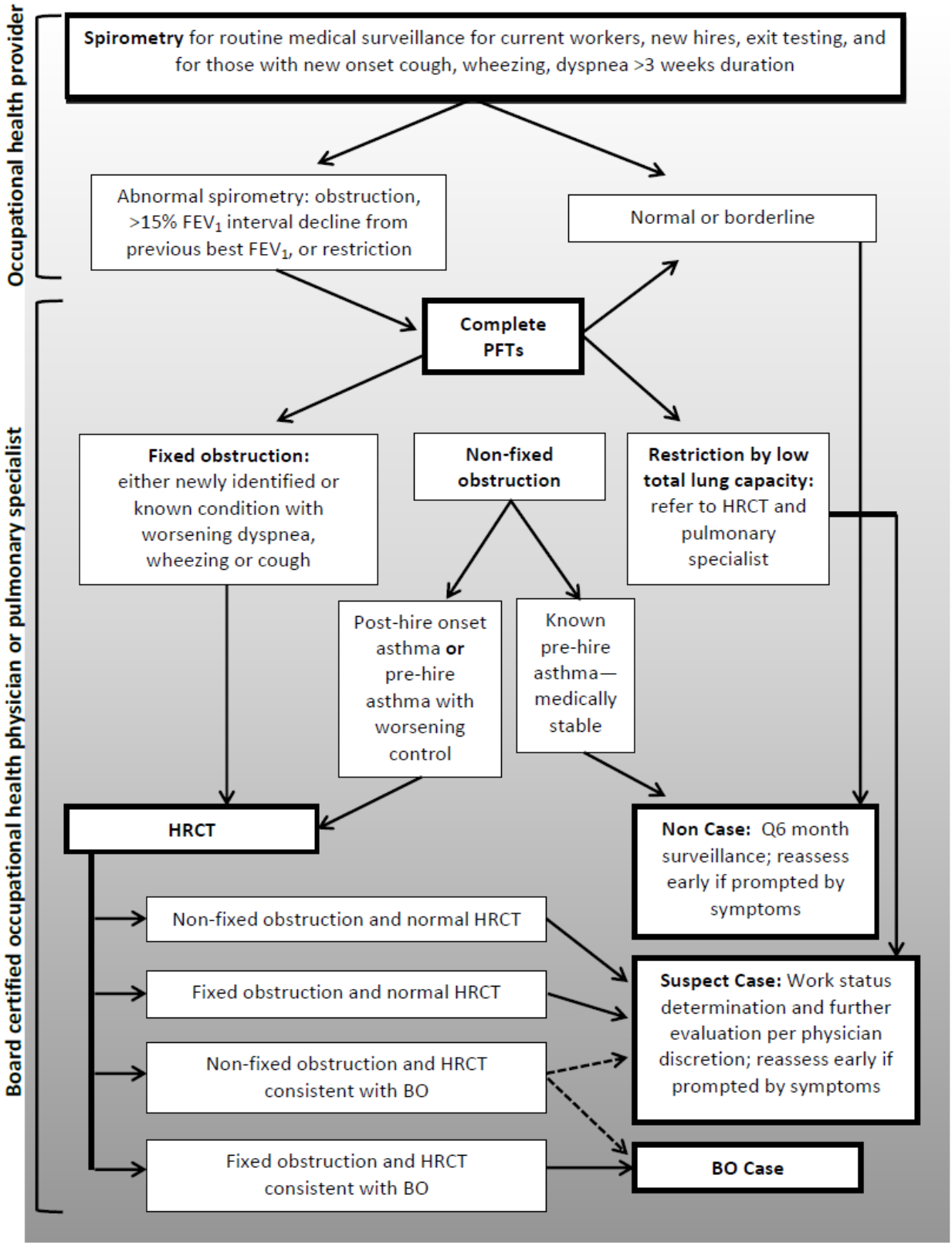
Finally, a lung biopsy is not generally necessary for diagnosis or classification of flavorings-related lung disease, but may be recommended by an evaluating pulmonary specialist. If a lung biopsy is desired, an open or thoracoscopic biopsy should be performed, and the reviewing pathologist should be notified that constrictive bronchiolitis is suspected so that appropriate tissue staining and sectioning will be performed to identify this type of lesion. Even so, many cases demonstrating fixed obstruction in the microwave popcorn and flavoring industries have not had pathologic confirmation of BO. Pathology should not be considered the gold standard in the presence of characteristic HRCT findings in a flavorings-exposed worker without other evident cause.

