Findings from Industrial Hygiene Air Sampling, Ventilation Assessment, and a Medical Survey at a Facility that Manufactures Flavorings, Modified Dairy Products, and Bacterial Additives

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Health Hazard Evaluation Report
HETA 2007-0327-3083
Chr. Hansen, Inc.
New Berlin, Wisconsin
May 2009

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
NIOSH *National Institute for Occupational Safety and Health*

The employer shall post a copy of this report for a period of 30 calendar days at or near the workplace(s) of affected employees. The employer shall take steps to insure that the posted determinations are not altered, defaced, or covered by other material during such period. [37 FR 23640, November 7, 1972, as amended at 45 FR 2653, January 14, 1980].

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ABBREVIATIONS

ACGIH	American Conference of Governmental Industrial Hygienists
AH	absolute humidity
ATS	American Thoracic Society
BO	bronchiolitis obliterans
cfm	cubic feet per minute
CT	computerized tomography
DL_{co}	diffusing capacity for carbon monoxide
ECRHS	European Community Respiratory Health Study
ESD	encapsulated starter distillate
°F	degrees Fahrenheit
fpm	feet per minute
FEMA	Flavor and Extract Manufacturers Association
FEV_1	forced expiratory volume in one second
FTIR	Fourier transform infrared
FVC	forced vital capacity
GM	geometric mean
GSD	geometric standard deviation
HEPA	high efficiency particulate air
HVAC	heating, ventilation, and air-conditioning
Max	maximum
mg/m^3	milligrams per cubic meter of air
mg/l	milligrams per liter of air
Min	minimum
NHANES III	Third National Health and Nutrition Examination Survey
NMAM	NIOSH Manual of Analytical Methods
NIOSH	National Institute for Occupational Safety and Health
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit
PID	photoionization detector
PPE	personal protective equipment
ppm	parts per million
QC	quality control
REL	recommended exposure limit
RH	relative humidity
STD	standard deviation
STEL	short-term exposure limit
TLV®	Threshold Limit Value
TWA	time-weighted average
VOC	volatile organic compound

Highlights of the NIOSH Health Hazard Evaluation

Workers at the Chr. Hansen, Inc. plant in New Berlin, Wisconsin, requested that the National Institute for Occupational Safety and Health (NIOSH) perform a health hazard evaluation to investigate the risk of respiratory and eye problems from exposures to diacetyl, butter flavorings, cheese flavorings, enzymes, colors, bacterial cultures, and cleaning agents at the plant.

What NIOSH Did

- Measured air concentrations of flavoring chemicals and dust in various work areas.
- Assessed the potential for air movement between production rooms and the warehouse area.
- Evaluated the effectiveness of ventilation systems in various work areas.
- Interviewed workers, measured their lung function with spirometry, and tested workers with methacholine to see if they had hyperreactive airways, a common finding in individuals who have asthma.

What NIOSH Found

- Diacetyl air concentrations in the spray dry, starter distillate, and flavors rooms and in the quality control (QC) laboratory were similar to air concentrations measured at other plants where workers have developed severe lung disease likely caused by exposure to diacetyl and possibly other flavoring chemicals.
- High diacetyl concentrations were measured during tasks involving the manual pouring of diacetyl or diacetyl-containing starter distillate and during cleaning activities.
- The Torit® local exhaust ventilation unit used during packaging of finished product in the spray dry room allowed some of the captured dust to escape back into the room air.
- Contaminants in the air of the flavors and spray dry rooms may occasionally migrate into the warehouse.
- Occasional peak dust exposures were measured in the animal health large and intermediate packaging rooms during ingredient mixing and product packaging activities.
- One worker in animal health and one worker who worked in flavoring production areas had abnormalities on spirometry tests that might be related to work exposures. For each of these workers, additional medical evaluation is required to determine the nature of the lung problem and the likely cause or causes.
- A higher percentage of workers in the animal and human health rooms reported work-related eye symptoms and skin problems compared to other workers.

What Chr. Hansen Managers Can Do

- Follow the recommendations in this report to decrease air concentrations of potentially hazardous agents in all production rooms, the QC laboratory, and the warehouse.
- Perform baseline spirometry tests and repeat spirometry tests at least every six months for maintenance workers and workers who enter or work in the starter distillate, enzymes, flavors, and spray dry rooms, and the QC laboratory; perform baseline spirometry tests and repeat spirometry tests at least annually for workers in the animal and human health rooms.
- Provide respiratory protection for all workers who enter the starter distillate, enzymes, flavors, spray dry, and animal and human health rooms. Follow the respiratory protection recommendations included in this report to ensure appropriate personal respiratory protection of permanent workers, temporary workers, and contract workers.
- Provide appropriate protective clothing, eye protection, and gloves for all production workers and educate workers on when to use this equipment.
- Perform lockout/tagout, confined space, and combustible dust assessments as recommended in this report.
- Ensure compliance with all applicable environmental protection regulations when disposing of residual flavoring chemicals such as diacetyl.
- Ensure that exposures to subtilisins are below the NIOSH recommended exposure limit (REL) if *B. subtilis* bacteria or subtilisins are being used.

What Chr. Hansen Workers Can Do

- Wear a full-face respirator with particulate filters and organic vapor cartridges when entering or working in the starter distillate, enzymes (when packaging starter distillate), flavors, and spray dry rooms.
- Wear an N-95 filtering-facepiece or a half- or full-face respirator with particulate filters when entering or working in the animal and human health rooms.
- Wear eye protection, protective clothing, and gloves as directed by management.
- Participate in all regularly-scheduled spirometry tests offered by management.

Workplace exposures to flavoring chemicals, enzymes, and organic dusts can put workers at risk for serious lung disease; eye and skin problems may also occur. This report provides recommendations for preventing these conditions through ventilation improvements, administrative and work practice changes, use of respirators and other personal protective equipment, worker education, and medical monitoring with regularly scheduled spirometry tests.

Background

Workers at Chr. Hansen, Inc., in New Berlin, Wisconsin, requested that NIOSH perform a health hazard evaluation to investigate the risk of respiratory and eye problems from exposures to diacetyl, butter flavorings, cheese flavorings, enzymes, colors, bacterial cultures, and cleaning agents. The plant has separate rooms for the production of the following products and product types:

- Starter distillate, a liquid which contains the flavoring chemical diacetyl, is produced in the starter distillate room.
- CHY-MAX®, a standardized solution of the enzyme chymosin (produced at another plant) is diluted and packaged in the enzymes room; starter distillate is also diluted and packaged in this room.
- Cheese, dairy, and other flavors and cheese products are produced in the flavors room.
- Powdered flavors and colors are produced through a spray drying process in the spray dry room.
- Bacterial blends for use in foods intended for human consumption are produced in the human health room. (Flavorings are not used or produced in this room.)
- Bacterial blends for use as feed supplements for farm animals are produced in the animal health rooms. (Flavorings are not used or produced in this room.)

Exposures related to production of flavorings are of particular concern to NIOSH. Previous NIOSH investigations have identified evidence of a severe disease of the small airways in the lung (bronchiolitis obliterans) among workers exposed to butter flavoring chemicals in microwave popcorn plants and among production workers in flavoring manufacturing plants. Exposures to enzymes and other organic dust are also of concern due to their potential to cause lung disease in some individuals. Workplace exposures to enzymes can cause asthma and other allergic problems. Repeated exposure to organic dusts (materials from living things such as plants, animals, bacteria, or fungi) can cause hypersensitivity pneumonitis, another serious lung disease.

Assessment

NIOSH staff visited the plant initially in September 2007 to meet with management and workers, conduct an initial walkthrough of the plant, learn about production processes, and do preliminary air sampling. NIOSH staff returned to the plant in December 2007 to do a detailed ventilation assessment and industrial hygiene air sampling, and to conduct a medical survey which included a questionnaire and lung function testing with spirometry. All current workers in production areas, the QC laboratory, the warehouse, and maintenance were invited to participate in the medical survey. For analyses of the medical survey results by type of potential exposure in the plant, workers were classified as follows:

- Flavoring workers: Current workers with potential exposure to diacetyl and other flavoring-related chemicals in the starter distillate, enzymes, flavors, or spray dry rooms, the QC laboratory, or in maintenance work.
- Bacterial products workers: Current workers with potential exposure to bacteria and other organic dusts in the animal health or human health rooms.
- Warehouse workers.

Results

Air sampling showed diacetyl air concentrations in the spray dry, starter distillate, and flavors rooms and in the quality control laboratory that were similar to those measured at some flavoring plants and microwave popcorn plants where some workers have developed severe lung disease likely caused by exposure to diacetyl and possibly other flavoring chemicals. This included both average air concentrations over the work shift and peak air concentrations during specific tasks. The atmospheric pressure in the spray dry and flavors rooms was neutral to positive relative to the warehouse; as a result, movement of air contaminants from those rooms into the warehouse is possible. The Torit® local exhaust ventilation unit used during packaging of finished product in the spray dry room allowed some of the captured dust to escape back into the room air. One worker in the flavoring worker group had mild fixed airways obstruction on spirometry testing. Although this finding might be related to flavoring chemical exposures, additional medical tests are required to establish if a particular lung disease is present and the likely cause; information from additional medical evaluation was not available to NIOSH investigators.

Among nine current and former workers in flavoring production areas who reported chest symptoms from work exposures, three workers reported chest symptoms from exposure to enzymes; three workers reported chest symptoms from exposure to acids; one worker reported chest symptoms from exposure to diacetyl; and one worker reported chest symptoms from exposure to encapsulated starter distillate. One worker reported eye burning from diacetyl and starter distillate.

Air sampling in the animal health large and intermediate packaging rooms showed intermittent peak exposures to dust during ingredient mixing and product packaging activities. For some processes, local exhaust ventilation in these rooms did not adequately control dust exposures. Of ten workers in the animal and human health rooms who participated in the medical survey, five reported post-hire skin problems, four reported chest symptoms from exposures, and three reported work-related eye and nasal symptoms. Two of the four with chest symptoms reported that these occurred with exposure to Biomax® and other powders. Spirometry tests in two animal health workers showed restriction, a decreased ability to fully expand the lungs. One of the two workers with restriction also reported weekly episodes of unusual tiredness and fatigue and monthly episodes of fever, chills, or night sweats. These symptoms in an individual with restriction on spirometry can be due to hypersensitivity pneumonitis, a lung disease which occurs in a small percentage of individuals exposed to organic dusts. Additional medical tests are necessary for a physician to establish if an individual has this disease

Conclusions and Recommendations

The levels of diacetyl measured in flavoring production areas at the Chr. Hansen plant may be high enough to put workers at risk of developing severe lung disease. Because flavoring-related lung disease can occur after only several months of exposure and can rapidly progress to severe irreversible disease, uncontrolled exposures should be minimized. Workers in the animal and human health rooms may also be at risk for respiratory symptoms and disease from exposure to organic dust. The Recommendations section of this report contains detailed guidance on what Chr. Hansen mangers should do to decrease exposures in all production rooms, the quality control laboratory, and the warehouse to minimize the potential for workers to develop respiratory and other health effects. The following approaches for prevention are

addressed: ventilation improvements, administrative and work practice changes, use of respirators and other personal protective equipment, worker education, and medical monitoring with regularly scheduled spirometry tests.

Keywords: NAICS 311930 (Flavoring Syrup and Concentrate Manufacturing), NAICS 31151 (Dairy Product [except Frozen] Manufacturing), NAICS 311942 (Spice and Extract Manufacturing), NAICS 32513 (Synthetic Dye and Pigment Manufacturing), NAICS 311119 (Other Animal Food Manufacturing), bronchiolitis, asthma, airways obstruction, respiratory symptoms, flavorings, diacetyl, modified cheese products, carmine, food coloring agents, animal feed supplements, probiotics.

