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Flavoring exposure in food manufacturing

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Abstract

Flavorings are substances that alter or enhance the taste of food. Workers in the food-manufacturing industry, where flavorings are added to many products, may be exposed to any number of flavoring compounds. Although thousands of flavoring substances are in use, little is known about most of these in terms of worker health effects, and few have occupational exposure guidelines. Exposure assessment surveys were conducted at nine food production facilities and one flavor manufacturer where a total of 105 area and 74 personal samples were collected for 13 flavoring compounds including five ketones, five aldehydes, and three acids. The majority of the samples were below the limit of detection (LOD) for most compounds. Diacetyl had eight area and four personal samples above the LOD, whereas 2,3-pentanedione had three area samples above the LOD. The detectable values ranged from 25–3124 ppb and 15–172 ppb for diacetyl and 2,3-pentanedione respectively. These values exceed the proposed National Institute for Occupational Safety and Health (NIOSH) recommended exposure limit for these compounds. The aldehydes had the most detectable samples, with each of them having >50% of the samples above the LOD. Acetaldehyde had all but two samples above the LOD, however, these samples were below the OSHA PEL. It appears that in the food-manufacturing facilities surveyed here, exposure to the ketones occurs infrequently, however levels above the proposed NIOSH REL were found. Conversely, aldehyde exposure appears to be ubiquitous.

Keywords

Exposure; flavorings; diacetyl; 2,3-pentanedione; food manufacturing

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

INTRODUCTION

Flavorings are substances that alter or enhance the taste of food. They are composed of various natural and manmade compounds and may consist of a single chemical, but more often they are complex mixtures of compounds. Workers in the flavoring production industry where flavorings are made, in the flavored food-manufacturing industry where flavorings are added to food products, and in the food industry where flavored foods are used, all may be exposed to any number of flavoring substances in the form of solids, liquids, vapors, or liquid or vapor encapsulated within a particulate. Although thousands of flavoring substances are in use, little is known about most of these in terms of worker health effects, and few have occupational exposure guidelines.

Diacetyl is one of the main components in flavoring that imparts a buttery taste and it has been identified as a prominent volatile organic compound (VOC) in air samples from microwave popcorn plants and flavoring manufacturing plants.[1–8] In flavor formulations, diacetyl and recently 2,3-pentanedione are typically found as components in liquid solutions, but can also be added to powders.

Occurrences of bronchiolitis obliterans (BO) were observed in the microwave popcorn industry in 2000 when eight workers were diagnosed with the disease after exposure to vapors from artificial butter flavoring substances including diacetyl.[1,9] Diacetyl is also used as a natural and artificial flavoring ingredient and aroma carrier in bakery products, dairy products, snack foods, and more. Initial research concerning occupational exposure to diacetyl has focused on workers who directly produce flavorings or use them in the microwave popcorn industry, however employment figures for the food production industry suggest that some other workers have potential exposure to diacetyl. For example, respiratory issues have been anecdotally reported for cheese production (Wisconsin), yogurt production (Ohio), and potato chip manufacturing.[10] Two cases of BO have been identified in workers employed in a small coffee-processing facility.[11] Although the microwave popcorn industry has received the most attention both in the media and in the scientific community, the first occurrences of BO in food production may have been observed in 1985 at a facility, which produced various products for the baking industry.[12]

Recently, facilities have begun producing and working with flavors without diacetyl, instead using alpha-diketone substitutes such as 2,3-pentanedione, 2,3-hexanedione, and 2,3-heptane-dione.[13,14] Reports on the toxicity of 2,3-pentanedione were first published in abstract form in 2010.[15,16] Subsequent animal inhalation studies by the National Institute for Occupational Safety and Health (NIOSH) and the National Institute of Environmental Health Sciences researchers[17] indicated similarities in pulmonary effects between 2,3-pentanedione and diacetyl exposures. Preliminary data from yet another study suggests that exposures to either 2,3-pentanedione or diacetyl can cause airway fibrosis in rats.[18] As a group, these publications illustrate that the toxicological effects of diacetyl may be shared with alpha-diketones that are close structural analogs such as 2,3-pentanedione, 2,3-hexanedione, and 2,3-heptanedione. Diacetyl substitutes should not be assumed to be safe until toxicology studies are completed.

In 2010, California promulgated a regulation for occupational exposure to food flavorings containing diacetyl that requires installation of exposure controls to reduce exposures to the lowest feasible levels, as well as follow-up by the employer if any concentration of diacetyl, diacetyl trimer, acetoin, 2,3-pentane-dione, 2,3-hexanedione or 2,3-heptanedione is used in a work-place where an employee is diagnosed with a fixed obstructive lung disease. In 2012, the American Conference for Governmental Industrial Hygienists (ACGIH) published a Threshold Limit Value (TLV) of 0.010 ppm with a short-term exposure limit (STEL) of 0.020 ppm for diacetyl.[19] In 2013, NIOSH published its draft recommended exposure limit (REL) for diacetyl and 2,3-pentanedione of 0.005 and 0.0093 ppm, with STELs of 0.025 and 0.031 ppm, respectively.[20]

Other flavor compounds are also of interest from a standpoint of worker health. The Flavor and Extract Manufacturers Association lists 34 substances that are high priorities for consideration as substances that may pose respiratory hazards in flavor-manufacturing workplaces.[21] Nine of these substances, in addition to diacetyl, 2,3-pentanedione, 2,3-hexanedone, and 2,3-heptanedione, were selected for this survey because of their potential for respiratory hazards in the workplace.

The purpose of this study is to characterize exposure to 13 flavoring compounds that are potential respiratory hazards in various food production facilities. To date, little exposure characterization of flavor compounds in food production other than microwave popcorn has been conducted.

