

06-OH-01

Title: Reducing the risk of bronchiolitis obliterans due to diacetyl and other food flavorings

Statement of the Problem:

In August 2000, the Missouri Department of Health and Senior Services requested technical assistance from NIOSH to investigate several cases of bronchiolitis obliterans (BO) in former workers of a microwave popcorn plant in Jasper, Missouri. Eight former workers at this plant developed illness characterized by fixed airways obstruction on lung function tests [Akpinar-Elci 2002]. An evaluation of the workforce at this plant showed an association between exposure to vapors from flavorings used in the production process and decreased lung function [Kreiss 2002]. Similar fixed obstructive lung disease has also occurred in workers at other plants that use or manufacture flavorings (NIOSH 1986; Lockey 2002). In animal tests, inhaling vapors from a heated butter flavoring used in microwave popcorn production caused severe injury to airways (Hubbs 2002). A 2004 NIOSH Alert, "[Preventing Lung Disease in Workers Who Use or Make Flavorings](http://www.cdc.gov/niosh/docs/2004-110/pdfs/2004-110.pdf)." (accessed May 28, 2006 at <http://www.cdc.gov/niosh/docs/2004-110/pdfs/2004-110.pdf>) recommended that employers and workers take steps to limit worker exposure, preferably by substitution and engineering controls. Studies at six microwave popcorn plants have shown that flavoring chemicals (including diacetyl) can cause BO in the workplace (Kanwal 2006). In these studies, peak exposures were hazardous even when ventilation maintained low average exposures, and respiratory protection and engineering controls were necessary to protect workers in these plants.

BO is characterized by inflammation and scarring in the smallest airways of the lung that may result in severe and disabling symptoms. One worker has recently died from BO due to exposure to diacetyl (accessed May 28, 2006 at <http://www.kansascity.com/mld/kansascity/news/local/14481628.htm>). The main respiratory symptoms experienced by diacetyl-exposed workers affected by BO include cough (usually without phlegm) and shortness of breath on exertion. Respiratory symptoms typically do not improve when the worker goes home at the end of the workday or on weekends or vacations. Respiratory symptoms are typically gradual in onset and progressive, but severe symptoms can occur suddenly. Some workers may experience fever, night sweats, and weight loss. The diagnosis of BO among diacetyl-exposed workers has been missed by some health care providers because they initially suspected asthma, chronic bronchitis or Chronic Obstructive Pulmonary Disease. Additional diagnostic studies should be performed and include pulmonary function studies (fixed airways obstruction, hyperinflation with air trapping, normal diffusing capacity), high-resolution computerized tomography scans of the chest (air trapping on the expiratory view with haziness and thickened airway walls) and lung biopsies (severe narrowing or complete obstruction of the small airways). Affected workers generally notice a gradual reduction or cessation of cough years after they are no longer exposed to diacetyl and other flavoring vapors, but shortness of breath on exertion may persist.

In the fall of 2004, the California Department of Health Services (CDHS) was notified of a case of BO in a worker exposed to diacetyl at a flavorings plant in Southern California. This case was the first to be reported after one case was summarized in a meeting abstract in 2002 (Lockey 2002). Further investigation by the California Division of Occupational Safety and Health (Cal/OSHA) determined that this worker was exposed to diacetyl during the formulation of artificial butter flavoring. Cal/OSHA and CDHS initiated discussions with the Flavoring and Extracts Manufacturers Association (FEMA) to conduct follow-up consultation and evaluation to determine if exposure to diacetyl poses a hazard to workers in other flavorings companies in California. As these discussions were ongoing, a second case of BO has been reported to CDHS in April 2006 in a worker exposed to diacetyl at a flavorings company. Similar to the first case, this worker also was exposed to diacetyl during the formulation of artificial butter flavoring.

Statement of the Desired Action to be Taken

The National Institute for Occupational Safety and Health (NIOSH), in collaboration with State health departments and the Council of State and Territorial Epidemiologists (CSTE), should take action to reduce and/or eliminate the risks of BO to workers due to exposure to diacetyl and other food flavorings. CSTE recommends that NIOSH:

- 1- Conduct animal inhalation toxicology studies to determine the mechanism of action, target organ effects and pharmacokinetics of diacetyl and other food flavorings
- 2- Develop and implement a nationwide system, based on State reporting under State public health authority, to report BO cases among workers exposed to diacetyl and other food flavorings. In conjunction with CSTE, NIOSH should establish appropriate case definitions, surveillance sources, reporting mechanisms, and case verification and follow-up protocols.
- 3- Conduct investigations of exposures and health effects among current and former diacetyl manufacturing and food flavoring industry workers. These studies should include identification of the manufacture, sales and distribution of diacetyl and other potentially hazardous food flavorings; determine exposure to diacetyl among all industries wherever workers may be exposed; exposure assessment in diacetyl manufacturing, food flavorings, and other work settings with potential exposure to diacetyl; and health effects studies to perform case finding and characterize exposure-response relationships.
- 4- Develop and evaluate control technologies to reduce and/or eliminate exposure to diacetyl and other hazardous food flavorings. These include closed systems, and the use of local and general exhaust ventilation during mixing and blending operations.
- 5- Conduct information dissemination to alert employers, employees and health care providers about the hazards of exposure to diacetyl and other food flavorings; availability of existing resources to assist with exposure assessment and controls; recommendations for medical monitoring and follow-up of abnormal results; and importance of early recognition of signs and symptoms of BO.
- 6- Convene meetings with the US Food and Drug Administration and the US Department of Labor OSHA to determine the mechanism to establish more effective regulatory policies to protect workers who are exposed to diacetyl and other hazardous food flavorings

Public Health Impact

The report of two additional cases of BO following exposure to diacetyl indicates that workers continue to be at risk of serious lung disease in the food flavoring industry. The 2004 NIOSH Alert served to highlight the importance of controlling exposures in this industry, but additional steps need to be taken to prevent future life-threatening lung disease in this worker population. A coordinated public health response by NIOSH and State Health Departments will lead to minimizing and/or eliminating diacetyl and/or other hazardous flavoring exposures, thereby preventing future disability and death due to BO.

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References

Akpinar-Elci M, Kanwal R, Kreiss K: Bronchiolitis obliterans syndrome in popcorn plant workers. *Am J Respir Crit Care Med* 165:A526, 2002.

Hubbs AF, Battelli LA, Goldsmith WT, Porter DW, Frazer D, Friend S, Schwegler-Berry D, Mercer RR, Reynolds JS, Grote A, Castranova V, Kullman G, Fedan JS, Dowdy J, Jones W.: Necrosis of nasal and airway epithelium in rats inhaling vapors of artificial butter flavoring. *Toxicol Appl Pharmacol* 185:128–135, 2002.

Kanwal R, Kullman G, Piacitelli C, Boylstein R, Sahakian N, Martin S, Fedan K, Kreiss K: Evaluation of flavorings-related lung disease risk at six microwave popcorn plants. *J Occup Environ Med* 48(2): 149-57, 2006.

Kreiss K, Gomaa A, Kullman G, Fedan K, Simoes EJ, Enright PL: Clinical bronchiolitis obliterans in workers at a microwave-popcorn plant. *N Engl J Med* 347:330–338, 2002.

Lockey J, McKay R, Barth E, Dahlsten J, Baughman R: Bronchiolitis obliterans in the food flavoring manufacturing industry. *Am J Respir Crit Care Med* 165:A461, 2002.

NIOSH Hazard evaluation and technical assistance report: International Bakers Services, Inc., South Bend, IN. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 85–171–1710, 1986.