INTRODUCTION

In August 2007, NIOSH received a confidential request from employees at the Chr. Hansen, Inc. plant in New Berlin, Wisconsin, to investigate the risk of work-related eye and respiratory disease at the plant. Exposures of concern included diacetyl, butter flavoring, cleaning agents, colors, bacterial cultures, enzymes, and cheese flavors.

The plant produces liquid starter distillates (that contain approximately 0.5%, 1.5%, and 4.5% diacetyl), CHY-MAX® (a standardized solution of the enzyme chymosin), liquid enzyme-modified cheese products, powdered food colors (paprika, carmine, tumeric, tartrazine), powdered encapsulated starter distillates (ESD-4X and ESD-50X), powdered butter flavors, powdered dairy flavors, and powdered bacterial blends. Starter distillate is used as a flavor enhancer for imitation cheese, bakery products, salad dressings, margarine, sour cream, whipped butter, and sauces. CHY-MAX® is used to curdle milk in the cheese production industry. Enzyme-modified cheese products are used as a flavor enhancer in the production of processed cheese, salad dressings, sauces, bakery products, and soups. Encapsulated starter distillate and powdered butter flavor are used as flavoring agents in cake mixes, frostings, dressings, margarine, instant potatoes and cottage cheese. Powdered dairy flavors are used in bakery products to boost flavor. Some bacterial blends are used as silage inoculants; others are used as probiotic additives for animal feed and human food products.

Flavoring-Related Lung Disease

Workplace investigations and animal studies conducted since the year 2000 have shown that workers can develop severe lung disease from exposures to butter flavoring chemicals such as diacetyl. Workers have become ill in plants using butter flavoring in the production of microwave popcorn, and in plants making butter flavorings and diacetyl [CDC 2007; Kreiss et al. 2002; Kanwal et al. 2006; NIOSH 1986; NIOSH 2007; NIOSH 2008a; van Rooy et al. 2007]. Some workers have been affected after only several months of exposure to butter flavoring chemicals. Most affected workers have ranged in age from their early 20s to late 40s. There is no known cure for the disease. Several severely affected workers have been placed on lung transplant waiting lists [Akpinar-Elci et al. 2004].

The lung disease in affected workers resembles bronchiolitis

obliterans, a condition in which the smallest airways in the lung develop scarring and become partially or completely blocked, limiting the movement of air in and out of the lungs (fixed airways obstruction) [King 1998; King 2000]. Symptoms include worsening shortness of breath on exertion, cough, and wheezing. These symptoms generally do not improve after the work shift or on weekends and vacations. Some workers have also reported eye problems (temporary eye burning) and skin problems from exposure to diacetyl and other flavoring chemicals.

Allergic Diseases from Exposures to Enzymes and Other Organic Matter

Workers exposed to enzymes can develop different types of allergic disease [Baur 2005; Bernstein et al. 2006]. These include rhinitis (stuffy, runny, itchy nose), conjunctivitis (tearing and itching of the outer lining of the eye), and asthma. Asthma is the most serious of these conditions because breathing difficulties can worsen over time (and possibly become life-threatening) if affected workers continue to be exposed.

Individuals with asthma have repeated episodes of reversible obstruction of the airways in the lung. Asthma symptoms include shortness of breath, chest tightness, wheezing, and cough. Asthma can occur from exposure to sensitizing agents (allergic asthma) or non-specific irritants (non-allergic asthma). Allergic asthma requires a period of time (from weeks to several years) between the first exposure and the start of symptoms. Symptoms of allergic asthma in workers generally follow one of two patterns: symptoms start within an hour of being exposed (immediate onset), with improvement away from work; or, symptoms start several hours after the start of exposure or after leaving work (delayed onset). With delayed-onset asthma, airways obstruction may not totally resolve before the affected worker's next work shift. Sometimes workers may have both immediate and delayed onset asthma symptoms.

Among the substances used at the Chr. Hansen plant, the following have been reported to be associated with allergic asthma in other facilities: carmine [Rodriquez et al. 1989; Lizaso et al. 2000; Tabar-Purroy et al. 2003], α-lactalbumin (found in whey) [Bernaola et al. 1994], paprika [Sastre et al. 1996], soy flour [Bush et al. 1988], protease derived from *Bacillus subtilis* [Bernstein 1972; Franz et al. 1971], and lipase from *Aspergillus oryzae* [Brant et al.

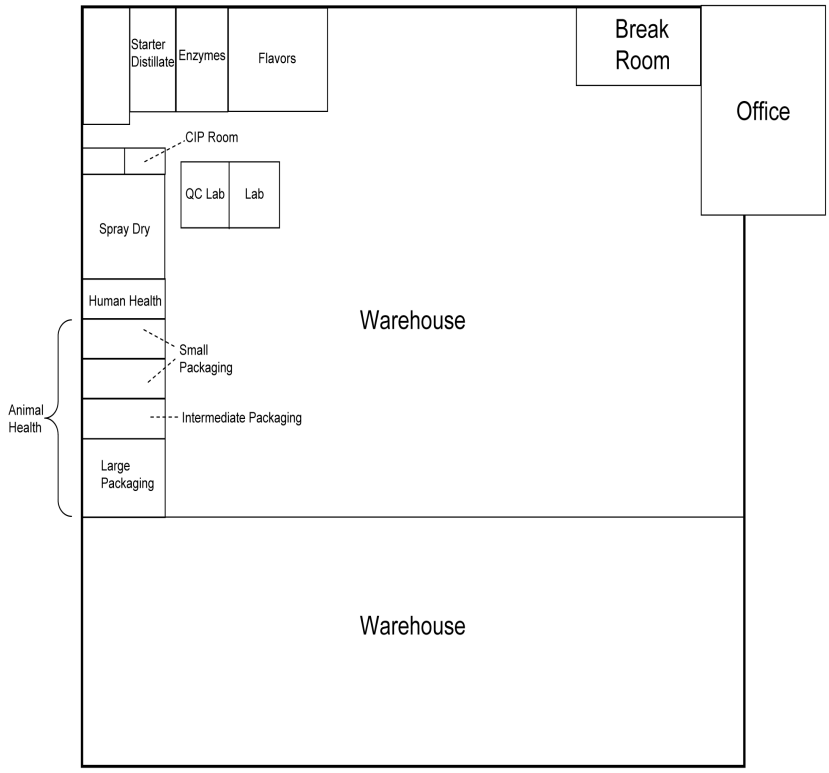
2004]. Individuals with stable preexisting asthma may experience worsening of their symptoms from workplace exposures. This can occur with exposure to a wide range of dusts, gasses, fumes, and mists (e.g., irritating cleaning agents).

Hypersensitivity pneumonitis (HP) is a serious lung disease in which an individuals' immune system responds to repeated exposure to organic dusts (materials from living things such as plants, animals, bacteria, or fungi) or other sensitizing agents [Patel et al. 2001]. Two symptom patterns exist in HP. Some individuals experience episodic shortness of breath and flu-like symptoms, including cough, muscle aches, chills, fever, sweating, and fatigue. These symptoms start within hours of exposure and last for one to three days. Other individuals do not develop flu-like symptoms; instead they develop gradual and progressive shortness of breath and cough, often accompanied by weight loss. In HP cases that are caused by occupational exposures, the first sign that the illness is due to exposures at work may be that a worker's symptoms and medical tests improve during a long period of time away from work and then worsen on return to work. Continued exposure can lead to lung scarring and permanent shortness of breath. Within the food color industry, HP has been identified in natural dye production workers exposed to carmine [Christiansen et al. 1981]. HP has also occurred in food workers exposed to moldy grains and cheese, paprika, flour, and coffee bean dust [Patel et al. 2001].

Process Description

The Chr. Hansen New Berlin plant has been in production since 1997. A schematic layout (Figure 1) shows the plant's separate rooms for the production of starter distillate (starter distillate room), dilution and packaging of starter distillate and CHY-MAX® (enzymes room), production of cheese, dairy, and other flavors and cheese products (flavors room), spray drying of flavors and colors (spray dry room), packaging of bacterial blends for use in foods intended for human consumption (human health room), and packaging of bacterial blends for use as feed supplements for farm animals (animal health rooms). There are four animal health production rooms: one for large blending and packaging operations; one for intermediate blending and packaging operations; and two for small packaging.

Figure 1. Plant layout



Forty workers work in production-related jobs (i.e., non-office jobs): one in the starter distillate room, two in the enzymes room, six in the flavors room, three in the spray dry room, ten in the animal and human health rooms, two in the quality control (QC) laboratory, ten in the warehouse, three in maintenance, and three as production supervisors. Most production workers are permanent employees; the company also uses temporary and contract workers. Administrative and clerical staff work in offices located across the warehouse from the production rooms (see Figure 1).

In the starter distillate room, a worker ferments dairy cultures in a tank to produce a milk stock. After incubation, the worker then manually transfers the fermented milk stock to stills which are heated to 230°F for distillation. The resulting distillate ("starter distillate") contains approximately 4.5% diacetyl. The worker manually transfers starter distillate to a large container several times during the work shift. The last transfer of the day is often performed by a worker from the adjacent enzyme room.

In the enzymes room, CHY-MAX® (a standardized solution of

the enzyme chymosin produced through a bacterial fermentation process at another plant) is diluted and packaged for sale. Once weekly, starter distillate is transferred to a large tank in the enzyme room, where it is diluted to a concentration of 1.5% or 0.5% diacetyl and packaged into 5- and 55-gallon containers for sale.

In the flavors room, workers add lipases, proteases, and other ingredients to solid cheese, water, and other dairy products (such as cultured whey and milk powder) in large mixing tanks and then incubate the mixtures. The lipases and proteases are generally in powder form. Enzyme-modified cheese products are directly packaged for sale or are spray dried. Workers use smaller mixing tanks to combine powder and liquid flavoring ingredients to make a variety of liquid flavors. Starter distillate (which contains diacetyl) or pure liquid diacetyl are used in the production of some enzyme-modified cheese products and some flavors; starter distillate is pumped from a large container into the mixing tank via a hose; pure liquid diacetyl is manually poured into the mixing tank. The liquid diacetyl is kept refrigerated in the warehouse.

In the spray dry room, a worker prepares different slurries (paprika, carmine, tumeric, tartrazine, starter distillate, butter flavoring, and enzyme-modified dairy ingredients) which are then spray-dried to form powdered products. In the spray-drying process, a mixture of liquid and powder ingredients (a slurry) is sprayed within a large sealed tank. Heat within the tank dries the slurry droplets, leaving a powder as the finished product. The worker observes much of the process from a control room, but enters the production area several times each hour to change product collection bags as they become filled with finished product. A Torit® portable local exhaust ventilation system is used when filling bags with encapsulated starter distillate powder or other powdered butter flavors. With encapsulated powder flavors, volatile flavor ingredients such as diacetyl are enclosed within an encapsulant material to decrease volatility.

Freeze- and spray-dried fermented products are produced in other facilities and then shipped to the New Berlin plant where they are used in the production of silage inoculants and animal and human probiotics. In the animal health large packaging room, bacteria and other ingredient powders are blended together and packaged into 50-pound containers. In the animal health intermediate packaging room, large totes (up to 1000 pounds) of probiotic products are blended and delivered to the adjacent small packaging

rooms for final product packaging. In the human health room, bacteria and other ingredient powders are blended and packaged. All bacteria used in the animal and human health rooms are gram-positive species.