METHODS

Food production facilities that use flavorings, or where fermentation takes place, were selected for sampling. After consulting a panel of food production experts, snack food, dairy, cereal and baked goods, wine, and confection production facilities were selected for inclusion in the study. One hundred and fifty-three companies were identified and contacted for participation in the study. Sixteen agreed to participate and surveys were conducted at ten facilities with 43 workers being sampled. The ten companies selected for a survey out of the 16 that agreed to participate were selected after a walkthrough survey and were felt to be the best representation of the food-manufacturing categories in the study. The ten facilities included three confection facilities, two dairy facilities, one bakery, one cereal facility, one snack food facility, one winery and one flavoring manufacturer. The workers were selected on the basis of having tasks associated with processes of interest as identified during the walkthrough survey. The main reasons for nonparticipation were no company response (after four attempts), ineligible (flavorings or fermentation were not part of the food production) or an unwillingness to participate. Of the 153 companies contacted, 12 were ineligible, 49 refused or declined to participate, and 76 could not be reached.

Sample Collection and Analysis

Full shift, time-weighted average (TWA) area and personal samples were collected for processes that involved fermentation, or the use or manufacture of flavorings. Sampling for aldehydes, acids, and ketones took place over 1–3 days, depending on processes and production schedules, at all facilities. Generally, one sample for each class of compound (i.e., aldehyde, acid, ketone) per worker was taken, but occasionally additional samples on subsequent days were taken on the same worker. The number of samples per facility varied and depended on the process of the facility. In places where solid flavoring compounds were used, respirable particulate samples were also collected. Sampling pumps were placed on workers and in places near to where flavorings were added or used in a process or where fermentation was actively occurring. Lastly, bulk samples were collected for various flavors used in the facilities. The analytes, and the sampling and analytical methods used are shown in Table 1 and were used for both area and personal samples and for production, handling, and control processes.

The aldehyde samples were collected using dinitrophenylhydrazine (DNPH)-treated silica tubes at a flow rate of 0.2 liters per minute (l/min). The tubes were changed out approximately every 3 h to avoid overloading and the sample results from all tubes collected during a shift were aggregated over time to obtain a TWA. The samples were analyzed by high performance liquid chromatography (HPLC) using Environmental Protection Agency (EPA) method TO-11a. The ketones samples were collected using two specially dried and cleaned 600-milligram (mg) silica gel tubes in series (an A and a B tube) at a flow rate of 0.05 l/min and were protected from light during sampling and shipping. The two tubes were used to determine whether breakthrough was occurring. As with the aldehyde sampling, both tubes were changed out approximately every 3 h and the sample results aggregated over time for a full shift. The samples were collected and analyzed by gas chromatography with a flame ionization detecter using Occupational Safety and Health Administration (OSHA) method 1013. The acids samples were collected using one 600-mg silica gel tube for the whole shift at a flow rate of 0.2 l/min. The samples were analyzed by HPLC using NIOSH Manual of Analytical Methods (NMAM) 5048. Respirable particulate samples were collected using 37-millimeter (mm) polyvinyl chloride filters attached to a Dorn-Oliver cyclone at a flow rate of 1.7 l/min. The samples were analyzed by gravimetric weighing using NMAM 0600.

Data Analysis

All statistical analyses were performed using SAS 9.3 (SAS Institute, Cary, NC, USA). The data were right skewed so a natural log transformation was applied to normalize the data. One half of the limit of detection (LOD) was the value used for samples that were below the LOD. ANOVA modeling was used to test for differences in the means of the log transformed data in three different categories: process, flavoring, and food. For the data, a Tukey adjusted multiple comparison test in the PROC MIXED procedure was used to simultaneously test for difference of means among the independent variables in each category. Levels with >50% censoring (below the LOD) were excluded from the analyses. The geometric SDs were in some cases large and different from each other, which contravenes the ANOVA assumption of equal variance. Therefore, an analysis was conducted on each category using a nonparametric Kruskal–Wallis test statistic to test differences, and then applying a Bonferroni adjustment. However, the results were similar for both the parametric and nonparametric tests for each category. Given that the Tukey adjustment is generally better than a Bonferroni adjustment, and that there is not an easy way to simultaneously test variables within a category using nonparametric tests, no further nonparametric analysis was conducted and the parametric tests are presented here.

RESULTS

A total of 105 area samples and 74 personal samples were collected from the 10 sites encompassing several food-manufacturing categories. The food categories included baked goods, cereal, chocolate, dairy, flavor manufacture, snack food, and wine. The processes observed can be placed into two broad categories: handling and production. Handling included tasks such as mixing, spraying, loading, packaging, pouring, or weighing when conducted manually. Production process included these tasks when conducted mechanically and also included fermentation, cooking, mechanical pumping, and milling. The flavors that were used and their ketone content can be found in Table 2. In some cases, no flavors were used, and other cases, natural products that included butter, margarine, milk powder, cream, milk chocolate, or chocolate liquor were used.

The majority of the samples for acids and ketones were non-detectable. Only the aldehydes and respirable particulate had >50% detectable samples (Tables 3 and 4). There were no special personal protective equipment (PPE) requirements or engineering controls at any of the facilities visited when handling flavors, with the exception of clothing requirements for food hygiene.