G. How to Handle Workers in Surveillance with Pre-Existing Lung Conditions

If a worker has either a known pre-existing lung condition such as COPD or asthma, or is found to have such a condition on initial pre-work evaluation, it is important to be aware that this does not preclude the possibility of additionally developing a flavorings-related lung condition. It may, however, complicate the identification and classification of such affected workers. For this reason, care must be taken to allow the worker to be fully evaluated without a premature assumption that his or her symptoms are related to the pre-existing lung condition. We recommend that the occupational health physician educate the worker on the health risks associated with diacetyl (Appendix D) and other flavoring chemicals, and arrange appropriate follow-up with the worker's primary care physician.

Frequency of surveillance for those with known pre-hire asthma that is medically stable and demonstrated not to have a fixed obstructive component is recommended to continue on the every-six-month schedule. However, if the worker develops post-hire asthma, or if asthma control worsens (i.e., increased use of rescue inhaler use, worsening peak flow measurements, or increase in frequency of symptoms), the worker should be evaluated by the surveillance physician and undergo an HRCT. Please refer to Figure 1.

Figure 1. Recommended Evaluation for Workers with Abnormal Spirometry



H. Evaluation Algorithm (Figure 1) and Case Definitions (Table 2)

The algorithm in Figure 1 on the previous page summarizes a recommended medical evaluation for workers with abnormal spirometry results.

The following table summarizes recommended criteria for the determination of flavorings-related lung disease classification.

Table 2

Determination of Flavorings-Related Lung Disease Status

- **No disease suspected**
  - o FEV_1/FVC at or above the lower limit of normal (LLN)
  - o AND, if two or more tests are available, the FEV_1 decline is within 15% of the worker's previous best FEV_1
  - → **Continue to monitor in surveillance program at six-month intervals**
- **Suspected**
  - o FEV_1/FVC below the lower limit of normal (LLN)*****
  - o OR, upon follow-up spirometry, a FEV_1 decline greater than 15% below the worker's previous best FEV_1*****
  - o AND high resolution CT (HRCT) findings not consistent with bronchiolitis obliterans
  - → **Recommend increasing surveillance frequency and continued pulmonary evaluation to determine or explain abnormal findings**
- **Confirmed BO Case**
  - o Fixed airways obstruction on complete pulmonary function tests
  - o AND high resolution CT (HRCT) findings consistent with bronchiolitis obliterans
  - o AND history of workplace diacetyl or other flavoring chemical exposure
  - → **Confirmation of diagnosis with pulmonary specialist if not already done**

*for asthmatics, these results should be obtained when under optimal medical control of asthma

I. Workplace interventions

If a worker is suspected of having or is confirmed to have flavorings-related lung disease, the physician should effectively and immediately remove the worker from further inhalation exposure to flavoring ingredients and compounds in any form. This work status change may be initiated when the worker begins further evaluation and before a full characterization of the worker's medical condition. The employer should be advised that

respirator use in an exposed environment is not equivalent to removal from exposure. Finally, caution should be exercised when considering returning a worker to his or her usual work tasks even when the lung condition has improved and engineering controls have been implemented.