Tanks in the starter distillate, flavors, and spray dry rooms are cleaned between product runs with a cleaning-in-place (CIP) process that uses a cleaning agent (Principal™, Ecolab, St. Paul, MN) and a sanitizer (Matrixx™, Ecolab, St. Paul, MN). Hoppers and ribbon blenders in the animal health large and intermediate packaging rooms are cleaned between blends with a foam chlorinated alkaline cleaner.

A written respiratory protection program was in place at the time of our initial visit to the plant in September 2007. According to management, workers have used respirators since the year 2000. Workers use disposable NIOSH-approved N-95 filtering–facepiece respirators (2200 Moldex™, Moldex-Metric Inc., Culver City, CA) when handling encapsulated starter distillate, powdered butter flavoring, powdered colors, powdered lipase, and powdered protease. Workers use full-face or half-face negative-pressure air-purifying respirators with organic vapor cartridges when handling starter distillate, diacetyl, or selected liquid ingredients such as acetic acid and butyric acid. Respirator cartridges are replaced monthly. Respirators are not used when packaging diacetyl-containing solutions in the enzymes room. Most workers who use negative-pressure air-purifying respirators are fit-tested. Workers who use disposable N-95 filtering-facepiece respirators are not fit-tested; only one size of this respirator (medium/large) is provided. Although not required by the company, workers in the animal and human health rooms usually can use disposable N-95 filtering-facepiece respirators when dumping ingredients into hoppers and during other dusty operations. Workers in the human health room are required to wear a protective suit, gloves, and eye protection for personal protection and to prevent product contamination.

The company obtains baseline and annual spirometry testing at a local occupational medicine clinic for permanent workers exposed to diacetyl (workers in the starter distillate, flavors, enzymes, and spray dry rooms, and maintenance workers). Permanent workers in the animal and human health rooms have a baseline spirometry test at the time of hire. Temporary workers are not fit-tested for respirators by the company and are not included in the company's spirometry program.

Ventilation System Description

There are four heating, ventilating, and air-conditioning (HVAC) units servicing the production areas within the plant. The flow rates for these HVAC units, as reported by the plant engineer, are shown in Table 1. Incoming air is heated or cooled as needed; both supply and return registers are located at ceiling height (approximately 24 feet above the floor). Room air is recirculated along with additional make-up air brought in from the outside. Make-up air reportedly ranges from 10-50% of total supply-air volume.

Table 1. Ventilation flow rates

Plant Area	Number of HVAC Units or Roof Exhausters	Reported Flow Rate (cfm*)
Enzyme Room	1 HVAC unit	10,000
Flavors Room	1 HVAC unit	10,000
Starter Distillate Room	2 Roof Exhausters	10,000
Animal Health Rooms (all production areas)	1 HVAC unit	26,300 (approximately 5,260 per room for the intermediate and small packaging rooms and 10,520 for the large packaging room)
Human Health Room	1 HVAC unit	9,000

*cfm – cubic feet per minute.

The starter distillate room receives its supply air from the enzymes room via a vent located in the wall that separates the two rooms. The starter distillate room has two roof-exhaust air registers. These rooftop exhausters maintain the starter distillate room at lower air pressure compared to the enzymes room. The resulting air movement between the two rooms is as follows: air enters the enzymes room through a supply-air vent; some of the air then moves into the starter distillate room (due to the lower air pressure there) and is then exhausted out of the room via the roof-exhaust vents. This ensures that starter distillate vapors do not migrate into the enzymes room. An exhaust-air register located at ceiling level also pulls air out of the enzyme room for recirculation. There were no local exhaust ventilation systems in the enzymes or starter distillate rooms.

The HVAC system for the flavors room re-circulates room air through a pre-filter and a high efficiency particulate air (HEPA) filtration system to remove airborne particulates (dust). This

filtration system is not designed to remove volatile organic compounds (VOCs) like diacetyl.

In the spray dry room, there is no forced-air supply, return, or exhaust. The plant engineer reported that when the spray dryer is operating, outside air is drawn into the room through two vents located in the outer walls of the building near the top of the spray dryer. This airflow is driven solely by the differential pressure. A Torit® portable fume extraction unit (Donaldson Company, Inc., Minneapolis, MN) is used during packaging activities. This is a local exhaust ventilation system which filters and recirculates air back into the room. It has a small articulating arm with a 4-inch simple circular hood at the end that can be positioned to capture dust with a pre-filter and a bank of pocket filters. This filtration system is not designed to remove VOCs like diacetyl.

All animal health production rooms are served by one shared HVAC unit. The HVAC unit reportedly provides an overall air supply of 26,300 cfm. Assuming that the air coming from the HVAC unit is evenly distributed to all animal health areas, the large packaging room would have an air supply of about 10,520 cfm and the other three animal health rooms would each have an air supply of about 5,260 cfm..

The local exhaust ventilation systems available in the animal health large packaging room are listed below:

- Bag Dump Station Hood—a single exhaust duct is connected to the rear of the bag dump station (at the top of the blender). An internal baffle helps to distribute the airflow across the width of the station.
- Product Discharge Hood—a ventilated collar hood is located on the outlet of the blender where product is discharged into a large tote.
- Product Packaging Hood—a flexible ventilation duct is located near the turboscrew packer (but it was disconnected).
- Hopper Hood—a flexible ventilation duct is located near the product packaging line.

All the hoods are connected to an air cleaner (baghouse) in the room which removes dust and re-circulates the air back into the room.

The animal health intermediate packaging room has a commercially available bag dump station that provides local exhaust ventilation at the top of the ribbon blender. The size of the hood opening is 26 by 41 inches. A baffle plate across the back of the station encloses the system filters and helps distribute airflow across the face of the hood. A pulsejet cleaning cycle occurs approximately every 25 seconds and consists of a high pressure pulse of air directed over the filters. There is no local exhaust ventilation at the discharge outlet of the ribbon blender in this room.

Both small packaging rooms have a local exhaust ventilation hood at the product discharge outlet which is connected to a portable HEPA vacuum. These hoods help contain dust as the product is being metered into the final package.

NIOSH staff (three physicians, two industrial hygienists, and a mechanical engineer) initially visited the plant from September 24 to 26, 2007. Activities during that visit included meetings with management, worker interviews, observation of production processes, and limited qualitative air sampling. NIOSH engineers and industrial hygienists assessed the ventilation systems in individual work areas from December 3 to 5, 2007, and conducted industrial hygiene air sampling from December 3 to 13, 2007. NIOSH staff conducted a medical survey for current workers at the plant from December 10 to 14, 2007. The survey included an interviewer-administered computerized questionnaire and lung function testing. Several former workers were invited to participate in the survey at an offsite location on December 15, 2007. Details on the industrial hygiene, ventilation, and medical assessments are provided below.

Industrial Hygiene Evaluation

Industrial hygiene air sampling measured contaminants generated during the production of bacterial blends and flavoring products. Air samples were collected from various plant areas, including the starter distillate, enzymes, flavors, spray dry, animal health, and human health rooms, the QC laboratory, and the warehouse. Area air samples were collected for VOCs, total hydrocarbons, ketones (diacetyl and acetoin), organic acids (acetic, butyric, caproic, caprylic, and lactic acids), inorganic acids (nitric and phosphoric acids), aldehydes (acetaldehyde and benzaldehyde), and respirable dust. Personal air samples were also collected for ketones (diacetyl and acetoin), organic acids (acetic, butyric, caproic, caprylic, lactic, and propionic acids), aldehydes (acetaldehyde and benzaldehyde), and respirable dust. Respirable dust consists of particles which are small enough to penetrate deep into the lungs upon inhalation. Both full-shift and partial-shift time-weighted average (TWA) samples were collected. Temperature and relative humidity were measured several times each day at each area sampling location.

Real-time diacetyl measurements were made using a Fourier transform infrared (FTIR) gas analyzer [Gasmet DX-4010, Temet Instruments Oy, Helsinki, Finland]. This instrument was used to obtain continuous one-minute concentration measurements for diacetyl. A photoionization detector (PID) was used to quantify real-time VOCs in air [ToxiRAE, Rae Systems, Inc., Sunnyvale, CA]. This instrument responds to a wide array of volatile chemicals with ionization potentials within the response range

of the instrument. It does not provide identification of specific chemicals but can be used for comparison of various task-specific exposures. The unit is calibrated with isobutylene and thus all measurements are shown in isobutylene-equivalent concentrations. Real-time personal dust measurements were taken using a PersonalDataRam®, model pDR-1000An/1200 [Thermo Electron Corporation, Franklin, MA] or a HazDust® IV, [Environmental Devices Corp., Plaistow, NH]. These instruments provide relative measures which can be used for comparison of various task-specific exposures. Additional detail on the industrial hygiene sampling methods used during this survey is provided in Appendix A. For statistical analyses, sampling results below detectable limits were assigned a value of one-half of the minimum detectable concentration.

Ventilation Systems Evaluation

We evaluated the ventilation systems in the starter distillate, spray dry, and animal health rooms. We used a thermal anemometer [Velocicalc®, TSI Incorporated, St. Paul, MN] to measure capture velocities of local exhaust ventilation hoods. The capture velocity of the hood is defined as the velocity created by the hood at the point of contaminant generation. A handheld smoke generator [Wizard Stick, Zero Toys, Inc., Concord, MA] was used to assess air capture of local exhaust ventilation hoods. We released smoke at the face of the hood and at points some distance from the face where contaminants would normally be released. If the smoke is captured quickly and directly by the hood, this indicates acceptable hood design and performance. If the smoke is slow to be captured or takes a circuitous route, the hood design is considered marginal.

We checked the pressurization status for all production areas by releasing smoke around the perimeter of the outer door (anteroom door) between each production room and the warehouse area. By releasing smoke at these interfaces, it can be easily observed whether air is moving into or out of the production rooms. Smoke moving out of a production room into the warehouse area would indicate that any potentially hazardous air contaminants in the production room would also move from that room into the warehouse area.

Medical Evaluation

All current workers in all production rooms, the QC laboratory, the warehouse, and in maintenance were invited to participate

in the medical survey. Former workers who had worked in any of the starter distillate, enzymes, flavors, or spray dry rooms during the past five years were also invited. (The names of former workers in these areas and contact information were provided by management.) Informed consent was obtained from all participants. A standardized questionnaire was used to collect information on symptoms, medical history, smoking history, work history, and work-related exposures (Appendix B). The questionnaire included questions from the American Thoracic Society (ATS) standardized adult respiratory symptoms questionnaire [Ferris 1978], the third National Health and Nutrition Examination Survey (NHANES III) [CDC 1996], and the European Community Respiratory Health Survey [Grassi et al. 2003]. In the work history, we collected information about use of fit-tested respirators and tasks for each job held at the plant.

Following ATS guidelines [ATS/ERS Task Force 2005a], a NIOSH technician administered spirometry tests using a dry rolling-seal spirometer interfaced to a personal computer. Spirometry results were compared to reference values generated from NHANES III data [Hankinson et al. 1999]. Each participating worker's largest forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) were selected for analysis.

We defined airways obstruction as an FEV_1/FVC ratio and FEV_1 below their respective lower limits of normal. We defined restriction as an FVC below the lower limit of normal with a normal FEV_1/FVC ratio. A mixed pattern (obstruction and restriction) was defined as an FEV_1/FVC ratio, FEV_1, and FVC below their respective lower limits of normal, and was considered an obstructive abnormality. Workers with airways obstruction were administered albuterol (a medication that relaxes lung airways and is used to treat obstructive lung disease such as asthma) and retested to assess reversibility of the obstruction. We defined reversible obstruction as an improvement in the FEV_1 of at least 12% and at least 200 milliliters (mL) after administration of albuterol [ATS/ERS Task Force 2005b].

