

Occupational Lung Disease Risk and Exposure to Butter-Flavoring Chemicals After Implementation of Controls at a Microwave Popcorn Plant

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ABSTRACT

Objectives. After an outbreak of severe lung disease among workers exposed to butter-flavoring chemicals at a microwave popcorn plant, we determined whether or not lung disease risk declined after implementation of exposure controls.

Methods. National Institute for Occupational Safety and Health staff performed eight serial cross-sectional medical and industrial hygiene surveys at the plant from November 2000 through August 2003. Medical surveys included standardized questionnaires and spirometry testing. Industrial hygiene surveys measured levels of production-related air contaminants, including butter-flavoring chemicals such as diacetyl. All diacetyl concentrations above detectable limits were corrected for the effects of absolute humidity and days to sample extraction.

Results. Ventilation and isolation of the production process resulted in one to three orders of magnitude reductions in diacetyl air concentrations in different areas of the plant. Workers with past high exposures had stable chest symptoms over time; nasal, eye, and skin irritation symptoms declined. New workers had lower symptom prevalences and higher lung function than workers with past high exposures, and they did not worsen over time. In workers who had at least three spirometry tests, those with past high exposures were more likely to experience rapid declines in lung function than new workers.

Conclusions. Implemented controls lowered exposures to butter-flavoring chemicals and decreased lung disease risk for much of the plant workforce. Some workers with continuing potential for intermittent, short-term peak and measurable time-weighted exposures remain at risk and should use respiratory protection and have regularly scheduled spirometry to detect rapid lung function declines that may be work-related. Close follow-up of such workers is likely to yield additional information on risks due to peak and time-weighted exposure levels.

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In May 2000, public health authorities were informed of a cluster of severe cases of bronchiolitis obliterans among former mixers and packaging line workers of a microwave popcorn plant (index plant).¹ A cross-sectional medical and environmental survey performed at the index plant by the National Institute for Occupational Safety and Health (NIOSH) in November 2000 linked this outbreak to inhalation exposure to butter flavorings used in the production process.² The finding of excess airways obstruction among current workers included a striking excess among quality control (QC) workers who performed microwave popping of approximately 100 bags of product per worker per work shift. (Five of six workers had airways obstruction.) Animal exposure studies demonstrated the severe respiratory epithelial toxicity of diacetyl, the chemical in butter flavorings that is primarily responsible for imparting butter flavor.³⁻⁵

Given the severe nature of the disease and its potential rapid onset and progression,^{6,7} it was important to quickly implement exposure controls, assess their effectiveness at lowering exposures, and determine whether workers were protected at the lower exposure levels achieved. After plant management began implementing recommended controls, NIOSH investigators conducted seven follow-up cross-sectional medical and environmental surveys and provided additional recommendations based on analyses of the survey data and what the investigators were learning from evaluations at other microwave popcorn plants.⁸

In this article, we present the results and limitations of our studies of intervention effectiveness at the index plant based on the surveys performed every four to six months from November 2000 through August 2003.

METHODS

Environmental surveys

We measured full-shift time-weighted average (TWA) diacetyl air concentrations obtained with area and personal sampling using NIOSH Method 2557.⁹ Relative humidity and temperature were recorded daily in different areas of the plant using an electronic psychrometer. In 2006, NIOSH investigators suspected that Method 2557 underestimated diacetyl concentration in proportion to increasing absolute humidity and days to sample extraction. From 2007 to 2009, NIOSH and Occupational Safety and Health Administration investigators conducted a series of laboratory chamber exposure studies, the results of which were used to derive a procedure to correct diacetyl air concentrations measured with Method 2557.¹⁰ This procedure was used to correct all diacetyl concentra-

tions above detectable limits, including the laboratory values between the limit of detection (LOD) and the limit of quantification. For statistical analyses, diacetyl concentrations that were below detectable limits were assigned a value of one-half of the uncorrected LOD in air. A detailed summary of all of the substances measured in the air of the plant during the environmental surveys, the sampling methods used, the uncorrected diacetyl concentrations, and environmental results can be found in the NIOSH Health Hazard Evaluation final report.⁷