Diacetyl was the most commonly detected ketone for both the area and personal samples. Eight area and four personal samples were above the LOD for diacetyl. All four personal samples and four of the eight area samples were collected at one facility that manufactured flavors using 4% diacetyl in oil. Three of the remaining four area samples above the LOD (Table 1) were collected at a site that manufactured cereal. These samples were collected from an enclosed unventilated room that contained 55 gallon drums of natural butter flavor and natural and artificial maple flavor that were pumped to a closed system. Workers only entered this room occasionally to move the closed system from one drum to another. In a bulk sample analysis, the natural butter flavor contained 4000 ppm of diacetyl. Another detectable diacetyl sample came from a chocolate manufacturer that was collected from the top of the conch tank during the conching process whereby milk chocolate was heated and stirred. No flavors were added during this process. Among the other ketones, 2,3-pentanedione was detected in three area samples only, all in cereal manufacturing; acetoin was detected in seven area samples in cereal and chocolate manufacturing, and three personal samples, all in cereal manufacturing; 2,3-hexanedione was detected in three area and three personal samples, all in cereal manufacturing, and 2,3-heptanedione was detected in three area and one personal sample, all in wine manufacturing. (Tables 5 and 6).

Acetic acid was the most commonly detected acid with 22% of the area samples and 14% of the personal samples being above the LOD (Table 1). Acetic acid was detected during cereal, chocolate, snack food, and wine manufacturing. The remaining acids were detected during cereal manufacturing, with one propionic acid sample being detected during chocolate production (Tables 5 and 6).

Aldehydes were the most commonly detected group of chemicals, with all aldehydes detected in >50% of the samples. Acetaldehyde was detected the most with 99% above the LOD. Respirable particulate was detected in >50% of the samples as well. As >50% of the aldehydes and respirable particulate were above the LOD, these results were further analyzed by food category (Tables 7 and 8), process (control, handling, production) (Table 9), and type of flavoring used (no flavor used, flavor used, natural product that might contain diacetyl, e.g., butter) (Table 10). Generally, baked goods had the highest percent of samples above the LOD and the highest geometric means (GM's) for all aldehydes and respirable particulate. Production process tended to have the highest GM's for respirable particulate and all aldehydes with a couple of exceptions, whereas the use of flavors appears to have resulted in the lowest respirable particulate and aldehyde GM's.

DISCUSSION

Exposure to flavoring compounds in food manufacturing, outside of microwave popcorn production, has been largely unstudied. Exposure to flavor compounds, in particular diacetyl, has been associated with BO in flavor manufacturing and microwave popcorn production. Two cases of BO have been identified in workers who handled flavors in a small coffee-processing facility.[11] However, it would appear in the food production and manufacturing industries surveyed here, little exposure to diacetyl is occurring. Only 8 of 105 area samples and 4 of the 74 personal samples were above the LOD for diacetyl at food-manufacturing facilities. The majority of detectable diacetyl samples came from a flavoring manufacturing facility and those sample results are consistent with other studies at flavor-manufacturing facilities.[6] The other ketones were also non-detectable in a large majority of the area and personal samples. 2,3-pentanedione was only detected in three area samples and no personal samples. However, among the detectable ketone samples, all exceeded the proposed NIOSH REL and ACGIH TLV TWA and STEL for diacetyl, and all but one sample exceeded the NIOSH REL and STEL for 2,3-pentanedione. Therefore, it appears when exposure is occurring, it is occurring at a sufficient level to cause some concern for health effects. Additionally, the diacetyl substitutes 2,3-heptanedione and 2,3-hexanedione were found above the LOD in six (three personal and three area) and four (one personal and three area) samples, respectively.

It is not entirely surprising that diacetyl and 2,3-pentanedione were not detected in the majority of samples. The amounts of liquid flavors used in the food production observed were generally small, with the largest addition being ~1–2 liters. Diacetyl and 2,3-pentanedione were detected in only nine and three bulk flavor samples, respectively, with the detected concentrations of diacetyl and 2,3-pentanedione generally <50 ppm despite a couple of notable exceptions. However, all but one of the detectable diacetyl air samples occurred when neat diacetyl or a flavor-containing diacetyl was being used at the time of sampling. In only one instance was diacetyl detected when a flavor or neat diacetyl was not used, and this process involved heating of milk powder, cocoa butter, and chocolate liquor during milk chocolate production. Similarly, 2,3-pentanedione was detected in air samples only when a flavor that contained 2,3-pentanedione was used. Conversely, there were several instances where diacetyl and 2,3-pentanedione were detected in flavors being used, but not detected in the air samples.

The aldehydes were detected in the majority of samples, with acetaldehyde found in all but two samples collected. In a NIOSH Health Hazard Evaluation[22] of a flavoring manufacturer, acetaldehyde was one of the most commonly used compounds, being used daily. However, in a VOC screen using thermal desorption tubes, acetaldehyde was not detected as a major peak. In a survey of 15 adult inhabitants of Helsinki, acetaldehyde levels found in their workplaces averaged 4700 microgram per cubic meter (μg/m^3).[23] Acetaldehyde occurs widely in nature and is produced in large scale industrially, and is a common contaminant in work-place, indoor, and ambient environments.[24] This may explain why acetaldehyde was so widely detected in our samples. However, acetaldehyde exposure is a concern. Acetaldehyde is classified as a probable human carcinogen (Group B2) by the United States EPA,[25] a potential occupational carcinogen by NIOSH,[26] and possibly carcinogenic to humans (Group 2B)[27] by the International Agency for Research on Cancer. The levels found in this study are well below the OSHA permissible exposure limit of 360 mg/m^3 and the ACGIH-ceiling limit of 45 mg/m^3. These exposure limits, however, are based on irritation and not carcinogenic effects. Further, acetaldehyde could not be ruled out as a possible causal or contributing agent for BO in a study of BO among workers in a diacetyl production facility.[28]

One area where exposure may be of concern is in the use of powders. Solid powdered flavor use ranged from one half pound to hundreds of pounds depending on the batch size. One of the bulk powdered flavor samples had a diacetyl concentration of over 3000 milligram per kilogram (mg/kg). However, to date there is no analytical method available for detecting diacetyl in particulate air samples. The sampling method used to measure diacetyl in the personal and area samples only detects diacetyl in vapor form. As a surrogate for exposure, respirable particulate samples were collected alongside the diacetyl samples when powdered flavors were used. With >50% of the respirable particulate samples above the LOD, and with an average of 357 and 425 μg/m^3 for area and personal samples, respectively, the potential for diacetyl and other ketone exposure exists from these respirable particles. However, sources other than powder flavors may be contributing to the detectable respirable particulate samples found. For example, flour, corn starch, and other non-flavor powders used in food manufacturing could also be contributing to the levels seen.