Methacholine challenge, a test commonly used in the evaluation of asthma symptoms, causes temporary airways obstruction in individuals. People with sensitive (hyperreactive) airways, such as asthmatic individuals, react to low concentrations of inhaled methacholine, whereas most people react only at higher concentrations. Workers who did not show evidence of airways

obstruction on initial spirometry testing were allowed to breathe increasingly higher concentrations of methacholine; spirometry was repeated after each administered dose. We defined airways hyperreactivity as a drop in FEV_1 of at least 20% following the administration of methacholine at a dosage of 16 milligrams (mg)/mL or less [ATS 2000]. We provided survey participants with their individual test results in letters mailed to their home addresses approximately one month after the survey.

Statistical Analyses

For statistical analyses, we grouped current workers according to work history as follows: 1) current workers with potential exposure to flavoring-related chemicals (in starter distillate, enzymes, flavors, or spray dry rooms, QC laboratory, or in maintenance work ("flavoring workers"); 2) workers currently working in animal health or human health rooms ("bacterial products workers"); and 3) workers with likely lower current exposures ("warehouse workers").

We compared the percentages of workers with spirometry test abnormalities and self-reported respiratory disease and symptoms among different worker groups and tested whether these differences were statistically significant with Fisher's exact test. We defined a statistically significant result (i.e., the difference was unlikely to be a random or chance occurrence) as a probability (*p* value) of less than 0.05.

Industrial Hygiene Survey

Predominant VOCs in Air

Table C1 in Appendix C provides semi-quantitative air sampling data identifying the predominant VOCs detected in different areas of the plant using thermal desorption tubes. In the starter distillate room, diacetyl was the predominant VOC on both days of sampling; other predominant chemicals were acetic acid, diethylphthalate, dimethylphthalate, and phthalic anhydride. (Diethylphthalate and dimethylphthalate were also detected on some of the control blank samples.) Diacetyl was a predominant chemical in the enzymes room during the bottling of starter distillate. The flavors room had a more variable VOC profile on different days due to the production of different cheese and flavoring products. Butyric acid was the predominant VOC detected during the three days of air sampling in the flavors room; diacetyl was a predominant chemical on two of the three days. In the spray dry room, diacetyl was one of the predominant VOCs detected during three different work shifts when powdered flavors were produced using diacetyl or starter distillate; diacetyl was also predominant during one work shift when cleanup was performed following production. Acetic acid, methyl ethyl ketone, furfural alcohol, cyclohexanone, and isopentane were also predominant VOCs in the spray dry room. In the QC laboratory, 1-butoxy-2-propanol, pentane, and diacetyl were among the predominant VOCs detected during one day of air sampling. Diacetyl was a predominant VOC in an area sample obtained in the warehouse at the end of the hallway across from the flavors room. In one of the animal health small packaging rooms, the predominant VOCs were methyl ethyl ketone, 3-buten-2-one, and diethylphthalate; diacetyl was not detected in the one sample collected from this area on a day when starter distillate was used in the adjacent spray dry room (See Figure 1). In summary, diacetyl was a predominant chemical in 11 of 13 samples from different plant areas during 4 days of sampling. The animal health small packaging room was the only area of those sampled where diacetyl was not detected or identified as a predominant VOC.

Average VOC Air Concentrations

Time-weighted average (TWA) air concentrations of total VOCs from full-shift area samples are presented in Table 2. The highest VOC concentrations were seen in the spray dry room (mean concentration 0.30 milligrams per cubic meter of air [mg/m^3]; highest concentration 0.58 mg/m^3). The flavors room had a mean VOC concentration of 0.11 mg/m^3; and a high of 0.22 mg/m^3. The starter distillate room had a mean VOC concentration of 0.05 mg/m^3 and a high of 0.11 mg/m^3. The one sample collected from the warehouse had a mean VOC concentration of 0.15 mg/m^3.

Table 2. Full-shift TWA VOC concentrations[1] by plant area

Plant Area	N	Mean	STD	GM	GSD	Min	Max
Starter Distillate	3	0.05	0.05	0.03	4.12	ND	0.11
Enzymes[2]	2	0.02	0.01	0.02	1.75	ND	0.03
Flavors	4	0.11	0.09	0.07	4.87	ND	0.22
Spray Dry	5	0.30	0.21	0.24	2.20	0.10	0.58
Warehouse	1	0.15	-	0.15	-	0.15	0.15

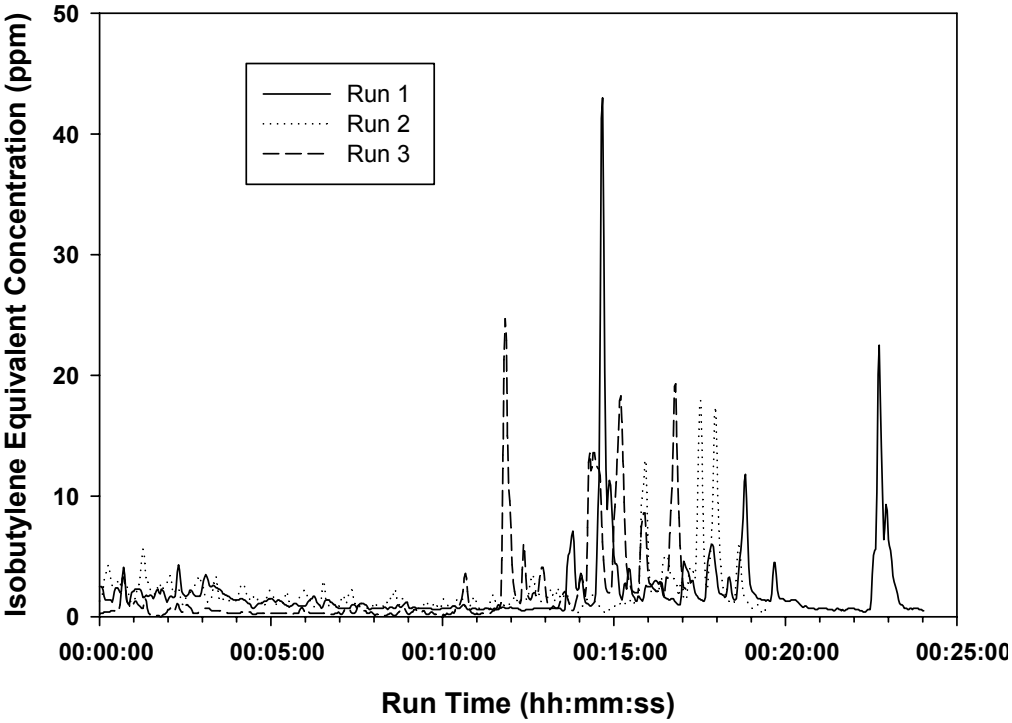
[1] Concentrations in mg/m^3.
[2] On day that workers packaged 1X starter distillate.
TWA – Time-weighted average; GM – geometric mean; GSD – geometric standard deviation; STD – standard deviation; Min – minimum; Max – maximum.
ND – below detectable limits in air, approximately 0.02 ppm depending on sample value.

Real-time VOC Air Concentrations

Starter Distillate Room

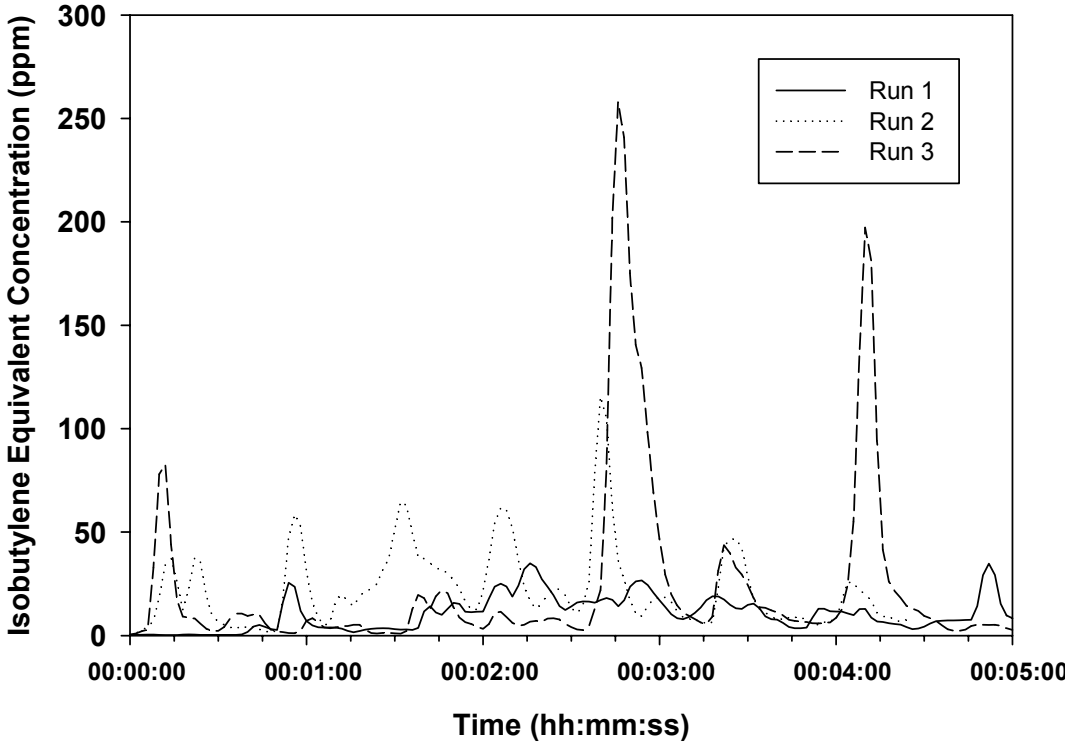
Real-time VOC exposure monitoring with a PID was performed on the starter distillate room worker during production activities, which included filling of the stills with fermented milk stock and manual transfer of starter distillate. Measurements during the filling of the stills ranged from 0.1 to 41 ppm, isobutylene equivalent (Figure 2). The peak exposures were recorded 11 to 23 minutes into the process. We were unable to reconstruct what work tasks corresponded to these peaks.

Figure 2. Real-time measurements of personal VOC concentrations for a worker in the starter distillate room during filling of the stills with fermented milk stock (three operations of filling the stills are overlaid on one graph), December 3, 2007



During manual transfer of the starter distillate, the VOC concentrations were generally higher than during other tasks, with a peak of approximately 250 ppm isobutylene equivalent measured during the third run (Figure 3). During this activity, the worker wore a half-face elastomeric respirator with organic vapor cartridges. Instantaneous area measurements of VOC concentrations near the individual stills cycled up and down; measurements up to 500 ppm isobutylene equivalent were recorded. PID measurements from this area indicated that the interface between the distillation unit outlet and the collection vessel did not form a good seal and allowed the release of VOCs into room air.