Medical surveys

After obtaining written informed consent approved by NIOSH's Human Subjects Review Board, NIOSH interviewers administered a standardized questionnaire to collect information on symptoms, medical diagnoses, smoking history, work history, and work-related exposures. NIOSH technicians administered spirometry tests to participating workers using a dry rolling-seal spirometer interfaced to a personal computer and following American Thoracic Society guidelines.¹¹ Spirometry results were compared with standard reference values.¹² After each survey, we mailed participants letters providing individual test results and interpretations. We recommended medical follow-up, flavoring exposure limitation, and smoking cessation (if appropriate) to individuals with abnormal results and/or evidence of rapid declines in lung function. Additional details on the methods for the medical surveys can be found in the NIOSH Health Hazard Evaluation final report.⁷

Statistical analyses

We analyzed participants' data according to whether or not they started work at the plant prior to the first NIOSH cross-sectional survey in November 2000 (i.e., before implementation of exposure controls). Group 1 participants included those who started work prior to November 4, 2000 (the last day of the first NIOSH survey). Group 2 participants were those who started work on or after November 4, 2000. Within each of these groups, we further analyzed health status according to history of work in mixing, QC, or maintenance because workers in these jobs, unlike those in packaging line jobs, had potential for intermittent peak exposures.

We compared health outcomes over time within each group and between groups. We used McNemar's test to identify statistically significant differences between prevalences from the first and last surveys. We used Chi-square and Student's t-tests to compare health outcomes data from initial surveys in the two groups. Probability values of $p \leq 0.05$ were considered unlikely

to be due to chance. To assess the occurrence of abnormally rapid declines in lung function by work area in each group, we identified survey participants who experienced a decline in a forced expiratory volume in one second (FEV₁) value of >300 milliliters (ml) and/or 10% from the first (baseline) spirometry test to last spirometry test.¹³ For this analysis, we excluded participants with fewer than three interpretable spirometry tests, as interpretation of change over time based on only two tests is less reliable. All analyses were generated using SAS[®] version 9.1.¹⁴

RESULTS

Interventions

Several controls were implemented to decrease air concentrations of flavoring chemicals in the mixing room, the main source of air contaminants in the plant. The Figure lists the industrial hygiene exposure control interventions by date of implementation. A respiratory protection program for mixing room workers was initiated at the time of the November 2000 NIOSH survey to minimize their exposures while engineering

Figure. Dates of NIOSH industrial hygiene surveys and exposure control interventions in a microwave popcorn plant in Missouri, 2000–2003

Date	Event
November 11–18, 2000	NIOSH industrial hygiene survey NIOSH staff conduct respiratory protection training and provide mixers with half-face mask respirators with organic vapor cartridges and particulate filters
January 17–19, 2001	NIOSH engineering control technology survey
February 2001	Exhaust fan installed in mixing room Heated liquid-flavoring tanks vented to exhaust fan
March 2001	Pump installed for closed transfer of flavorings between holding and mixing tanks
April 2–5, 2001	NIOSH industrial hygiene follow-up survey
May 2001	Local exhaust ventilation installed for two of seven oil tanks on mezzanine (but initially vented into packaging line area air)
June 2001	Flavoring storage cabinets completed for storing bulk flavorings
July 2001	Temperature control installed on one of two flavoring tanks
August 2001	Tempered outside supply air intake system completed, providing replacement air for microwave popcorn production areas
September 4–8, 2001	NIOSH industrial hygiene follow-up survey
September 2001	Exhaust fan installed in QC laboratory Fresh air intake installed in QC laboratory Completion of local exhaust ventilation to the outdoors for all mezzanine oil tanks
November 2001	Flavoring transfer pump installed for five-gallon containers Air lock installed outside of mixing room Mixers begin use of powered air-purifying respirators with organic vapor cartridges and particulate filters
November 6–8, 2001	NIOSH industrial hygiene follow-up survey
March 18–21, 2002	NIOSH industrial hygiene follow-up survey
August 2002	Mixers begin use of supplied-air respirators in mixing room and mezzanine Microwave ovens and testing counter in QC laboratory enclosed with plastic curtain
August 11–16, 2002	NIOSH industrial hygiene follow-up survey
September 2002	Started using new mixing room (ventilation incomplete) Discontinued use of one paste butter flavoring
October 2002	New mixing room wall exhaust fan operational
January 27–31, 2003	NIOSH industrial hygiene follow-up survey
March 2003	Enclosure of tanks on mezzanine completed
April 2003	Air-handler functional on mezzanine New exhaust fan operational in QC laboratory (in new “popping room”) Two additional exhaust fans operational (for mezzanine and mixing room)
May 2003	Microwave ovens moved into isolated popping room in QC laboratory
July 14–18, 2003	NIOSH industrial hygiene follow-up survey