It is difficult to determine which type of food production studied might have the greatest flavor compound exposure, given the large number of non-detectable samples. It is also difficult to ascertain whether the type of food production was a factor or if the recipes used was the driving factor. Cereal manufacturing had the greatest number of detectable analytes, and both cereal and chocolate had a relatively higher percentage of detectable samples. However, baked goods had either the highest or second highest GM aldehyde and respirable particulate values for both personal and area samples. The differences between food production type were not always significant however. For process type, aldehydes GM's were generally higher during production tasks than handling or control tasks, however, in two cases the control samples were higher for propionaldehyde and benzaldehyde. It is not clear why this may have occurred. Interestingly, the GM's tended to be the lowest when flavorings were used, and highest for either no flavors or natural products. It appears that aldehydes are fairly ubiquitous in food production, and may not necessarily relate to flavoring use.

There are a few limitations to the study. First, it is not clear if company recruitment had an impact on the generalizability or bias of the results. Forty-nine companies declined to participate, and whereas most companies did not give a reason, anecdotal evidence suggest that some reasons were liability concerns and busy operations. Perhaps some of the companies that refused to participate might have had higher exposures. Unfortunately, the reason to not participate and company statistics were not collected from refusing companies, therefore any potential exposure bias cannot be determined. Second, the large number of non-detectable samples and relatively small sample size once broken out by food and flavor category make it difficult to conduct any inferential statistics. Last, although the focus was on food production that had a high potential to use flavors, and the food categories were selected based on expert opinion, there are likely other food production industries that would warrant inclusion in this study.

CONCLUSION

On the days sampled, the majority of exposures to diacetyl, 2,3-pentanedione were below the limit of detection in the facilities surveyed in this study. However, for detectible samples, all were above the proposed NIOSH TWA RELs for diacetyl and 2,3-pentanedione. In addition, all diacetyl samples above the LOD were also above the ACGIH TWA. In facilities where exposures were observed above existing and proposed occupational exposure limits, exposures should be controlled using appropriate engineering controls and PPE, if necessary. This study also illustrated that the diacetyl substitiutes 2,3-heptanedione and 2,3-hexanedione are in use. Conversely, the aldehydes appear to be ubiquitous in food production. Acetaldehyde was detected in nearly every sample, and is classified as a possible human carcinogen.

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References

1. Akpinar-Elci M, Travis WD, Lynch DA, Kreiss K. Bronchiolitis obliterans syndrome in popcorn production plant workers. Eur Respir J. 2004; 24(2):298–302. [PubMed: 15332401]
2. Kanwal, R. Letter of July 2, 2003, from R. Kanwal, Division of Respiratory Disease Studies. National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Department of Health and Human Services, to Frank Morrison, Nebraska Popcorn; Clearwater, NE: 2003.
3. Kanwal, R.; Martin, S. Letter of May 13, 2003, from R. Kanwal and S. Martin. Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Department of Health and Human Services, to Keith Heuermann, B.K. Heuermann Popcorn, Inc; Phillips, NE: 2003.
4. Kanwal R, Kullman G, Piacitelli C, Boylstein R, Sahakian N, Martin S, et al. Evaluation of flavorings-related lung disease risk at six microwave popcorn plants. J Occup Environ Med. 2006; 48(2):149–157. [PubMed: 16474263]