If flavorings-related lung disease is suspected in a worker, the physician should request an industrial hygiene evaluation of that worker's workstation(s) to characterize the extent and type of exposures and to obtain recommendations for worker protection. This assessment will also assist in determining appropriate steps for protecting and screening other workers. Additionally, the occupational health physician should annually coordinate with the industrial hygienist to assess work areas and observe job tasks of workers in companies with suspect or confirmed cases to determine if additional control measures are needed.

J. Reporting of workers with suspected or confirmed flavorings-related fixed obstructive lung disease

Several lines of reporting should be completed by the occupational health physician once a worker is found to have suspected or confirmed flavorings-related lung disease. If the worker's lung condition is deemed to be work-related, the provider is responsible for submitting a **Doctor's First Report of Occupational Injury and Illness** found at http://www.dir.ca.gov/DLSR/dlsrform5021.pdf and is encouraged to assist the worker in the workers' compensation claim process. Workers should have appropriate changes to their work status based on their condition, their exposures, and the potential for progression of disease.

Occupational health providers should also notify the **California Department of Public Health, Occupational Health Branch** (see below), about any identified workers with "suspected" or "confirmed" flavorings-related lung disease.

The provider should advise the employer of their obligation to report serious illness to the nearest **Cal/OSHA district office** per Title 8, California Code of Regulations, Section 342(a).

Conclusion

While flavorings-related lung disease can be severe and irreversible, we believe it can be prevented when proper steps are taken to protect workers. Health care providers play an essential role in the early identification of affected symptomatic and asymptomatic workers and in their appropriate clinical management. Through the collaboration of industry, workers, and government agencies, we are learning more about this new health hazard, the risk factors, and best practices for prevention and control. The information in these guidelines is intended to assist you in creating an effective medical surveillance program that will protect California workers against potential harm from flavoring exposures.

Since the original publication of this document, our colleagues at NIOSH have produced a number of valuable new resources on spirometry and its use in medical surveillance of workers exposed to respiratory hazards:

- The NIOSH Spirometry topic page includes information on spirometry training, free SPIROLA software to analyze longitudinal data, a poster "Get Valid Spirometry Results EVERY Time," and information sheets for employers and workers. (http://www.cdc.gov/niosh/topics/spirometry/)
- Spirometry Quality Assurance: Common Errors and Their Impact on Test Results: http://www.cdc.gov/niosh/docs/2012-116/pdfs/2012-116.pdf

The Occupational Health Branch of the California Department of Public Health is available for consultation regarding surveillance or spirometry program design, appropriate work status for affected workers, and any other related questions. Please contact:

HESIS Workplace Hazard Helpline
1-510-620-5817 or 1-866-282-5516 (toll-free in California)

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Appendices and Additional Resources

- **Appendix A: Definition of Key Terms**
- **Appendix B: Spirometry Quality Guidelines**
- **Appendix C: Scoring Criteria for Spirometry Test Quality**
- **Appendix D: Health Hazard Alert: Diacetyl (Butter Flavor Chemical) Use in Flavoring Manufacturing Companies (English and Spanish)**
- **Appendix E: Respiratory Health Questionnaires: Initial and Follow-Up (English and Spanish)**

Appendix A: Definition of Key Terms

Airways Obstruction

FEV_1/FVC below the lower limit of normal (14) as determined by NHANES LLN values.

Reversible Airways Obstruction

In workers found to have airways obstruction, two separate doses of 100 µg of a short-acting $ß_2$ agonist (such as salbutamol or albuterol) should be given using a spacer and the spirometry test repeated after 10 minutes. Reversibility is defined as an increase in FEV_1 and/or FVC of at least 12% and 200 milliliters, compared to pre-bronchodilator values (14).

Fixed Airways Obstruction

Airways obstruction that persists despite the administration of two separate doses of a short-acting $ß_2$ agonist.

Restrictive Pattern

FEV_1/FVC at or above the lower limit of normal and FVC below the lower limit of normal on screening spirometry and confirmed by lung volume tests demonstrating a total lung capacity $<5^{th}$ percentile of the predicted value.