NIOSH = National Institute for Occupational Safety and Health

QC = quality control

controls were being implemented. An exhaust fan was installed in an outer wall of the mixing room to move contaminated air from this room to the outdoors and maintain this room under negative air pressure relative to the rest of the plant. An air lock was installed at the entrance to the mixing room to further isolate the room from the rest of the plant. Local exhaust ventilation of the air space (headspace) above the contents of the heated flavoring tanks and the mixing tank (where flavorings are mixed into heated soybean oil) was accomplished via ducts connecting the tank lids to the wall exhaust fan. A pump was installed to facilitate closed transfer of heated butter flavorings from the flavor-holding tanks into the mixing tank (Photos 1 through 7). (Prior to this intervention, workers used open five-gallon buckets to manually transfer the heated butter flavorings.) The temperatures of the heated tanks were lowered to decrease evaporation of butter-flavoring chemicals into plant air.

Additional general dilution ventilation was implemented in the microwave popcorn packaging line area. Local exhaust ventilation was implemented for seven heated holding tanks (located on a mezzanine above the packaging lines) that contained soybean oil and butter-flavoring mixtures (transferred via pipes from the mixing room). Eventually, the entire mezzanine

was walled off from the packaging line area (Photos 8 and 9).

Additional general dilution ventilation was also implemented in the QC laboratory, where workers repeatedly popped product in five microwave ovens. Eventually, all microwave ovens were moved into a separate “popping room” adjacent to the QC laboratory with additional exhaust ventilation (Photos 10 and 11).

Effects of engineering controls on diacetyl air concentrations

As exposure controls were implemented, mean TWA diacetyl air concentrations for mixers, machine operators on the microwave popcorn packaging lines, and the QC laboratory workers decreased over time (Table 1). After implementation of exposure controls in the mixing room in 2001, the mean TWA diacetyl air concentration decreased from 57.2 parts per million (ppm) in November 2000 to 2.24 ppm in November 2001. After the company began using a new mixing room in September 2002, the mean TWA diacetyl air concentration in the mixing room was 0.310 ppm in January 2003 and 2.88 ppm in July 2003.

With the additional ventilation in the packaging line area and the isolation of the mixing room, the mean TWA diacetyl air concentration for machine operators on the microwave popcorn packaging lines declined from 2.76 ppm in November 2000 to 0.426 ppm in November 2001. After implementation of the new mixing room in September and October 2002, the mean TWA diacetyl air concentration for machine operators was below quantifiable or detectable levels in July 2003. Similar diacetyl exposure reductions were seen for microwave popcorn packaging line workers in other job categories (e.g., packers and stackers).

After implementation of additional general dilution ventilation in



Photo 1: The original entrance to the mixing room was open to the packaging line area. Courtesy of the National Institute for Occupational Safety and Health.



Photo 2: Mixing and flavor-holding tanks before implementation of controls. Note the five-gallon buckets used for open transfer of flavorings, and evidence of spills on outside of the mixing tank. Courtesy of the National Institute for Occupational Safety and Health.



Photo 3: Mixer near open mixing tank prior to implementation of respiratory protection program. Courtesy of the National Institute for Occupational Safety and Health.



Photo 4: Mixing room after implementation of exposure controls shows exhaust fan on wall and local exhaust ventilation hoses on tanks. Courtesy of the National Institute for Occupational Safety and Health.