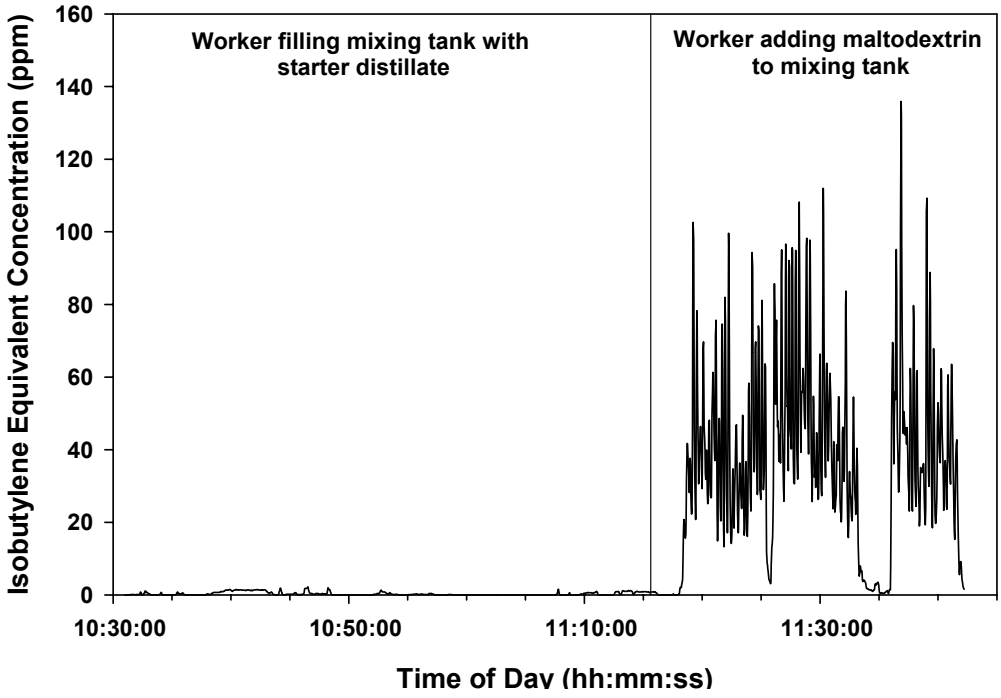
Figure 3. Real-time measurements of personal VOC concentrations for a worker in the starter distillate room during the manual transfer of the starter distillate (three transferring operations are overlaid on one graph), December 3, 2007



Spray Dry Room

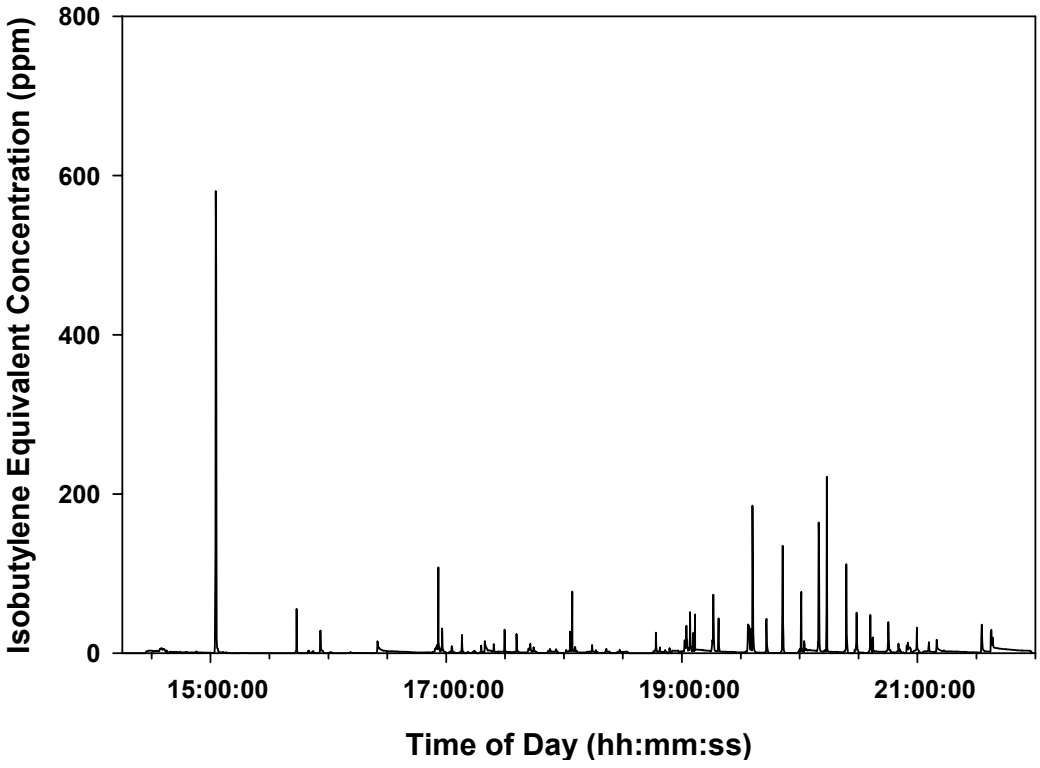
Real-time personal exposure monitoring was performed while a worker prepared the slurry feed for ESD-50X (Encapsulated Starter Distillate 50X) and during product packaging activities. In the preparation of the slurry feed, the worker used a forklift to position a 280-gallon tote of starter distillate above the mixing tank. The worker then opened the discharge valve and moved away from the tank opening and remained away until the container had drained completely. After this, the worker added 68 bags of maltodextrin to the starter distillate in the mixing tank. Worker VOC exposure measurements during the preparation of the slurry feed ranged from 0-136 ppm isobutylene equivalent. The initial addition of starter distillate resulted in minimal VOC exposure because the worker was mostly positioned away from the mixing tank during this operation. The highest concentrations were measured during the addition of the bags of maltodextrin to the mixing tank after starter distillate had been poured into the tank (Figure 4).

Figure 4. Real-time measurements of personal VOC concentrations for a worker in the spray dry room during the preparation of the slurry feed for ESD-50X, December 3, 2007



Additional real-time VOC monitoring of a spray dry worker during slurry preparation and packaging activities for Natural Butter 50X on second shift showed some transient peak concentrations (see Figure 5). The large peak during the early part of the shift most likely occurred when the worker obtained a sample of the mixture from the mixing tank. The series of smaller, yet still substantial, peaks later in the shift most likely occurred during product packaging activities.

Figure 5. Real-time measurements of personal VOC concentrations for a worker in the spray dry room during slurry preparation and packaging activities for Natural Butter 50X, December 4, 2007



Average Ketone Air Concentrations

Modified OSHA Method PV 2118 (diacetyl)

Personal and area air concentrations of diacetyl from full-shift, TWA samples collected using the modified OSHA Method PV 2118 are presented by plant area in Table 3.

Table 3. Full-shift TWA diacetyl air concentrations[1] by sample type and location using the modified OSHA Method PV 2118

Plant Area	Type	N	Mean	SD	GM	GSD	Min	Max
Starter Distillate	Personal	3	1.78	0.112	1.78	1.06	1.71	1.91
	Area	15	1.13	0.405	1.06	1.43	0.532	2.09
Enzymes[2]	Personal	2	0.186	0.018	0.186	1.10	0.174	0.199
	Area	2	0.040	0.020	0.037	1.69	ND	0.054
Flavors	Personal	5	0.909	0.861	0.329	7.84	ND	1.93
	Area	4	0.599	0.697	0.171	9.09	ND	1.44
Spray Dry	Personal	7	1.53	1.44	0.756	5.79	ND	4.30
	Area	5	1.31	0.773	1.07	2.27	0.270	2.44
Quality Control	Personal	2	1.59	2.21	0.265	33.1	ND	3.15
Animal Health	Area	2	ND	-	ND	-	ND	ND
Warehouse	Personal	2	0.052	0.029	0.048	1.80	0.032	0.072
	Area	1	0.207	-	0.207	-	0.207	0.207

[1] Concentrations in parts per million parts air (ppm)..
[2] On day that workers packaged 1X starter distillate.
TWA – Time-weighted average; GM – geometric mean; GSD – geometric standard deviation; STD – standard deviation; Min – minimum; Max – maximum.
ND – below detectable limits in air, approximately 0.02 ppm depending on sample volume.

The starter distillate room had the highest TWA diacetyl exposures, with a mean of 1.78 ppm from three personal samples; the mean TWA diacetyl air concentration from 15 area samples was 1.13 ppm (range 0.532 ppm to 2.09 ppm). Starter distillate was produced in this room for two full days (December 3 and 4) and for one-half day on December 5 (production was at near full capacity on all three days). The diacetyl content of the starter distillate produced on these days was approximately 4 to 4.5 % by weight. The worker in this room used a full-facepiece, negative-pressure respirator with combined organic vapor and particulate cartridges during starter distillate pours; respiratory protection was not used for other tasks.

In the spray dry room, full-shift TWA diacetyl air concentrations from personal samples ranged from below detectable levels (less than approximately 0.02 ppm) to a high of 4.30 ppm. A 50X encapsulated starter distillate (ESD) powder was produced in this room on December 3 and a natural butter flavored powder (50X) was produced on December 4. The butter flavored powder was produced using pure concentrated diacetyl, whereas the ESD used starter distillate in which diacetyl was a component. Both products contained substantial quantities of diacetyl (a total of approximately 90 pounds) in the liquid formulation that was subsequently spray dried on December 3 and 4. The mean TWA diacetyl air concentration from area samples in the spray dry room was 1.31 ppm (range 0.270 to 2.44 ppm). A 3rd-shift worker who performed cleaning activities following production of ESD and natural butter flavor powders had a TWA diacetyl exposure of 1.68 ppm, indicating that diacetyl exposure can occur during spray dryer cleaning activities. The spray dry operator used a full-facepiece, negative-pressure air-purifying respirator with combined organic vapor and particulate cartridges when handling liquid diacetyl or starter distillate; he used an N-95 filtering-facepiece respirator during the bagging of powdered flavorings.

In the flavors room, the mean TWA diacetyl air concentration from full-shift personal samples was 0.909 ppm; concentrations ranged from below detectable levels (less than approximately 0.02 ppm) to 1.93 ppm. The mean TWA air concentration from full-shift area samples was 0.599 ppm (range from below detectable levels to 1.44 ppm). Diacetyl was reportedly used in the flavors room on two of the four days sampled (December 5 and 6). Short-term, task-based samples for diacetyl were collected on December 5 and 6 during mixing operations when workers handled diacetyl and starter distillate. A short-term (113 minute) diacetyl air concentration of 2.9 ppm was measured on December 5 when a worker prepared a flavor containing approximately 50 pounds of 15X starter distillate. On December 6, a short-term (133 minute) diacetyl air concentration of 17.1 ppm was measured when a worker prepared a flavor using approximately 9 pounds of 45X starter distillate and approximately 0.05 pounds of pure diacetyl. Workers in the flavors room used respiratory protection according to company policies for the specific chemicals being used in the flavoring formulation; a full-facepiece, negative-pressure air-purifying respirator with combined organic vapor and particulate cartridges was used when handling liquid diacetyl or starter distillate.

In the enzymes room on a day when workers packaged 1X starter distillate, two personal air samples showed TWA diacetyl air concentrations of 0.174 and 0.199 ppm, respectively (mean 0.186 ppm). The processing of 15X or 45X starter distillate in the enzymes room would likely have resulted in higher diacetyl concentrations; we did not have the opportunity to perform air sampling during packaging operations with these more concentrated starter distillate products.

In the QC laboratory, two personal air samples showed a mean TWA diacetyl air concentration of 1.59 ppm. Workers handled starter distillate on both days of sampling. On December 3, when the starter distillate tested in the QC laboratory included 1X, 15X, and undiluted starter distillate, the TWA diacetyl concentration was below detectable levels; on December 4, when 15X and undiluted starter distillate were tested, the TWA diacetyl concentration was 3.15 ppm. The QC worker did not use respiratory protection.

Other plant areas had lower diacetyl concentrations from personal and area air samples; the two area samples collected from the animal health area were below detectable levels for diacetyl (less than approximately 0.02 ppm).