Excessive Decline in FEV_1

Excessive decline in FEV_1 is a decline greater than 15% below the worker's previous best FEV_1.

Appendix B: Spirometry Quality Guidelines

Spirometry testing standards

- Equipment:
  - Written verification from a third party (not the manufacturer or distributor) that the spirometer has successfully passed its validation checks using the most current ATS protocol. The manufacturer may be able to provide a copy of the letter from an independent testing laboratory detailing the validation results for the specific model of spirometer being used.

  - Spirometer must store and print all results from the best three acceptable maneuvers, including volume-time and flow-volume curves.

- Spirometry Technician:
  - Should have successfully completed a NIOSH-approved spirometry training course (http://www.cdc.gov/niosh/topics/spirometry/training.html) within the previous five years or should be certified by the National Board for Respiratory Care as a Certified Pulmonary Function Technologist (CPFT). Copies of certificates of completion of a NIOSH-approved spirometry training course and/or CPFT certification should be maintained.

  - Spirometry reports should be periodically reviewed for quality and should demonstrate that at least 80% of tests completed by each technician have three acceptable maneuvers with two maneuvers within ATS repeatability criteria.

- Testing Procedures:
  - Spirometer volume accuracy checks should be performed using a currently calibrated (per manufacturer recommendations) three-liter syringe on each day of testing and other checks performed according to the frequency established by the ATS/ERS spirometry standardization statement (11). A copy of the spirometer calibration report should be maintained either electronically or in hard copy form.

  - Spirometry should be performed in the same documented position (either sitting or standing) during the initial and all subsequent tests.

  - A minimum of three forced exhalation maneuvers producing **"Acceptable Curves"** on the spirometry report should be characterized by all of the following:
    - Lack of hesitation (back-extrapolation volume should be less than 5% of FVC or 150 mL, whichever is larger).
    - Free of cough in the first second.

- No evidence of airflow cessation, variable effort, leak, obstructed mouthpiece, a positive or negative zero flow error, or extra breath(s).
- At least six seconds in duration (However, young healthy adults may empty their lungs before six seconds. As long as there are no other technical errors and the worker reaches end-of-test criteria, then the trial is valid).
- Meeting acceptable end-of-test criteria ($\leq$ 25 mL increase in volume for one second) or a maneuver greater than 15 seconds in duration.

- Less than 150 mL difference between the two highest FVC measurements and the two highest FEV_1 measurements is the goal.

- Spirometry report should include:
  - Name of the person being tested;
  - Spirometry values and volume-time and flow-volume curves for the three best blows;
  - Test date;
  - Date of last calibration check;
  - Reference values used;
  - Initials or name of the technician; and
  - Name of the medical provider.

Since all spirometry software packages cannot identify all possible technical errors encountered during testing, NIOSH developed a poster for use in clinical testing areas that provides guidance to identify and correct common testing errors and improve spirometry test quality (16). This document has been translated into several languages for non-English speaking technicians and can be accessed from: http://www.cdc.gov/niosh/docs/2011-135/.

Spirometry Predicted Values

If spirometry software allows a choice of predicted values, NHANES III should be used (12). NHANES III predicted values are recommended by ATS and are based on a much larger population, compared to other studies. NHANES III predicted values are not available for Asians. Predicted values for Asians born in the United States can be calculated by multiplying the NHANES III Caucasian predicted values for FEV_1 and FVC by 0.94 (14) or by 0.88 (17). If spirometry software does not include lower limits of normal values, the Web link http://www.cdc.gov/niosh/topics/spirometry/RefCalculator.html can be used to calculate lower limits of normal for NHANES III reference values. Be aware that all predicted values and lower limits of normal should be from the same reference paper.

Appendix C: Scoring Criteria for Spirometry Test Quality

Using the definition of "Acceptable Curves" described earlier in **Spirometry Quality Guidelines (Appendix B)**, the following quality codes should be used.