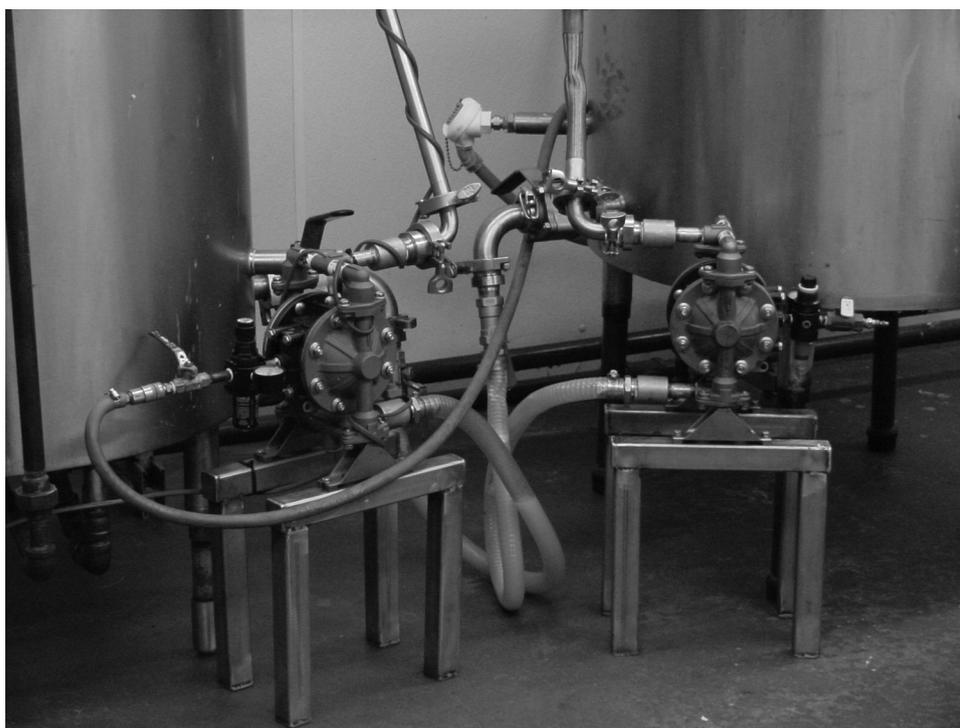


Photo 5: Device for closed transfer of heated butter flavorings. Courtesy of the National Institute for Occupational Safety and Health.



Photo 6: Closed door to mixing room for exposure control. Courtesy of the National Institute for Occupational Safety and Health.



Photo 7: Mixer using supplied-air respirator while manually adding powdered butter flavoring to heated soybean oil in the open mixing tank. Courtesy of the National Institute for Occupational Safety and Health.



Photo 8: Microwave popcorn packaging line area before implementation of exposure controls. Note heated holding tanks for the oil and flavoring mixture located on a mezzanine above the packaging lines. Courtesy of the National Institute for Occupational Safety and Health.



Photo 9: Mezzanine tank area walled off from the rest of the packaging line area. Courtesy of the National Institute for Occupational Safety and Health.



Photo 10: Workers in quality control laboratory before implementation of exposure controls. Courtesy of the National Institute for Occupational Safety and Health.



Photo 11: Microwave ovens in new “popping room” with additional exhaust ventilation. Courtesy of the National Institute for Occupational Safety and Health.

Table 1. Diacetyl air concentrations in ppm corrected for absolute humidity and days to extraction (area and personal measurements combined) by job category and survey date, in a microwave popcorn plant in Missouri, 2000–2003

Survey date	Corrected time-weighted average (in ppm)											
	Mixers			Packaging line machine operators			Quality control laboratory workers					
	N	Mean	Range	N	Mean	Range	N	Mean	Range			
November 2000	10	57.2	5.43–147	9	2.76	0.479–8.19	3	0.823	0.451–1.47			
January 2001	4	36.1	4.92–109	6	2.13 ^a	0.291 ^a –4.61	2	1.92 ^a	0.300 ^a –3.53			
April 2001	9	2.24 ^a	0.691 ^a –4.38	9	0.711 ^a	0.249 ^a –1.66	5	0.827	0.281–1.27			
September 2001	5	1.73 ^{a,b}	LOD ^b –3.51	9	0.143 ^b	LOD ^b –1.23	3	LOD ^b	All LOD ^b			
November 2001	8	2.24	0.228–6.80	9	0.426	0.146–0.748	8	0.401	0.083–0.893			
March 2002	4	4.56	2.40–7.31	5	0.734	0.459–1.03	4	0.482	0.364–0.698			
August 2002	6	6.22	0.762–16.8	7	0.513 ^a	0.085 ^a –1.57	5	0.146 ^{a,b}	LOD ^b –0.519			
January 2003	12	0.310 ^a	0.006 ^a –1.25	6	0.004 ^{a,b}	LOD ^b –0.007 ^a	5	0.107 ^a	0.015 ^a –0.468			
July 2003	8	2.88 ^{a,b}	LOD ^b –12.6	8	LOD ^b	All LOD ^b	10	LOD ^b	All LOD ^b			

^aDesignates those diacetyl ranges or means with concentrations below quantifiable limits and provides the estimated, corrected diacetyl concentration for each mean or range.