5. NIOSH. Hazard evaluation and technical assistance report: American Pop Corn Company, Sioux City, IA. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health; Cincinnati, OH: 2004.
6. Martyny JW, Van Dyke MV, Arbuckle S, Towle M, Rose CS. Diacetyl exposures in the flavor manufacturing industry. J Occup Environ Hyg. 2008; 5(11):679–688. [PubMed: 18720288]
7. Parmet AJ, Von Essen S. Rapidly progressive, fixed airway obstructive disease in popcorn workers: a new occupational pulmonary illness? J Occup Environ Med. 2002; 44(3):216–218. [PubMed: 11911019]
8. Ashley K, McKernan LT, Burroughs E, Deddens J, Pendergrass S, Streicher RP. Analytical performance criteria. Field evaluation of diacetyl sampling and analytical methods. J Occup Environ Hyg. 2008; 5(11):D111–D116. [PubMed: 18726763]
9. Kreiss K, Kullman GA, Fedan G, Simoes K, Enright EJPL. Clinical bronchiolitis obliterans in workers at a microwave-popcorn plant. N Engl J Med. 2002; 347(5):330–338. [PubMed: 12151470]
10. Alleman T. Case report: bronchiolitis obliterans organizing pneumonia in a spice process technician. J Occup Environ Med. 2002; 44(3):215–216. [PubMed: 11911018]
11. CDC. Obliterative bronchiolitis in workers in a coffee-processing facility - Texas, 2008–2012. MMWR Morb Mortal Wkly Rep. 2013; 62(16):305–307. [PubMed: 23615673]
12. NIOSH. US Department of Health and Human Services, Centers for Disease Control and Prevention. National Insituitute for Occupational Safety and Health; Cincinnati, OH: 1986. Health Hazard Evaluation: International Bakers Services - Indiana; July 1986. HETA 85-171-1710.
13. Day G, LeBouf R, Grote A, Pendergrass S, Cummings K, Kreiss K, et al. Identification and measurement of diacetyl substitutes in dry bakery mix production. J Occup Environ Hyg. 2011; 8(2):93–103. [PubMed: 21253982]
14. Boylstein R. Case study: identification of diacetyl substitutes at a microwave popcorn production plant. J Occup Environ Hyg. 2012; 9:D33–D34. [PubMed: 22233226]
15. Hubbs AF, Moseley AE, Goldsmith WT, Jackson MC, Kashon ML, Battelli LA, et al. Airway epithelial toxicity of the flavoring agent, 2,3-pentanedione. J Soc Toxicol. 2010; 114(S-1):319.
16. Morgan DL, Jokinen MP, Price HC, Bosquet RW, Taylor GJ, Gage N, et al. Inhalation toxicity of acetyl proprionyl in rats and mice Abstract 1492. The Toxicologist. 2010; 114(S-1):316.
17. Morgan DL, Jokinen MP, Price HC, Gwinn WM, Palmer SM, Flake GP. Bronchial and bronchiolar fibrosis in rats exposed to 2,3-pentanedione vapors: implications for bronchiolitis obliterans in humans. Toxicol Pathol. 2012a; 40(3):448–465. [PubMed: 22215510]
18. Morgan DL, Jokinen MP, Johnson CL, Gwinn WM, Price HC, Flake GP. Bronchial fibrosis in rats exposed to 2,3-butanedione and 2,3-pentanedione vapors. Toxicol Sci. 2012b; 126:186.
19. ACGIH. 2012 TLVs and BEIs: threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists; 2012.
20. NIOSH. Criteria for a Recommended Standard, Diacetyl and 2, 3-Pentanedione, National Institute for Occupational Safety and Health Pub # xxxxxx. US Department of Health and Human Services, Centers for Disease Control and Prevention; National Insituitute for Occupational Safety and Health; Cincinnati, OH: 2013.
21. FEMA. Respiratory Health and Safety in the Flavor Manufacturing Workplace. The Flavor and Extract Manufacturers Association of the United States; Washington: 2004.
22. NIOSH. Health Hazard Evaluation: Lung function (Spirometry) testing in employees at a flavorings manufacturing plant – Indiana; June 2011. HETA 2008-0155-3131. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Insituitute for Occupational Safety and Health; Atlanta, GA: 2011.
23. Jurvelin J, Vartiainen M, Jantunen M, Pasanen P. Personal exposure levels and microenvironmental concentrations of formaldehyde and acetaldehyde in the Helsinki metropolitan area, Finland. J Air Waste Manag Assoc. 2001; 51(1):17–24. [PubMed: 11218421]
24. Spengler, JD.; McCarthy, JF.; Samet, JM. Indoor Air Quality Handbook. McGraw-Hill Professional Publishing; New York, NY: 2000.
25. EPA. Health Assessment Document for Acetaldehyde. EPA/600/8-86-015A. US Environmental Protection Agency, Environmental Criteria and Assessment Office, Office of Health and

Environmental Assessment, Office of Research and Development; Research Triangle Park, NC: 1987.

26. NIOSH. NIOSH Pocket Guide to Chemcial Hazards. DHHS (NIOSH) Publication No. 2005-149. US Department of Health and Human Services, Centers for Disease Control and Prevention; National Institute for Occupational Safety and Health; Cincinnati, OH: 2007.
27. IARC. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 71: Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide. World Health Organization; International Agency for Research on Cancer; Lyon, France: 1999.
28. van Rooy FG, Rooyackers JM, Prokop M, Houba R, Smit LA, Heederik DJ. Bronchiolitis obliterans syndrome in chemical workers producing diacetyl for food flavorings. Am J Respir Crit Care Med. 2007; 176(5):498–504. [PubMed: 17541015]

Table 1

Sampling and analytical methods and analytes.

Compound	Analysis method	Media	Analytes	LOD
Aldehydes (µg/sample)	EPA TO-11a	Dinitrophenylhydrazine (DNPH)-treated silica	2-Furaldehyde Acetaldehyde Benzaldehyde Isovaleraldehyde Propionaldehyde	0.03–0.5 0.008–0.4 0.02–0.40 0.02–0.3 0.01–0.1
Acids (µg/sample)	Draft NIOSH NMAM 5048	Silica gel (600 mg)	Acetic Acid Butyric Acid Propionic Acid	4–30 5–20 5–20
Ketones (µg/sample)	OSHA 1013	Silica gel (600 mg)	Diacetyl Acetoin 2,3 pentanedione 2,3-hexanedione 2,3-heptanedione	0.5–1 0.3–2 0.2–1 0.5–1 0.5–1
Bulk sample Ketones (mg/kg)	Bureau Veritas internal method for bulks	N/A	Diacetyl Acetoin 2,3 pentanedione 2,3 hexanedione 2,3-heptanedione	0.2–10 0.4–20 0.2–10 0.2–9 0.3–9
Size selective particulates (µg/sample)	NMAM 0600	37-mm PVC filter	Respirable particulate	40–100

Table 2

Flavors used and their ketone content (mg/kg).