FEV_1 Quality Codes

Grade A: At least three acceptable curves, FEV_1 repeatable within
- 50 mL if FEV_1 is derived from the last curve
- 100 mL otherwise

Grade B: At least two acceptable curves, FEV_1 repeatable within 150 mL

Grade C: At least two acceptable curves, FEV_1 repeatable within 250 mL

Grade D: Only one acceptable curve

Grade F: No acceptable curve

FVC Quality Codes

Grade A: At least three acceptable curves,
- If best FVC derived from last curve, repeatability within 50 mL; otherwise, FVC repeatable within 100 mL
- FVC acceptable curve demonstrates
  - Greater than six second exhalation
  - Achievement of exhalation volume plateau

Grade B: At least two acceptable curves,
- FVC acceptable curve requirements
  - Greater than six second exhalation
  - Achievement of exhalation volume plateau
- FVC repeatability within 150 mL

Grade C: At least two acceptable curves,
- FVC acceptable curve requirements
  - Greater than six second exhalation
  - Achievement of exhalation volume plateau
- FVC repeatability within 250 mL

Grade D: Only one acceptable curve

Grade F: No acceptable curves

Appendix D: Health Hazard Alert: Diacetyl (Butter Flavor Chemical) Use in Flavoring Manufacturing Companies (in English and Spanish)

English version found at http://www.cdph.ca.gov/programs/hesis/Documents/diacetyl.pdf

Diacetyl (Butter Flavor Chemical) Use in Flavoring Manufacturing Companies

Exposure to diacetyl used in flavoring manufacturing companies may cause a serious lung disease called bronchiolitis obliterans. Workers from two California flavoring companies that use diacetyl have been diagnosed with this disease. Damage to the lungs can be permanent, canrequire a lung transplant, and can lead to death. The main symptoms are a persistent cough and shortness of breath when using extra energy (such as walking fast or up a slight hill) and wheezing when you do not have a cold. The symptoms do not go away in the evenings, on weekends, and on vacations. They can start gradually and get worse over time, or they can suddenly be very severe. Doctors sometimes think the symptoms are due to asthma, chronic bronchitis, emphysema, pneumonia, or smoking. If you work at a flavoring company that uses diacetyl, see a doctor immediately to make sure that your health is not being affected. Take this information sheet with you. Your company should follow the recommendations on page 2 to reduce exposure to diacetyl and other flavoring chemicals.

Health Hazard ALERT

How to know if you are working with diacetyl

Diacetyl is a yellowish liquid that is usually mixed with other ingredients to produce butter flavor or other flavors in a variety of food products. If you think diacetyl is used in your workplace, read labels on containers and ask to see a Material Safety Data Sheet (MSDS). The MSDS must list diacetyl in Section 2 by the Chemical Abstract Service (CAS) number 431-03-8. Cal/OSHA's Hazard Communication Standard (Title 8, Section 5194), requires your employer to tell you if you are using diacetyl, and to train you on the health hazards and how to use it safely.

How you are exposed to diacetyl

Diacetyl enters your body when you breathe vapors, droplets of spray, or dust containing diacetyl in the air.

Your risk of health effects depends on how much diacetyl enters your body. The amount of diacetyl in the air and how long you are exposed, determines how much enters your body.

How diacetyl can affect your health

Lungs. Diacetyl can damage your lungs. Symptoms include a dry cough, shortness of breath when using extra energy, and wheezing. The symptoms can start gradually, or severe symptoms can occur suddenly. The symptoms continue when you are not at work. Asthma medicines are not effective. Some workers do not have symptoms. See Medical Tests (page 2). Diacetyl damages the respiratory system of test animals.

Eyes, nose, and throat. Diacetyl vapors can sting or burn your eyes. They can cause your nose and throat to burn and feel sore. Eye contact with vapors can also cause chemical burns which require medical treatment to heal.