^bLOD designates diacetyl ranges or arithmetic means with concentrations below detectable limits. LOD concentrations could not be corrected for the effects of absolute humidity and days to extraction using the National Institute for Occupational Safety and Health correction equation and, for statistical purposes, a value of one-half of the uncorrected LOD in air was assigned.

ppm = parts per million

LOD = limit of detection

the QC laboratory in September 2001, the mean TWA diacetyl air concentration declined from 0.823 ppm in November 2000 to 0.401 ppm in November 2001. With the additional ventilation and enclosure controls added by July 2003, all diacetyl concentrations in the QC laboratory were below detectable limits.

Follow-up medical surveys

Out of a total of 373 current workers who participated in one or more NIOSH surveys, 146 started work at the plant prior to November 4, 2000 (Group 1), and 227 started work on or after this date (Group 2). Group 2 was younger on average, had higher proportions of male and nonwhite workers, and had shorter employment durations (Table 2). The total workforce at the plant varied from survey to survey, ranging from 135 to 165 workers. Participation at each survey ranged from 71% to 91%. Participation in more than one survey was much greater for Group 1 (101 of 146 participants, 69%) than for Group 2 (86 of 227 participants, 38%), as turnover among new workers was high (data not shown).

Among Group 1 workers who participated in one of the last two surveys as well as in one or more previous surveys, those who worked in the QC laboratory or in maintenance, or had ever worked as mixers of oil and flavorings, had initial prevalences of trouble breathing and shortness of breath on exertion that were similar to those of microwave popcorn packaging line workers (range for both: 46.3%–54.5%). Prevalences of reported eye, nose, or throat irritation were similar (68.3% vs. 63.6%), but the prevalence of usual cough was higher among the ever mixer, maintenance, and QC worker subgroup than among packaging line

workers (47.8% vs. 36.6%). Both subgroups had a high prevalence of airways obstruction on spirometry (30.4% in the mixer, maintenance, and QC worker subgroup and 20.0% among packaging line workers) and a low mean percent predicted FEV₁ (87.0% in packaging line workers vs. 85.8% in the mixer, maintenance, and QC worker subgroup). The only statistically significant change in symptom prevalence in either subgroup over time, from first to last survey, was a decline in reported eye, nose, or throat irritation. There were no statistically significant changes in the prevalence of airways obstruction or in mean percent predicted FEV₁ over time in either subgroup, nor in the difference in mean annualized change in FEV₁ between the subgroups (Table 3).

Most Group 2 participants who took part in more than one NIOSH survey worked in microwave popcorn packaging line jobs; only six worked in the QC laboratory, in maintenance, or as ever mixers. For packaging line workers, symptom prevalence based on data from each participant's first survey ranged from 13.7% for trouble breathing to 32.9% for shortness of breath on exertion; the prevalence of airways obstruction was low (4.1%) (Table 4). Compared with packaging line workers in Group 1 (Table 3), these prevalences were significantly lower, and mean percent predicted FEV₁ was significantly higher. Among the Group 2 mixer, maintenance, and QC workers, 66.7% (four of six participants) reported usual cough on their first survey (Table 4). The prevalence of other chest symptoms; eye, nose, or throat irritation; and airways obstruction was 33.3% in this group. Based on last survey data, the prevalence of eye, nose, or throat irritation increased to 66.7% and the prevalence of airways obstruction

Table 2. Characteristics of NIOSH medical survey participants hired before or after November 4, 2000 (the last day of the first NIOSH medical survey), at a microwave popcorn plant in Missouri, 2000–2003

Characteristic	Group 1 ^a	Group 2 ^a	P-value
Number of participants	146	227	
Age (in years)			
Mean	36.5	28.7	<0.0001
Median	34.5	25.0	
Range	18.0–67.0	18.0–63.0	
Male [N (percent)]	70 (48.0)	131 (57.7)	0.07
White [N (percent)]	132 (90.4)	160 (70.5)	<0.0001
Smoking status [N (percent)]			0.08
Current	62 (42.5)	123 (54.2)	
Former	20 (13.7)	22 (9.7)	
Never	64 (43.8)	82 (36.1)	
Length of employment (in months) at time of last survey [mean]	72.3	6.2	<0.0001

^aGroup 1 = workers hired before November 4, 2000; Group 2 = workers hired on or after November 4, 2000

NIOSH = National Institute for Occupational Safety and Health

Table 3. Health characteristics over time for Group 1 microwave popcorn production workers at a microwave popcorn plant in Missouri, 2000–2003