Flavor	Type	Heptanedione	Hexanedione	Pentanedione	Acetoin	Diacetyl
Cheese	P	34	0	0	0	0
Cheese blend	P	54	0	0	57	0
Blueberry cream	P	0	0	0	0	0
Creamer	P	0	0	0	0	0
Vanilla ice cream	P	0	0	0	0	3300
Peach cream	P	0	0	0	0	0
Butter berry	L	0	0	0	0	990
Strawberry juice concentrate	L	0	0	0	0	0
Natural butter	L	0	NA	460	4500	4000
Natural and artificial maple	L	0	0	0	0	0
Strawberry cream	P	0	0	0	0	0
Acid and flavor	L	NA	0	0	0	64
Peppermint double distilled	L	5.7	5	0	3.3	11
Natural blackberry	L	0	1.4	0.57	0	0.81
Natural rasberry	L	0	0	0	0	0
Natural lemon	L	2.1	9.1	4.7	0	11
Peppermint oil redistilled	L	2.6	0.55	0	0	8.1
Peanut butter	L	0	0	0	24	2.1
Loaded spud	P	0	39	0	22	0
Cheddar and sour cream	P	0	43	0	0	0
Parmesan and garlic	P	0	69	0	0	0
Jalapeno and cheddar	P	0	0	0	11	0
Buffalo blue cheese	P	0	35	0	17	0
French onion	P	0	17	0	13	0
Sour cream and onion	P	0	13	0	16	0
Sour cream and green onion	P	0	20	0	5.1	0
Au gratin	P	0	25	0	0	0

Abbreviations: L, liquid; NA, not analyzed owing to analytical interferences; P, powder.

Zero indicates below the LOD.

Table 3

Number and percent of detectable area samples for each flavoring compound.

Flavoring class	Flavoring compound	*N*	No. detected (%)	Min[a]	Max	Avg[a]
Aldehydes (μg/m^3)	Acetaldehyde	105	104 (99)	2.81	3495.81	307.34
	Benzaldehyde	105	73 (70)	0.29	663.22	71.44
	Isovaleraldehyde	105	77 (73)	0.55	2398.80	162.19
	Propionaldehyde	105	81 (77)	0.24	376.59	24.91
	2-Furaldehyde	105	60 (57)	0.30	10349.85	540.35
Acids (μg/m^3)	Acetic acid	105	23 (22)	79.29	5244.73	761.06
	Butyric acid	105	6 (6)	66.45	297.69	175.15
	Propionic acid	105	5 (5)	141.39	3654.40	1185.17
Ketones (ppb)	Diacetyl	105	8 (8)	25.15	3123.99	856.70
	Acetoin	105	7 (7)	11.79	96.40	52.75
	2,3-Pentanedione	105	3 (3)	15.14	172.07	76.22
	2,3-Hexanedione	105	3 (3)	30.09	991.67	432.83
	2,3-Heptanedione	105	3 (3)	37.13	174.06	95.19
Particulate (μg/m^3)	Respirable particulate[b]	43	24 (56)	52.79	2966.83	357.04

[a] Minimum and arithmetic mean value for detectable samples only. Excludes non-detectable samples.

[b] Respirable particulate samples were taken only where powdered flavors were used or where particulate exposure might occur.

Table 4

Number and percent of detectable personal samples for each flavoring compound.

Flavoring class	Flavoring compound	N[a]	No. detected (%)	Min[b]	Max	Avg[b]
Aldehydes (µg/m^3)	Acetaldehyde	73	72 (99)	1.47	3569.29	266.20
	Benzaldehyde	73	60 (82)	0.32	848.12	63.75
	Isovaleraldehyde	73	54 (74)	1.22	2218.00	167.74
	Propionaldehyde	73	59 (81)	0.81	3889.92	103.11
	2-Furaldehyde	73	47 (64)	0.46	1505.72	113.12
Acids (µg/m^3)	Acetic acid	72	10 (14)	127.67	11009.70	1507.38
	Butyric acid	72	3 (4)	75.27	28950.34	9704.31
	Propionic acid	72	2 (3)	150.55	9310.22	4730.38
Ketones (ppb)	Diacetyl	74	4 (5)	60.63	631.88	324.53
	Acetoin	74	3 (4)	9.63	18.79	13.08
	2,3-Pentanedione	74	0 (0)	ND	ND	ND
	2,3-Hexanedione	74	3 (4)	31.84	821.79	313.61
	2,3-Heptanedione	74	1 (1)	119.03	119.03	119.03
Particulate (µg/m^3)	Respirable particulate[1]	29	15 (52)	61.15	2139.04	425.32

[1]Respirable particulate samples were taken only where powdered flavors were used or where particulate exposure might occur.

[a]Seventy-four personal samples were taken, however two acid samples and one aldehyde sample were not processed owing to pump failures or sampling errors.

[b]Minimum and arithmetic mean value for detectable samples only. Excludes non-detectable samples.

Table 5

Number of area samples above the LOD by food production category.

Food category		Aldehydes					Acids			Ketones					
	N	Acetal	Ben	Iso	Propional	Fur	Acetic	Butyric	Propionic	Dia	Acetoin	Pent	Hex	Hept	RP[a]
Baked goods	24	23	23	23	23	23	0	0	0	0	0	0	0	0	7 (8)
Cereal	21	21	7	14	7	15	6	6	4	3	3	3	3	0	11 (18)
Chocolate	21	21	20	19	20	10	9	0	1	1	4	0	0	0	0 (3)
Dairy	7	7	3	3	3	0	0	0	0	0	0	0	0	0	NS
Flavor manufacture	8	8	8	8	8	1	0	0	0	4	0	0	0	0	NS
Snack food	14	14	6	0	14	10	6	0	0	0	0	0	0	0	6 (14)
Wine	10	10	6	10	6	1	2	0	0	0	0	0	0	3	NS

Abbreviations: Acetal, acetaldehyde; Ben, benzaldehyde; Dia, diacetyl; Fur, 2-furaldehyde; Hept, 2,3, heptanedione; Hex, 2,3-hexanedione; Iso, isovaleraldehyde; N, number of samples collected; NS, not sampled; Pent, 2,3-penanedione; Propional, propionaldehyde; RP, respirable particulate.