Skin. Diacetyl can irritate the skin. It can cause a rash with dryness, redness, flaking, and cracking of the skin.

Cancer and reproductive effects. Diacetyl has not been tested for these effects. Reducing exposure (page 2) to prevent lung disease will help to protect you.

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Medical tests for health effects

Breathing tests (spirometry) that measure how well your lungs are working, and a respiratory symptom questionnaire, are the best ways to detect bronchiolitis obliterans and other serious lung disease. Early detection is critical. You should have a lung function test before you begin working in a company that uses diacetyl and on a regular basis while you are working.

How to reduce exposure to diacetyl

Substitution. Less hazardous flavoring ingredients should be used whenever possible. Make sure that substitutes are safe.

Closed production processes. Handling open containers of diacetyl and other flavoring ingredients should be avoided.

Ventilation. Maintain air levels of diacetyl as low as possible using local exhaust ventilation. A safe exposure level has not been identified.

Respiratory protection. Respirators should be used until ventilation and other controls are determined to be effective. Use NIOSH-approved air-purifying respirators with organic vapor cartridges and particulate filters, or supplied-air respirators. Employers must comply with the Cal/OSHA Respiratory Protection Standard (Title 8, Section 5144). See **www.dir.ca.gov/title8/5144.html**

Skin and eye protection. Employers must provide protective gloves, goggles, and other protective equipment.

WHERE TO GET HELP

- **HESIS** can answer questions about diacetyl, other workplace hazards, and information in this fact sheet. Call **(866) 282-5516**.
- **California Division of Occupational Safety and Health (Cal/OSHA)** investigates workers' complaints and makes enforcement inspections. Complainants' identities are kept confidential. Call the nearest office to your workplace, or see **www.dir.ca.gov/DOSH/districtoffices.htm**
- **Cal/OSHA Consultation Service** helps employers who want free, non-enforcement help to evaluate the workplace and improve health and safety conditions. Flavoring companies can call **(562) 944-9366**.
- **National Institute for Occupational Safety and Health (NIOSH).** See **www.cdc.gov/niosh/topics/flavorings/**
- **Occupational health services can be found at:**
  - University of California (UC) San Francisco: **(415) 885-7580**
  - UC Davis: **(530) 754-7635**
  - UC Irvine: **(949) 824-8641**
  - UC San Diego: **(619) 471-9210**
  - UCLA: **(310) 794-8144**
- **Flavor and Extract Manufacturers Association of the United States (FEMA).** See **www.femaflavor.org/html/public/RespiratoryRpt.pdf**

REGULATIONS THAT HELP TO PROTECT WORKERS

- **Injury and Illness Prevention Program.** See **www.dir.ca.gov/title8/3203.html**
- **Hazard Communication.** See **www.dir.ca.gov/title8/5194.html**
- **Control of Harmful Exposures to Employees.** See **www.dir.ca.gov/title8/5141.html**
- **Access to Employee Exposure and Medical Records.** See **www.dir.ca.gov/title8/3204.html**

Arnold Schwarzenegger, Governor
State of California
Kimberly Belshé, Secretary
California Health and Human Services Agency
Victoria L. Bradshaw, Secretary
Labor and Workforce Development Agency
Sandra Shewry, Director
California Department of Health Services
John Rea, Acting Director
Department of Industrial Relations

JANE NORLING DESIGN

Spanish version found at http://www.cdph.ca.gov/programs/hesis/Documents/diacetyl.pdf

Uso de diacetil (aromatizante químico con sabor a mantequilla) en compañías que fabrican aromatizantes