Health characteristics	Packaging line workers (n=41 ^a)		Mixers, maintenance, and quality control workers (n=23 ^a)	
	First survey	Last survey	First survey	Last survey
Usual cough ^b [N (percent)]	15 (36.6)	17 (41.5)	11 (47.8)	5 (21.7)
Trouble breathing ^c [N (percent)]	19 (46.3)	15 (36.6)	12 (52.2)	7 (30.4)
Shortness of breath on exertion ^d [N (percent)]	20 ^e (54.1)	23 (56.1)	12 ^f (54.5)	10 (43.5)
Work exposure irritating to eyes, nose, or throat ^g [N (percent)]	28 (68.3)	12 ^h (33.3)	14 ⁱ (63.6)	7 ⁱ (33.3)
Obstruction on spirometry [N (percent)]	8 ^j (20.0)	6 ^j (15.0)	7 (30.4)	7 (30.4)
Mean percent predicted FEV ₁	87.0 ^k	85.7 ^k	85.8	83.4
Mean annualized change in FEV ₁ (≥ 2 tests; ml/year)	NA	-43.5 ^k	NA	-71.0
Mean annualized change in FEV ₁ (≥ 3 tests; ml/year)	NA	-44.6 ^k	NA	-58.7 ^k

^aTotal number of survey participants in subgroup

^bThe questionnaire asked, "Do you usually have a cough?" (first survey and follow-up surveys).

^cThe questionnaire asked, "During the last 12 months, have you had any trouble with your breathing?" (first survey) and "Since the last time we saw you, have you had any trouble with your breathing?" (follow-up surveys).

^dThe questionnaire asked, "Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?" (first survey and follow-up surveys).

^eFour of 41 survey participants in the subgroup did not answer the question.

^fOne of 23 survey participants in the subgroup did not answer the question.

^gThe questionnaire asked, "Is there an exposure in your work environment that you find irritating to your eyes, nose, or throat?" (first survey and follow-up surveys).

^hFive of 41 survey participants in the subgroup did not answer the question.

ⁱTwo of 23 survey participants in the subgroup did not answer the question.

^jOne of 41 survey participants in the subgroup did not have at least two interpretable spirometry tests.

^kTwo of 41 survey participants in the subgroup did not have at least three interpretable spirometry tests.

^lOne of 23 survey participants in the subgroup did not have at least three interpretable spirometry tests.

FEV₁ = forced expiratory volume in one second

ml = milliliter

NA = not applicable

decreased to 16.7% (one of six participants). There were no statistically significant changes in the prevalence of symptoms and airways obstruction or in mean percent predicted FEV₁ from first to last survey in either of the Group 2 subgroups.

Of the 87 Group 1 participants who participated in at least three of the medical surveys, 19 (22%) had FEV₁ declines >300 ml and/or 10% from their first to last spirometry test. Of the 40 Group 2 participants who participated in at least three surveys, three (8%) had FEV₁ declines >300 ml and/or 10% from their first to last spirometry test (Table 5).

Nine workers who worked as mixers for at least one month after the November 2000 survey participated in at least three of the medical surveys. Four of these nine workers, all from Group 1, had excessive FEV₁ declines. One mixer experienced an extreme decline in lung function during the eight NIOSH surveys. (That mixer's FEV₁ declined 1,300 ml during nine

months; after stopping work as a mixer, it continued to fall, resulting in a total decline of 2,800 ml in 2.75 years, representing a decline from 96% predicted to 39% predicted.) The four workers with excessive FEV₁ declines averaged 34 months of work as mixers (range: 7–67 months) compared with 10 months (range: 5–13 months) in the five mixers without excessive FEV₁ declines.

Of the nine workers who worked in the QC laboratory at some point after the November 2000 survey and who participated in three or more surveys, seven had stable lung function over time. Two workers, both from Group 1, had excessive FEV₁ declines.

DISCUSSION

The implementation of exposure controls at the index plant had a substantial effect on air concentrations of flavoring chemicals. Compared with November 2000,

mean TWA diacetyl air concentrations measured in November 2001 were approximately 96% lower in the mixing room, 85% lower in the microwave popcorn packaging line area, and 51% lower in the QC laboratory. After the implementation of a new, more isolated mixing room in the fall of 2002 and enclosure of the mezzanine area in March 2003, mean TWA diacetyl air concentrations in the microwave popcorn packaging line area further declined below detectable limits in July 2003. With the microwave oven relocation and ventilation changes implemented in the QC laboratory by May 2003, diacetyl concentrations were also reduced below detectable levels in this area.