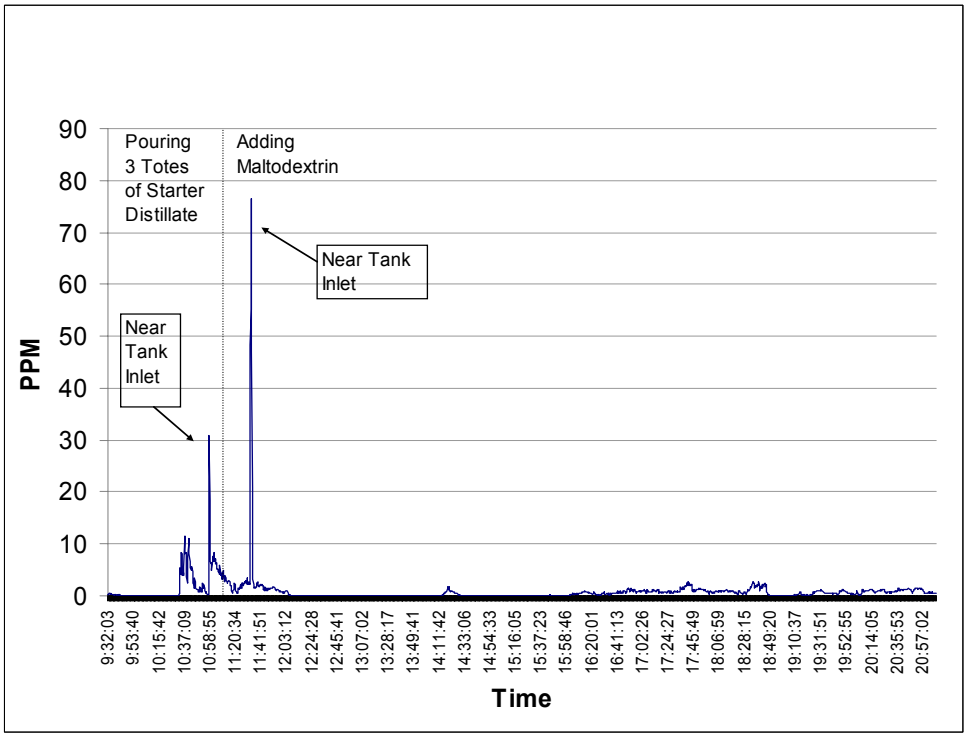
NIOSH Methods 2557 and 2558 (Diacetyl and Acetoin)

Table C2 in Appendix C shows mean TWA air concentrations of diacetyl and acetoin from full-shift personal and area samples collected using NIOSH Methods 2557 (diacetyl) and 2558 (acetoin). In general, the diacetyl concentrations measured using NIOSH Method 2557 were lower than those collected using the modified OSHA method; this is likely due to the effect of humidity on diacetyl recoveries with NIOSH Method 2557, as described on the *NIOSH Flavorings-Related Lung Disease* Topic Page at: http://www.cdc.gov/niosh/topics/flavorings/. (Table C3 in Appendix C provides mean air temperatures, relative humidity, and absolute humidity by plant location and date.) Acetoin concentrations (from air samples obtained on the same dates and in the same plant areas as diacetyl) were lower than diacetyl. The highest acetoin concentration, 0.089 ppm, was measured in a personal sample from a worker in the starter distillate area.

Real-Time Measurements of Diacetyl Air Concentrations

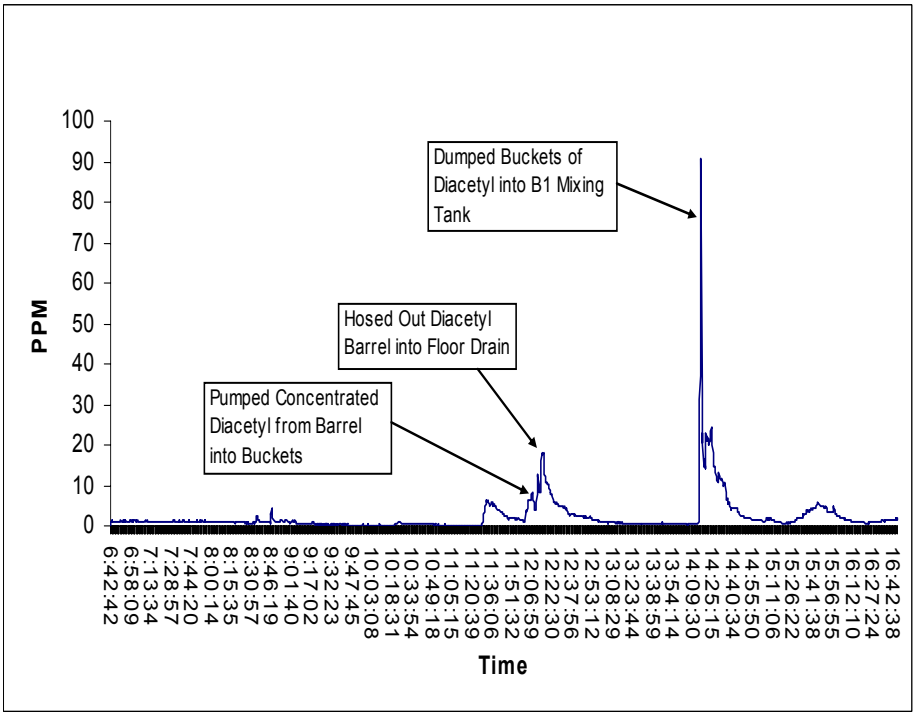
Figures 6–8 present real-time diacetyl air concentrations measured by FTIR in the spray dry (December 3 and 4) and starter distillate (December 5) rooms. On December 3 (Figure 6), a 50X encapsulated starter distillate powder was produced in the spray dry room. At the start of this process, approximately 280 gallons of starter distillate were poured into the B1 mixing tank. During this pouring, the FTIR was positioned near the B1 mixing tank and the sampling inlet was positioned in the worker's breathing zone when he was in the room. A peak diacetyl concentration of approximately 31 ppm was measured at the B1 tank inlet during the starter distillate pour. A second peak concentration of approximately 80 ppm was measured at the tank inlet as bags of maltodextrin were manually emptied into the mixing tank after the addition of starter distillate. Following the initial mixing steps, the FTIR was repositioned next to the bagging operations for the remainder of the first and second shifts. Diacetyl concentrations throughout the remainder of the two shifts were lower, as seen in Figure 6.

Figure 6. Real-time measurements of diacetyl air concentrations measured by FTIR in the spray dry room on December 3, 2007 during the production of butter flavored powder using starter distillate (50X)



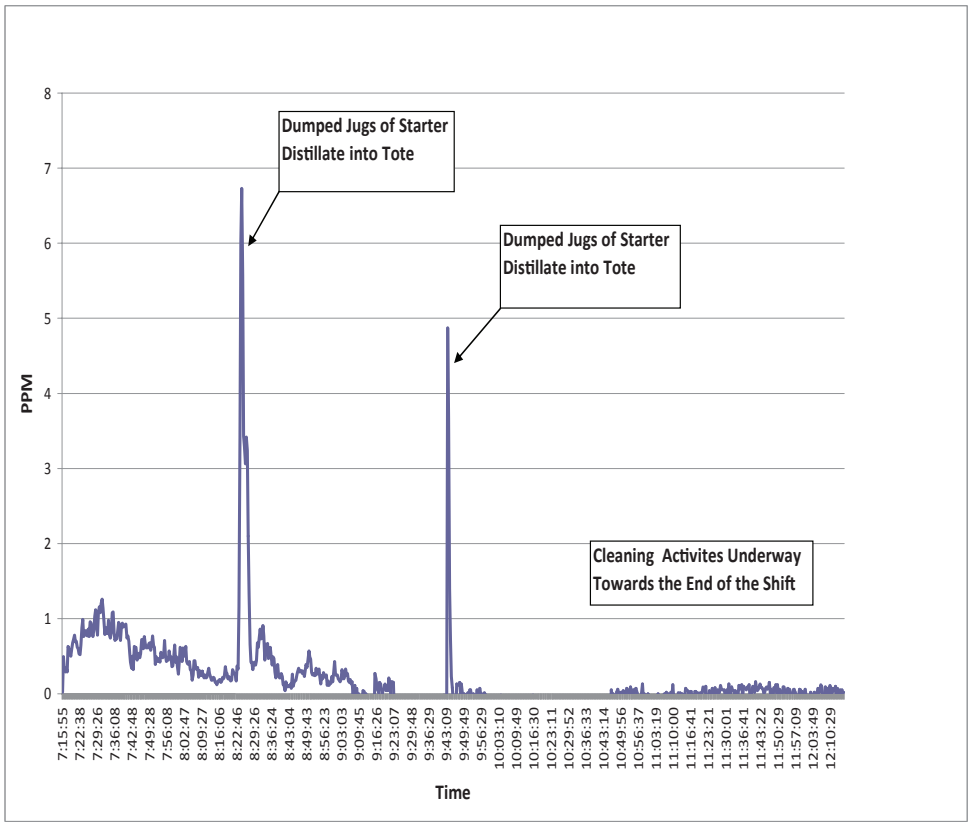
On December 4, a natural butter flavored 50X powder was produced in the spray dry room using concentrated diacetyl from a food ingredient supplier. A worker pumped concentrated diacetyl from a large barrel into three metal buckets; these buckets had lids. A peak concentration of approximately 8 ppm diacetyl was measured in the worker's breathing zone during this activity (Figure 7). The worker then cleaned the barrel of diacetyl using water from a hose; the barrel contents were dumped into a floor drain in the center of the room. This cleaning activity resulted in a higher diacetyl concentration (approximately18 ppm) in the worker's breathing zone. At approximately 2:15 pm on December 4, the three buckets of concentrated diacetyl were dumped into the B1 mixing tank; this produced a peak diacetyl concentration of approximately 90 ppm in the general work area. (On this day, the maltodextrin was added prior to the diacetyl, compared to the previous day where maltodextrin was added after the starter distillate.) The 3 buckets of concentrated diacetyl were added to the B1 mixing tank at about the time of the plant shift change and we were not present to observe this task (or to position the FTIR sampling inlet in the workers breathing zone); consequently, for this measure, the FTIR measurement was for the general area next to the mixing tank.

Figure 7. Real-time measurements of diacetyl air concentrations measured by FTIR in the spray dry area on December 4, 2007 during the production of a butter flavored powder using concentrated diacetyl



On December 5, FTIR sampling was performed in the starter distillate room (Figure 8). Peak diacetyl concentrations of approximately 5 and 7 ppm were observed when the operator manually transferred starter distillate. The FTIR sampling inlet was positioned in the worker's breathing zone for these two transfers; the FTIR was operated as a general area sampler at other times during this shift. Between the transfers, diacetyl concentrations in the room ranged from below detectable levels to approximately 1 ppm. Starter distillate was not produced during the second half of the shift on December 5; instead, cleaning operations were underway and diacetyl concentrations were lower (sometimes below detectable limits) for the rest of the work shift.

Figure 8. Real-time measurements of diacetyl air concentrations measured by FTIR in the starter distillate room during starter distillate production on December 5, 2007



Aldehyde Air Concentrations

Table 4 shows mean TWA air concentrations of acetaldehyde from full-shift personal and area samples by plant area. The limit of detection was approximately 0.0001 ppm depending on sample air volume. The starter distillate room had the highest mean personal acetaldehyde exposure at 3.49 ppm. The highest mean area acetaldehyde air concentrations were in starter distillate and spray dry (2.33 and 2.24 ppm, respectively). All benzaldehyde concentrations were below detectable limits (approximately 0.0003 ppm depending on sample volume) or quantifiable limits (approximately 0.002 ppm depending on sample volume).