La exposición al diacetil utilizado por las compañías que fabrican aromatizantes puede causar una enfermedad seria en los pulmones llamada bronquiolitis obliterante. Trabajadores de dos fabricantes de aromatizantes en California que usan diacetil fueron diagnosticados con esta enfermedad. Los pulmones pueden quedar dañados en forma permanente, y la enfermedad puede requerir un transplante de pulmón o ser fatal. Los síntomas principales son una tos persistente y falta de aire cuando se hace un esfuerzo (como caminar rápido o subir una pendiente suave), y sibilancias sin tener un resfriado. Los síntomas no desaparecen por la noche, en los fines de semana o cuando está de vacaciones. Pueden comenzar en forma gradual y empeorar con el tiempo, o se pueden hacer muy severos de golpe. Los médicos creen a veces que los síntomas son causados por el asma, bronquitis crónica, enfisema, pulmonía, o el fumar. Si trabaja en una empresa que fabrica aromatizantes y que usa diacetil, vea a un médico inmediatamente para comprobar que no le haya afectado la salud. Lleve esta hoja informativa a la consulta. Su empresa debe seguir las recomendaciones de la página 2 para reducir su exposición al diacetil y otros aromatizantes químicos.

ALERTA de peligro de salud

Cómo saber si está trabajando con diacetil

El diacetil es un líquido amarillento que generalmente se mezcla con otros ingredientes para producir un aromatizante con sabor a mantequilla u otros sabores. Estos se usan en una variedad de productos alimenticios. Si cree que se está usando diacetil en su lugar de trabajo, lea las etiquetas de los recipientes y pida ver una Hoja Informativa de Seguridad de Material (MSDS, por sus siglas en inglés). La MSDS deberá incluir el diacetil en la sección 2 con el número 431-03-8 del Servicio de Resumen Químico (CAS, por sus siglas en inglés). La Norma de Comunicación de Sustancias Peligrosas de Cal/OSHA (Título 8, Sección 5194) exige que su empleador le informe si usted está usando diacetil, y que lo capacite sobre los peligros para la salud y cómo usarlo de manera segura.

Cómo se expone al diacetil

El diacetil entra en el cuerpo cuando respira aire que contiene vapores, gotas de rocío o polvo de diacetil.

El riesgo para la salud depende de cuánto diacetil entra en el cuerpo. La cantidad de diacetil que entra en el cuerpo depende de la cantidad que haya en el aire, y del tiempo de exposición.

Cómo puede afectar su salud el diacetil

Pulmones. El diacetil puede dañar los pulmones. Los síntomas incluyen tos seca, falta de aire cuando hace un esfuerzo, y sibilancias. Los síntomas pueden comenzar gradualmente o pueden aparecer de golpe en forma de síntomas graves. Los síntomas continuarán aunque no esté trabajando. Los medicamentos contra el asma no son efectivos. Algunos trabajadores no tienen síntomas. Vea la sección sobre pruebas médicas (página 2). El diacetil daña el sistema respiratorio en animales de laboratorio.

Ojos, nariz y garganta. Los vapores de diacetil pueden causar escozor o ardor en los ojos. Pueden causar dolor y ardor en la nariz y la garganta. El contacto de estos vapores con los ojos también puede causar quemaduras químicas que sólo se pueden curar con tratamiento médico.

Piel. El diacetil puede irritar la piel. Puede causar un sarpullido con sequedad, enrojecimiento, escamas y grietas en la piel.

Cáncer y efectos reproductivos. No se han estudiado estos efectos en el diacetil. Si reduce su exposición para prevenir enfermedades de los pulmones (página 2) se protegerá también contra estos efectos.

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Pruebas médicas para ver si hay efectos sobre la salud

Las mejores maneras de detectar la bronquiolitis obliterante y otras enfermedades serias de los pulmones son pruebas de respiración (espirometría) para medir cómo funcionan los pulmones, y un cuestionario sobre sus síntomas respiratorios. La detección temprana es crítica. Debería hacerse una prueba de funcionamiento del pulmón antes de comenzar a trabajar en una empresa que usa diacetil, y en forma periódica mientras siga trabajando allí.