In addition to the engineering controls described previously, mixers began using respiratory protection in November 2000, including supplied-air respirators in August 2002, further reducing their diacetyl exposures. Analyses of data from follow-up medical surveys revealed evidence that the workforce was at lower risk for lung disease after exposures were controlled. Prevalences of chest symptoms and abnormal lung

function in workers with past high exposures (Group 1) remained mostly unchanged over time. This is to be expected with an irreversible lung disease process. In contrast, the prevalence of mucous membrane irritant symptoms declined following exposure control. The limited follow-up data on new workers (Group 2) showed that packaging line workers had lower symptom prevalences and better lung function than their Group 1 counterparts on their initial medical surveys and did not appear to worsen over time. Additionally, among 27 Group 1 participants who participated in all eight medical surveys, annualized declines in FEV₁ improved from 144 ml per year to 40 ml per year to 22 ml per year, the last being consistent with normal aging-related lung function decline.¹⁵

The TWA air concentration of diacetyl is not the only exposure metric that may be pertinent to lung disease risk in workers exposed to butter-flavoring chemicals. The former and current workers at highest risk in this plant worked in the mixing room and in the QC laboratory. While mixers had the highest mean TWA

Table 4. Health characteristics over time for Group 2 microwave popcorn production workers at a microwave popcorn plant in Missouri, 2000–2003

Health characteristic	Packaging line workers (n=73 ^a)		Mixers, maintenance, and quality control workers (n=6 ^a)	
	First survey	Last survey	First survey	Last survey
Usual cough ^b [N (percent)]	14 (19.2)	17 (23.3)	4 (66.7)	4 (66.7)
Trouble breathing ^c [N (percent)]	10 (13.7)	8 (11.0)	2 (33.3)	2 (33.3)
Shortness of breath on exertion ^d [N (percent)]	24 (32.9)	19 (26.0)	2 (33.3)	1 (16.7)
Work exposure irritating to eyes, nose, or throat ^e [N (percent)]	18 (24.7)	19 ^f (26.4)	2 (33.3)	4 (66.7)
Obstruction on spirometry [N (percent)]	3 (4.1)	4 ^g (5.6)	2 (33.3)	1 (16.7)
Mean percent predicted FEV ₁	97.0	95.8 ^g	94.9	94.8
Mean annualized change in FEV ₁ (≥2 tests; ml/year)	NA	-83.0 ^g	NA	-162.7
Mean annualized change in FEV ₁ (≥3 tests; ml/year)	NA	-21.3 ^h	NA	17.0 ⁱ

^aTotal number of survey participants in subgroup

^bThe questionnaire asked, "Do you usually have a cough?" (first survey and follow-up surveys).

^cThe questionnaire asked, "During the last 12 months, have you had any trouble with your breathing?" (first survey) and "Since the last time we saw you, have you had any trouble with your breathing?" (follow-up surveys).

^dThe questionnaire asked, "Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?" (first survey and follow-up surveys).

^eThe questionnaire asked, "Is there an exposure in your work environment that you find irritating to your eyes, nose, or throat?" (first survey and follow-up surveys).

^fOne of 73 survey participants in the subgroup did not answer the question.

^gOne of 73 survey participants in the subgroup did not have at least two interpretable spirometry tests.

^hOnly 31 of 73 survey participants in the subgroup had at least three interpretable spirometry tests.

ⁱTwo of six survey participants in the subgroup did not have at least three interpretable spirometry tests.

FEV₁ = forced expiratory volume in one second

ml = milliliter

NA = not applicable

diacetyl exposures (57.2 ppm), QC laboratory workers' exposures were approximately two orders of magnitude lower (0.823 ppm) in November 2000. At three other microwave popcorn plants where mixers had developed bronchiolitis obliterans, mean humidity-corrected TWA diacetyl air concentrations from NIOSH air sampling in the mixing area were much lower, ranging from 0.759 ppm to 1.54 ppm. What these high-risk areas have in common is the potential for repeated, short-term, intense peak exposures to butter-flavoring chemicals (up to 13 ppm diacetyl when a QC laboratory worker opens a just-popped bag; as high as 1,200 ppm if a worker lifts the lid to look into a tank of heated butter flavoring;⁷ and up to 80 ppm when a mixer pours liquid butter flavorings into a mixing tank).⁸