[a] The number in parenthesis indicates the number of samples collected. The number of particulate samples collected depended on the process being sampled and differed from the other samples.

Table 6

Number of personal samples above the LOD by food production category.

Food category	*N*	Aldehydes					Acids			Ketones					RP[a]
		Acetal	Ben	Iso	Propional	Fur	Acetic	Butyric	Propionic	Dia	Acetoin	Pent	Hex	Hept	
Baked goods	22	21	21	20	20	21	1	1	1	0	0	0	0	0	6 (8)
Cereal	9	9	6	4	2	7	0	2	1	0	3	0	3	0	5 (9)
Chocolate	17	17	15	15	16	8	6	0	0	0	0	0	0	0	0 (3)
Dairy	5	5	2	3	3	0	0	0	0	0	0	0	0	0	NS
Flavor manufacture	6	6	6	6	6	3	0	0	0	4	0	0	0	0	NS
Snack food	9	9	7	1	9	7	3	0	0	0	0	0	0	0	4 (9)
Wine	6[b]	5	3	5	3	1	0	0	0	0	0	0	0	1	NS

Abbreviations: Acetal, acetaldehyde; Ben, benzaldehyde; Dia, diacetyl; Fur, 2-furaldehyde; Hept, 2,3, heptanedione; Hex, 2,3-hexanedione; Iso, isovaleraldehyde; N, number of samples collected; NS, not sampled; Pent, 2,3-penanedione; Propional, propionaldehyde; RP, respirable particulate.

[a]The number in parenthesis indicates the number of samples collected. The number of samples collected depended on the process being sampled and differed from the other samples.

[b]Only five aldehyde samples were collected.

Table 7

Aldehyde and respirable particulate area sample concentrations by food category (μg/m^3).

Food category	*n*	*n*>LOD	GM	GSD	Diff[a]
Ace					
Baked goods	24	23	108.64	8.58	A
Cereal	21	21	56.15	4.74	A,B
Chocolate	21	21	42.59	1.93	A,B
Dairy	7	7	6.48	1.46	C
Flavor manufacture	8	8	10.64	2.12	B,C
Snack food	14	14	30.19	1.38	A,B,C
Wine	10	10	1000.55	2.62	D
Ben					
Baked goods	24	23	57.33	7.41	A
Cereal	21	7	1.34	2.60	B,C
Chocolate	21	20	3.62	2.09	B
Dairy	7	3	0.95	1.26	B,C
Flavor manufacture	8	8	39.65	3.98	A
Snack Food	14	6	0.40	1.34	C
Wine	10	6	0.73	2.32	C
Iso					
Baked goods	24	23	55.69	7.45	A
Cereal	21	14	3.17	3.12	B
Chocolate	21	19	28.08	10.71	A,C
Dairy	7	3	1.47	1.31	B,C
Flavor manufacture	8	8	4.11	1.82	B,C
Snack food	14	0	NA		
Wine	10	10	13.24	2.05	A,B,C
Pro					
Baked goods	24	23	22.46	4.89	A
Cereal	21	7	1.21	2.18	B,C
Chocolate	21	20	2.29	2.10	B,C,D

Food category	***n***	***n*>LOD**	**GM**	**GSD**	**Diff[a]**
Dairy	7	3	0.98	1.34	B,C
Flavor manufacture	8	8	0.96	1.43	B,C
Snack food	14	14	3.58	1.10	D
Wine	10	6	2.99	1.52	C,D
Fur					
Baked goods	24	23	38.26	7.25	A
Cereal	21	15	29.21	18.71	A
Chocolate	21	10	2.02	4.0	B
Dairy	7	0	NA		
Flavor manufacture	8	1	NA		
Snack food	14	10	2.16	5.66	B
Wine	10	1	NA		
RP					
Baked goods	8	7	162.60	2.02	A
Cereal	18	11	88.59	4.47	AB
Chocolate	3	0	NA		
Dairy	0	0			
Flavor manufacture	0	0			
Snack food	14	6	39.21	1.84	B
Wine	0	0			

Abbreviations: Ace, acetaldehyde; Ben, benzaldehyde; Fur, 2-furaldehyde; Iso, isovaleraldehyde; Pro, propionaldehyde; RP, respirable particulate.

[a]Levels with the same letter are not significantly different in a Tukey multiple comparison procedure with a level of significance of 0.05.

Table 8

Aldehyde and respirable particulate personal sample concentrations by food category (μg/m^3).

Food Category	*n*	*n*>LOD	GM	GSD	Diff[a]
Ace					
Baked goods	22	21	175.62	8.16	A,B
Cereal	9	9	21.74	1.68	C
Chocolate	17	17	43.70	1.63	C
Dairy	5	5	9.74	1.50	C
Flavor manufacture	6	6	36.44	4.73	B,C
Snack food	9	9	31.12	1.31	C
Wine	5	5	929.42	2.23	A
Ben					
Baked goods	22	21	19.01	9.98	A
Cereal	9	6	2.15	2.26	B
Chocolate	17	15	2.63	1.96	B
Dairy	5	2	0.99	1.17	B
Flavor manufacture	6	6	116.85	1.36	A
Snack food	9	7	0.60	1.51	B
Wine	5	3	0.58	1.78	B
Iso					
Baked goods	22	20	25.40	10.83	A
Cereal	9	4	2.11	2.61	B
Chocolate	17	15	25.10	10.79	A,B
Dairy	5	3	1.60	1.20	A,B
Flavor manufacture	6	6	5.56	2.0	A,B
Snack food	9	1	NA		
Wine	5	5	10.74	2.69	A,B
Pro					
Baked goods	22	20	14.98	10.40	A
Cereal	9	2	1.34	2.04	B
Chocolate	17	16	2.45	1.91	B