Cómo reducir la exposición al diacetil

Sustitución. Use ingredientes aromatizantes menos peligrosos en la medida de lo posible. Compruebe que los sustitutos sean seguros.

Procesos de producción cerrada. Evite el manejo de recipientes abiertos de diacetil y otros ingredientes aromatizantes.

Ventilación. Use un sistema de extracción de contaminantes para mantener más bajo posible el nivel de diacetil en el aire. No se ha identificado cuál es un nivel de exposición segura.

Protección respiratoria. Se deben usar respiradores hasta que se haya comprobado la efectividad de la ventilación y otros controles. Use respiradores purificadores de aire aprobados por NIOSH, con cartuchos de vapor orgánico y filtros de partículas, o respiradores con suministro de aire propio. Los empleadores deben cumplir con la Norma de Protección Respiratoria de Cal/OSHA (Título 8, Sección 5144). Visite: www.dir.ca.gov/title8/5144.html.

Protección de la piel y los ojos. Los empleadores deben proporcionar guantes, lentes protectores, y otros equipos de protección.

DÓNDE OBTENER AYUDA

- **HESIS** puede responder a preguntas sobre el diacetil, otras sustancias peligrosas en el lugar de trabajo, y esta hoja informativa. Llame al **(866) 282-5516**.
- **La División de Seguridad y Salud Ocupacional de California (Cal/OSHA)** investiga las quejas de los trabajadores y efectúa inspecciones para verificar el cumplimiento de las normas. No se divulgará la identidad de las personas que presentan quejas. Llame a la oficina más cercana a su lugar de trabajo o visite: **www.dir.ca.gov/DOSH/districtoffices.htm**
- **El Servicio de Consultoría de Cal/OSHA** ayuda a los empleadores que quieren obtener información gratis y sin ser multados para evaluar su lugar de trabajo y mejorar las condiciones de salud y seguridad. Compañías que fabrican aromatizantes pueden llamar al: **(562) 944-9366**.
- **Instituto Nacional para la Salud y Seguridad Ocupacional (NIOSH)** Visite: **www.cdc.gov/niosh/topics/flavorings/**
- **Se pueden encontrar servicios de salud ocupacional en:**
  - Universidad de California (UC) San Francisco: **(415) 885-7580**
  - UC Davis: **(530) 754-7635**
  - UC Irvine: **(949) 824-8641**
  - UC San Diego: **(619) 471-9210**
  - UCLA: **(310) 794-8144**
- **Asociación de Fabricantes de Aromatizantes y Extractos de EE UU. (FEMA).** Visite: **www.femaflavor.org/html/public/RespiratoryRpt.pdf**

REGLAMENTOS QUE AYUDAN A PROTEGER A LOS TRABAJADORES

- **Programa de prevención de lesiones y enfermedad.** Visite **www.dir.ca.gov/title8/3203.html**
- **Comunicación de sustancias peligrosas.** Visite: **www.dir.ca.gov/title8/5194.html**
- **Control de exposiciones peligrosas a los empleados.** Visite: **www.dir.ca.gov/title8/5141.html**
- **Acceso a los registros médicos y de exposición de los empleados.** Visite: **www.dir.ca.gov/title8/3204.html**

Appendix E: Respiratory Health Questionnaires

1. **Initial Questionnaire in English**
   Available at: http://www.cdph.ca.gov/programs/ohb/Documents/flavor-initial.doc

2. **Initial Questionnaire in Spanish**
   Available at: http://www.cdph.ca.gov/programs/ohb/Documents/flavor-initial-sp.doc

3. **Follow-Up Questionnaire in English**
   Available at: http://www.cdph.ca.gov/programs/ohb/Documents/flavor-followup.doc

4. **Follow-Up Questionnaire in Spanish**
   Available at: http://www.cdph.ca.gov/programs/ohb/Documents/flavor-followup-sp.doc