Because only one Group 2 participant had worked in the QC laboratory, data were insufficient to assess ongoing risk to workers in this area. QC laboratory workers with lower mean exposures at other microwave popcorn plants appeared to be at much lower risk for lung disease.⁸ While none of the four Group 2 workers who had worked in the mixing room and participated in at least three medical surveys had excessive FEV₁ declines, three of them had worked fewer than 12 months in mixing and the fourth had worked only 13 months in mixing. In analyses of medical survey data from NIOSH surveys at six microwave popcorn plants (including the index plant), we found that mixers with >12 months work experience had significantly lower lung function than mixers with ≤12 months work experience.⁸

Although mandatory respiratory protection can help limit ongoing risk to workers in the mixing room, workers may still experience hazardous exposures due to improper respirator use or fit, respirator malfunction, or failure to wear the respirator at all times when they are exposed. We recommend that the mixing operation be engineered to a closed process. Baseline spirometry and regularly scheduled follow-up tests for mixing room, QC laboratory, and maintenance workers are necessary to detect abnormalities or rapid declines in lung function that might be due to work-related exposures. Additional interventions to limit exposures in these areas may be necessary if excessive lung function declines are identified.

Limitations

We were limited in assessing ongoing lung disease risk as interventions lowered exposures because the company did not implement spirometry testing for new workers until June 2003. Thus, new workers had often been in the plant for weeks or months prior to their first NIOSH survey. If they had abnormal lung function

on their first NIOSH test, there was no way to know whether or not the abnormality predated their start of work in the plant. Even with normal lung function on their first NIOSH test, there was no way to know if a worker, who may have had above-normal lung function before working at the plant, had experienced a rapid decline in lung function due to hazardous exposure at the plant. Another limitation was the short duration of follow-up for most new workers due to rapid turnover of the workforce.

Intervention by substitution of safer butter flavorings has been a difficult issue. Flavorings are complex mixtures of many volatile organic compounds (VOCs) that are formulated as liquids, pastes, and powders. Flavoring chemicals are usually assessed for safety to consume in small quantities in food, but few have been evaluated for safety to inhale at the concentrations to which some workers are exposed. Diacetyl is one butter-flavoring chemical with known potential to cause airway injury,^{4,5} but other highly irritating butter-flavoring chemicals may contribute to the overall toxic effects of butter flavorings. A flavoring that contains less diacetyl may or may not be safer depending on the composition of the rest of the mixture. Another diacetyl flavor substitute, 2,3-pentanedione, can cause respiratory epithelial necrosis similar to diacetyl, and other alpha-diketones may have similar toxicity.¹⁶ Additionally, some powdered flavorings are encapsulated to minimize release of VOCs during incorporation into food in the production process. While these powders may pose less risk to workers from VOC emissions, airborne respirable particulate can be generated when workers handle them during production.¹⁷ The potential risk to workers from inhalation of such powders is currently unknown, but the encapsulated flavorings

Table 5. Prevalences of FEV₁ declines of 300 ml and/or 10% from first to last test in workers who had three or more spirometry tests at a microwave popcorn plant in Missouri, 2000–2003

Workers	Group 1 N (percent)	Group 2 N (percent)
All workers ^a	19/87 (22)	3/40 (8)
Worked as mixer after November 2000	4/5 (80)	0/4 (0)
Worked in quality control laboratory after November 2000	2/8 (25)	0/1 (0)

^ap=0.07

FEV₁ = forced expiratory volume in one second

ml = milliliter

are released upon contact with moisture, which may happen on mucosal surfaces of the respiratory tract.

CONCLUSIONS

In a plant where workers with uncontrolled exposures to butter-flavoring chemicals in microwave popcorn production had rapidly developed severe, irreversible lung disease, increased ventilation and isolation of flavor sources in mixing, holding tanks, and microwave popping decreased the risk for most workers. However, some workers with continuing potential for intermittent peak exposures and measurable TWA exposures remain at risk; these worker subgroups should have respiratory protection and medical surveillance with regularly scheduled spirometry to detect rapid declines in lung function that may be work-related, possibly due to failure or inadequacy of implemented control strategies. The success of this approach for protecting workers depends on a good understanding of the nature of the risk by management, workers, health and safety professionals, physicians, and public health authorities, as well as a firm commitment by management to regularly evaluate and maintain the effectiveness of exposure controls and the quality of serial spirometry in medical surveillance.

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