Food Category	*n*	*n*>LOD	GM	GSD	Diff[a]
Dairy	5	3	1.05	1.37	B
Flavor manufacture	6	6	1.22	1.28	B
Snack food	9	9	3.81	1.14	A,B
Wine	5	3	2.34	1.71	A,B
Fur					
Baked goods	22	21	15.14	9.77	A
Cereal	9	7	30.48	10.67	A,B
Chocolate	17	8	1.94	3.68	C
Dairy	5	0	NA		
Flavor manufacture	6	3	0.92	1.34	C
Snack food	9	7	3.49	5.78	A,B,C
Wine	5	1	NA		
RP					
Baked goods	8	6	148.96	3.55	A
Cereal	9	5	133.27	4.62	A
Chocolate	3	0	NA		
Dairy	0	0			
Flavor manufacture	0	0			
Snack food	9	4	44.93	1.78	A
Wine	0	0			

Abbreviations: Ace, acetaldehyde; Ben, benzaldehyde; Fur, 2-furaldehyde; Iso, isovaleraldehyde; Pro, propionaldehyde; RP, respirable particulate.

[a] Levels with the same letter are not significantly different in a Tukey multiple comparison procedure with a level of significance of 0.05.

Table 9

Aldehyde and respirable particulate area and personal sample concentrations by process (μg/m^3).

Type	Flavor	*n*	*n*>LOD	GM	GSD	Diff[a]
Ace						
Area	Control	6	6	46.20	11.31	A
	Handling	53	52	43.31	3.95	A
	Production	46	46	80.66	8.05	A
Personal	Handling	41	40	54.94	4.76	A
	Production	32	32	78.07	6.59	A
Ben						
Area	Control	6	6	80.52	9.69	A
	Handling	53	34	2.82	8.83	B
	Production	46	33	3.86	6.79	B
Personal	Handling	41	34	2.66	5.75	A
	Production	32	26	8.66	10.25	B
Iso						
Area	Control	6	4	5.28	3.98	A,B
	Handling	53	33	4.62	12.01	A
	Production	46	40	14.54	7.78	B
Personal	Handling	41	27	5.74	12.68	A
	Production	32	27	11.63	7.20	A
Pro						
Area	Control	6	5	4.81	10.53	A
	Handling	53	43	3.55	3.35	A
	Production	46	33	2.83	4.88	A
Personal	Handling	41	34	3.74	4.69	A
	Production	32	25	3.61	6.24	A
Fur						
Area	Control	6	4	6.06	9.68	A
	Handling	53	38	7.45	10.40	A
	Production	46	18	5.51	10.87	A

Type	Flavor	*n*	*n*>LOD	GM	GSD	Diff[a]
Personal	Handling	41	28	5.78	8.52	A
	Production	32	19	4.44	7.36	A
RP						
Area	Handling	33	29	69.82	2.96	A
	Production	10	4	133.74	4.56	A
Personal	Handling	25	13	86.25	3.17	A
	Production	4	2	258.99	3.78	A

Abbreviations: Ace, acetaldehyde; Ben, benzaldehyde; Fur, 2-furaldehyde; Iso, isovaleraldehyde; Pro, propionaldehyde; RP, respirable particulate.

[a]Levels with the same letter are not significantly different in a Tukey multiple comparison procedure with a level of significance of 0.05.

Table 10

Aldehyde and respirable particulate area and personal sample concentrations by flavor used (µg/m^3).

Type	Flavor	*n*	*n*>LOD	GM	GSD	Diff[a]
Ace						
Area	None	32	32	110.36	9.57	A
	Flavor	56	56	38.53	4.21	B
	Natural	17	16	60.23	4.73	A,B
Personal	None	18	18	155.2	6.19	A
	Flavor	40	39	39.56	5.35	B
	Natural	15	15	80.29	3.27	A,B
Ben						
Area	None	32	21	4.89	13.32	A,B
	Flavor	56	35	2.52	6.86	A
	Natural	17	17	11.0	6.49	B
Personal	None	18	12	1.92	4.44	A
	Flavor	40	34	4.66	8.71	A,B
	Natural	15	14	10.95	9.32	B
Iso						
Area	None	32	25	11.72	6.92	A
	Flavor	56	37	3.28	7.18	B
	Natural	17	15	57.56	13.54	C
Personal	None	18	13	17.18	9.79	A
	Flavor	40	28	3.34	6.63	B
	Natural	15	13	29.34	13.27	A
Pro						
Area	None	32	21	4.75	6.56	A
	Flavor	56	44	2.61	3.39	A
	Natural	17	16	3.40	3.09	A
Personal	None	18	11	3.91	6.02	A
	Flavor	40	34	3.11	5.03	A
	Natural	15	14	5.38	5.38	A

Type	Flavor	*n*	*n*>LOD	GM	GSD	Diff[a]
Fur						
Area	None	32	13	5.06	6.18	A
	Flavor	56	33	6.15	14.01	A
	Natural	17	14	11.96	8.71	A
Personal	None	18	10	6.72	6.23	A
	Flavor	40	24	4.27	9.85	A
	Natural	15	13	6.17	5.90	A
RP						
Area	None	7	3	195.22	4.84	A
	Flavor	33	19	63.56	2.97	A
	Natural	3	2	155.38	1.23	A
Personal	None	6	3	248.16	3.99	A
	Flavor	19	9	72.33	3.20	A
	Natural	4	3	122.43	1.44	A

Abbreviations: Ace, acetaldehyde; Ben, benzaldehyde; Fur, 2-furaldehyde; Iso, isovaleraldehyde; Pro, propionaldehyde; RP, respirable particulate.

[a] Levels with the same letter are not significantly different in a Tukey multiple comparison procedure with a level of significance of 0.05.