Table 4. Full-shift TWA acetaldehyde air concentrations[1] by sample type and location

Plant Area	Type	N	Mean	SD	GM	GSD	Min	Max
Starter Distillate	Area	3	2.33	1.65	1.94	2.14	0.903	4.14
	Personal	1	3.49	-	3.49	-	-	-
Enzymes[2]	Area	2	0.044	0.034	0.037	2.40	0.020	0.069
Flavors	Area	5	1.24	1.42	0.327	11.6	0.011	3.52
	Personal	1	0.058	-		-	-	-
Spray Dry	Area	5	2.24	1.19	1.57	3.48	0.170	3.05
Warehouse	Area	1	0.039	-	0.039	-	-	-

[1] Concentrations in parts per million parts air (ppm).
[2] Enzymes room was sampled on the day that workers packaged 1X starter distillate.
TWA – Time-weighted average; GM – geometric mean; GSD – geometric standard deviation;
STD - standard deviation; Min - minimum; Max - maximum.

Organic Acid Air Concentrations

All of the air samples for caproic, caprylic, and lactic acids were below detectable limits; the limits of detection were 0.14, 0.11, and 0.05 ppm, respectively. The air samples for acetic, butyric, and propionic acids were below detectable or quantifiable limits; the detection and quantification limits for these organic acids were 0.24 and 0.78 ppm for acetic acid, 0.12 and 0.40 ppm for butyric acid, and 0.07 and 0.22 ppm for propionic acid.

Inorganic Acid Air Concentrations

One personal and six area samples were collected for nitric and phosphoric acids during cleaning-in-place (CIP) operations. All the air samples for phosphoric acid were below detectable limits (approximately 0.03 ppm). All of the air samples for nitric acid

were below detectable (approximately 0.03 ppm) or quantifiable (approximately 0.07 ppm) limits.

Comparison to Existing Exposure Limits

Table C4 in Appendix C lists the chemicals that we measured with air sampling and provides the regulatory and/or recommended exposure limits that are currently available. None of the air concentrations we measured exceeded any currently available regulatory or recommended exposure limits. For several of these chemicals, regulatory or recommended exposure limits do not exist.

Average Respirable Dust Air Concentrations

Mean respirable dust air concentrations from gravimetric analyses of full-shift personal and area samples are presented by plant location in Table 5. The highest mean TWA respirable dust air concentrations from personal samples were measured in the animal health and human health rooms (0.517 and 0.401 mg/m^3, respectively); the highest TWA respirable dust air concentration was measured in animal health (1.25 mg/m^3). The animal health air samples were collected in the large and small packaging rooms. The mean TWA respirable dust air concentration from personal samples in the spray dry room was 0.175 mg/m^3. All respirable dust air concentrations measured in the warehouse and in the starter distillate, enzymes, and flavors rooms were less than 0.06 mg/m^3.

Table 5. TWA respirable dust concentrations[1] by location

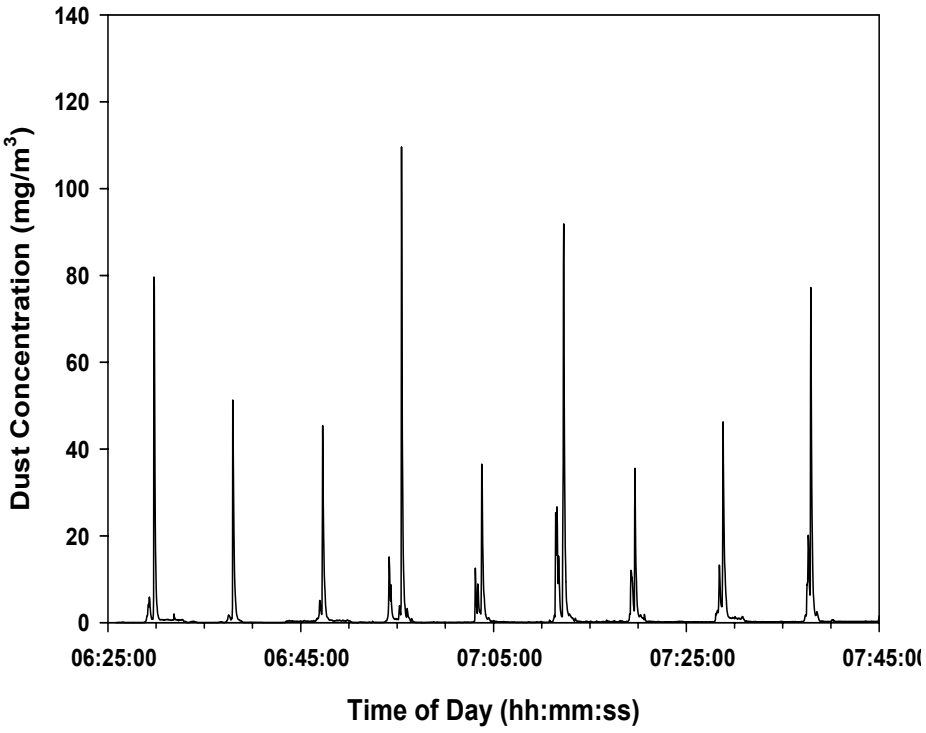
Plant Area	Type	N	Mean	SD	GM	GSD	Min	Max
Starter Distillate	Area	3	0.031	0.022	0.027	1.95	ND	0.057
Enzymes	Area	2	ND	-	ND	-	ND	ND
Flavors	Area	4	0.029	0.017	0.026	1.69	ND	0.054
Spray Dry	Area	5	0.102	0.056	0.083	2.35	ND	0.171
	Personal	5	0.175	0.178	0.094	4.08	ND	0.454
Animal Health	Area	4	0.203	0.140	0.158	2.50	0.044	0.364
	Personal	8	0.517	0.455	0.279	4.28	ND	1.25
Human Health	Area	1	ND	-	ND	-	ND	ND
	Personal	2	0.401	0.264	0.356	2.04	0.215	0.588
Warehouse	Area	1	ND	-	ND	-	ND	ND

[1] Concentrations in mg/m^3.
TWA – Time-weighted average; GM – geometric mean; GSD – geometric standard deviation; STD – standard deviation; Min – minimum; Max – maximum.
ND – Below detectable limits, less than approximately 0.037 mg/m^3 depending on sample volume.

Real-time Measurements of Dust Exposures

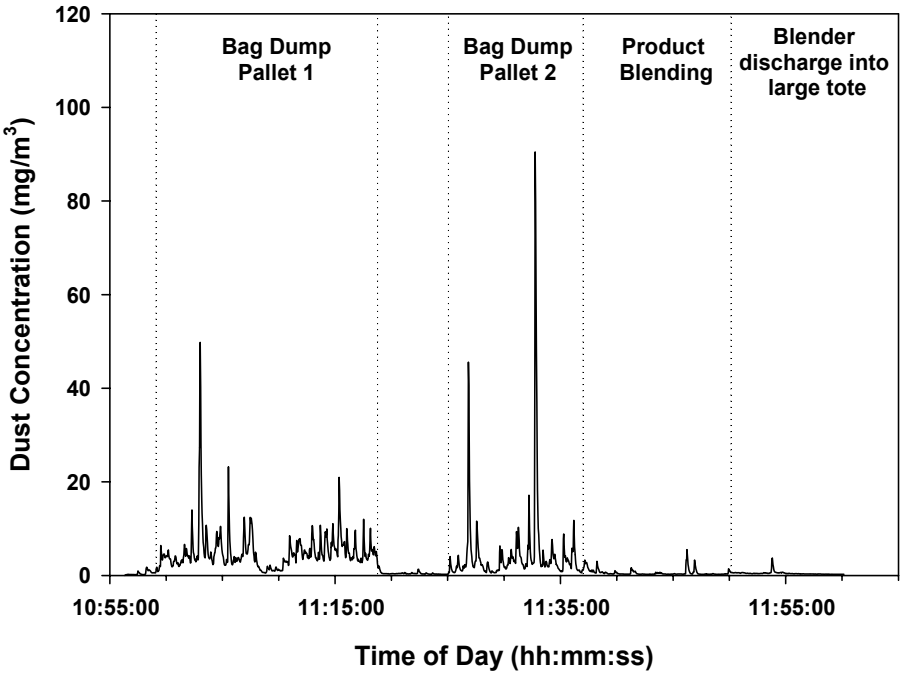
Real-time measurements of personal dust exposures in the spray dry room during product packaging activities ranged from 0.02 to 110 mg/m^3 (Figure 9). During packaging, the worker manually places a bag on the discharge chute under the hopper, then generally leaves the room to monitor (on a computer in an adjacent room) discharge of a defined amount of product from the hopper into the bag. The worker then returns to the spray dry room to manually scoop out or add product to the bag to adjust the final weight, and then ties off the inner poly liner, stitches the outer bag, and places the bag on a pallet. The sequence is repeated approximately every 7 to 8 minutes. The peaks in dust concentration seen in Figure 9 correspond to the worker manually adjusting the final weight of the bag and sealing the bag. Sources of exposure during this process include dust generated during the discharge of product into the bag and the handling and tying-off of the bag, and dust emitted from the Torit® local exhaust ventilation unit.

Figure 9. Real-time measurements of dust exposure for a worker in the spray dry room during the packaging of ESD-50X, December 4, 2007



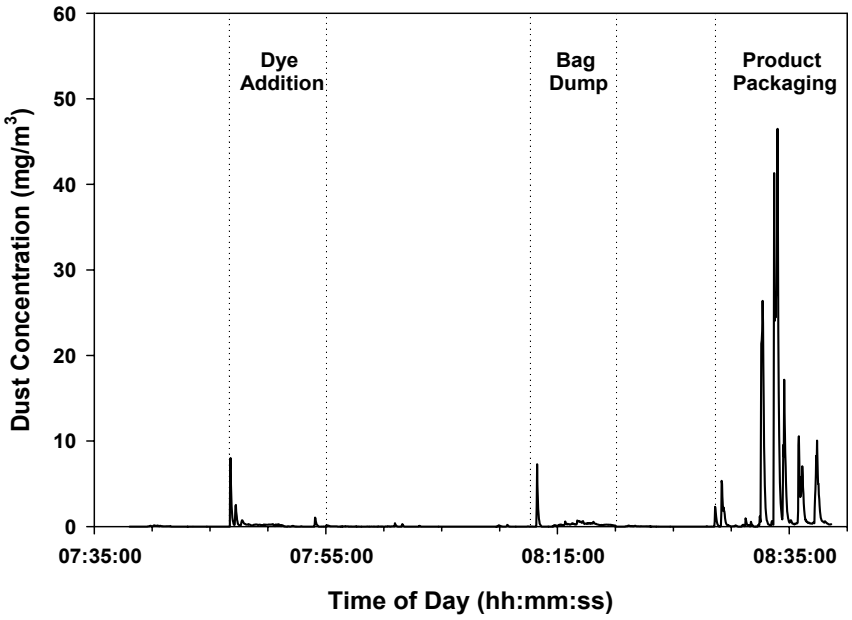
In the animal health large packaging room, real-time personal dust exposure measurements ranged from 0.03 to 90 mg/m^3 during bag dumping, blending, and blender discharge activities (Figure 10). The highest concentrations were measured during bag dumping. A gap between the blender and its lid allows substantial amounts of dust to escape into the work area during bag dumping. When the lid was clamped to the blender, visible dust emissions diminished, although real-time exposure monitoring still indicated peak dust concentrations during bag dumping. Substantial amounts of visible dust were released during the discharge of the blender into the large totes. Worker dust exposure was low during this task, however, because the worker moved away from the powder discharge point when emptying the blender. Real-time measurements of personal dust air concentrations ranged from 0.14 to 2.81 mg/m^3 during the packaging of the final product.

Figure 10. Real-time measurements of dust exposure for a worker in the large packaging room during bag dumping, blending, and blender discharge activities, December 4, 2007



In the intermediate packaging room, real-time personal dust exposure measurements ranged from 0 to 46 mg/m^3 during the preparation of BioPlus® and packaging in paper bags holding 25 pounds of final product (Figure 11). The production cycle included addition of dye into the blender, dumping of bulk powder carrier material, and packaging of the final product. Product packaging included discharge of powders from the blender through a valve into paper bags. The highest dust concentrations were associated with packaging of the final product. Dust was seen to escape when the powder dropped into the bag and when the operator shook the chute to make powder fall into the bag.

Figure 11. Real-time measurements of dust exposure for a worker in the intermediate packaging room during dye addition, bag dumping, and product packaging activities for BioPlus®, December 5, 2007



Respiratory Protection Observations

Workers in the spray dry room used N-95 filtering-facepiece respirators during bagging operations; however, workers had not been fit-tested for these respirators, and temporary workers and some permanent workers in flavoring production areas had not been included in the respiratory protection program. Other deficiencies in the respiratory protection program included intermittent usage of respirators in flavoring production rooms, and workers with beards using tight-fitting respirators. (A beard

prevents a tight seal between the respirator and the worker's face, allowing the worker to inhale unfiltered air.)

Ventilation Survey

Production Room Air Pressures Relative to the Warehouse

The results of room pressurization tests are shown in Table 6. Some production rooms had negative air pressure relative to the warehouse; this should prevent migration of contaminants out of these rooms. The exceptions were the flavors, spray dry, and human health rooms. The flavors and spray dry rooms were neutral to positive relative to the warehouse; contaminants in the air of these areas could at times migrate into the warehouse. The air pressure in the human health room is by design positive relative to the warehouse to prevent migration of contaminants in the air of the warehouse into this room where products intended for human food are produced; contaminants in the air of this room could at times migrate into the warehouse.

Table 6. Room air pressure relative to adjacent areas

Plant Area	Air Pressure Relative to Adjacent Areas
Starter Distillate	Negative relative to warehouse Negative relative to enzyme room
Enzymes	Negative relative to warehouse Positive relative to the starter distillate room
Flavors	**Neutral to positive** relative to warehouse
Spray Dry	**Neutral to positive** relative to warehouse
Animal Health: Large Packaging	Negative relative to warehouse
Animal Health: Intermediate Packaging	Negative relative to warehouse
Animal Health: Small Packaging	Both small packaging rooms were negative relative to warehouse
Human Health	Positive relative to warehouse (by design)

Bold indicates sub-optimal pressurization status.

Spray Dry Room

Air velocity measurements of the Torit® unit taken at the center of the circular hood ranged from 3,300 to 3,400 feet per minute (fpm). Smoke tests showed effective capture up to 12 inches from the hood face. The hood of the Torit® unit was positioned approximately 10 inches from the discharge chute during product packaging. We observed good capture of airborne powder by the Torit® unit during powder discharge into the final product bags. However, measurement of dust concentrations at the exhaust outlet from the Torit® unit indicated that a substantial amount of airborne powder is not removed by the filters and is released back into the spray dry room air. Real-time dust measurements near the exhaust outlet ranged from 0.3 to 0.4 mg/m^3 when no powder was being actively discharged from the spray dryer and up to 13 mg/m^3 when product was being discharged. The filter for the local exhaust unit is reportedly changed out when the unit loses suction, which may occur after a week or a longer time period depending on usage. There is no gauge on the Torit® unit to indicate when the old filter should be replaced with a new filter based on differential pressure.

Animal Health Rooms

In the large packaging room, air velocities at the face of the bag dump station showed an average capture velocity of approximately 70 fpm. Smoke tests showed that air generally moved towards the hood; however, the air velocity was low and the overall capture effectiveness was marginal to poor. The bag dump station sits on top of the blender and the worker stands on the lid of the blender when dumping materials into the blender. There is a gap between the blender lid and the blender which allows substantial amounts of dust to escape during bag dumping. When the lid was clamped to the blender, visible dust emissions diminished.

During packaging of final product in the large packaging room, bags are filled, sealed, and palletized two at a time. Dust was emitted into the air from the top of the bag during filling and when the bag was compressed (to settle ingredients and expel air) prior to sealing. A 6-inch flexible duct with a simple circular hood was positioned approximately 2 feet away from the powder discharge point. The centerline velocity at the duct entrance was 2200 fpm. Smoke released at the powder discharge point was not captured by the hood.

In the intermediate packaging room, air velocities at the face of the bag dump station located on top of the blender showed an average capture velocity of approximately 90 fpm. However, the exhaust airflow was not well distributed across the face of the bag dump station, with air velocities of approximately 130 fpm on one side and 50 fpm on the other side. Smoke tests showed reasonably good capture except at the left side of the bag dump station (due to excessive air turbulence). Airborne dust was released from the bag dump station hood unit into the air of the room during each pulsejet cleaning cycle.

Each of the small packaging rooms has a small annular ventilation hood at the product discharge outlet which is connected to a small HEPA vacuum. These hoods appeared to adequately contain the powder during discharge. Compressed air was used to blow dust off the containers of finished product; the containers were then wiped down with a damp cloth and palletized.

Medical Survey

Participation

Of 40 current workers invited to participate, 34 (85%) took part in the medical survey at the plant in December 2007 (Table 7). Three of ten former production workers who were invited also participated in the medical survey at an off-site location. Most (82%) of the current workers who participated were male. About half were current or former smokers. The average age and work tenure were 42.0 and 5.5 years, respectively

Table 7. Worker demographics by current work area

Demographics	Flavoring Workers[1] (N=15)	Bacterial Products Workers[2] (N=10)	Warehouse Workers (N=9)	All Workers (N=34)
Average age (years)	39.7	42.5	45.4	42.0
Gender, males (%)	13 (87%)	6 (60%)	9 (100%)	28 (82%)
Current and former smokers (%)	8 (53%)	4 (40%)	6 (67%)	18 (53%)
Smoking history (pack-years) Mean Range	 13.8 (1.5–36.6)	 17.3 (0.15–31.5)	 14.3 (3.15–27.0)	 14.7 (0.15–36.6)
Average length of employment (years)	3.9	7.3	6.2	5.5
Participation rate (%)	15 (83%)	10 (91%)	9 (82%)	34 (85%)

[1]Flavoring Workers – workers who currently work in the starter distillate, enzymes, flavors, or spray dry rooms, the QC laboratory, or in maintenance.
[2]Bacterial Products Workers – workers who currently work in the animal health or human health rooms.

Work History

Of the 34 current workers who participated in the medical survey, one currently worked in the starter distillate room, two worked in the enzymes room, five worked in the flavors room, three worked in the spray dry room, two worked in the QC laboratory, two worked in maintenance, 10 worked in the animal or human health rooms, and nine worked in the warehouse.

Of the 34 participating current workers, 14 reported using full- or half-face respirators (for which they had been fit-tested) as follows: the worker who reported ever working in the starter distillate room; three of four workers who reported ever working in the enzymes room; six of nine workers who reported ever working in the flavors room; four of seven workers who reported ever working in the spray drying room; two of four workers who reported ever working in maintenance; two of 12 workers who reported ever working in the animal health rooms; and one of 14 workers who reported ever working in the warehouse. None of the workers who had ever worked in the QC laboratory or in the human health room reported having worn a respirator. (Respirator use was not required by management in the warehouse, in the QC laboratory, or in the animal health or human health rooms.)

With respect to work assignments, one of three workers who reported ever working in the enzymes room reported completing afternoon transfers in the starter distillate room. All six workers who reported ever working in the flavors room reported handling diacetyl; one handled diacetyl daily; two handled it at least once per week; two handled it at least once per month; and one handled it less than once per month. All five workers who reported ever working in the spray dry room reported making encapsulated starter distillate at least once per month; all five also reported making carmine powder; three of the five reported making powdered enzyme-modified dairy products.

Worker Symptoms and Asthma History

Table 8 shows the percentages of flavoring workers, bacterial products workers, and warehouse workers who reported various symptoms on the questionnaire. Work-related eye symptoms were about four times more common among bacterial products workers than among flavoring and warehouse workers combined (p=0.05). Post-hire skin problems were about four times more common among bacterial products workers than among flavoring and warehouse workers combined (p=0.03). Three of ten bacterial products workers reported monthly or more frequent occurrence of unusual tiredness, fatigue, fever, chills, or night-sweats. Forty percent of both flavoring workers and bacterial products workers reported chest (lower respiratory) symptoms from work exposures compared to 22% of warehouse workers.

Table 8. Worker symptoms

Health Outcome	Flavoring Workers[1] (N=15)	Bacterial Products Workers[2] (N=10)	Warehouse Workers (N=9)
Wheeze in the last 12 months	4 (27%)	2 (20%)	1 (11%)
Usual cough on most days for three consecutive months or more during the year	0 (0%)	2 (20%)	0 (0%)
Shortness of breath when hurrying on level ground or walking up a slight hill	0 (0%)	2 (20%)	1 (11%)
Work-related lower respiratory symptoms during the last 12 months[3]	1 (7%)	3 (30%)	1 (11%)
Work-related nasal symptoms (stuffy, itchy, runny, burning, or stinging nose) during the last 12 months	4 (27%)	3 (30%)	2 (22%)
Work-related eye symptoms (watery, itchy, burning, or stinging eyes) during the last 12 months	1 (7%)	3 (30%)	1 (11%)
Post-hire skin problem	2 (13%)	5 (50%)	1 (11%)
Cough, shortness of breath, chest tightness, or wheezing brought on by work chemicals or substances	6 (40%)	4 (40%)	2 (22%)
At least monthly fever, chills, night sweats or monthly unusual fatigue during the last 12 months	2 (13%)	3 (30%)	1 (11%)

[1]Flavoring Workers – workers who currently work in the starter distillate, enzymes, flavors, or spray dry rooms, in the QC laboratory, or in maintenance.
[2]Bacterial Products Workers – workers who currently work in the animal health or human health rooms .
[3]Work-related lower respiratory symptoms: Feeling of tightness in the chest in the last 12 months that was better away from work; OR Attack of shortness of breath on awakening in the last 12 months that was better away from work; OR Wheezing in the last 12 months that was better away from work? OR Attack of asthma in the last 12 months that was better away from work.

Among nine current and former workers in flavoring production rooms who reported chest symptoms from work exposures, three workers reported chest symptoms from enzymes; three workers reported chest symptoms from acids; one worker reported chest symptoms from diacetyl; and one worker reported chest symptoms from encapsulated starter distillate. One worker reported eye burning from diacetyl and starter distillate. Another reported developing a skin rash from a "sanitizing solution." Two workers reported nasal symptoms from exposure to carmine or paprika. Two of the four workers who worked in the animal health rooms and reported chest symptoms from exposures said these occurred with exposure to Biomax® and other powders. Three workers in different production rooms reported either chest symptoms or nasal and eye symptoms from exposures to Matrixx™.

Eight workers reported ever having physician-diagnosed asthma (Table 9); all of them indicated that their asthma was diagnosed before they started work at the plant; five of them (all of them flavoring workers) indicated that their asthma was still active. No workers reported post-hire recurrence of pre-existing asthma that had been inactive for two or more years prior to hire.

Table 9. Physician-diagnosed asthma and medication use as reported by workers

Health Outcome	Flavoring Workers[1] (N=15)	Bacterial Products Workers[2] (N=10)	Warehouse Workers (N=9)
Ever diagnosed by a physician with asthma	6 (40%)	2 (20%)	0 (0%)
Currently active physician-diagnosed asthma	5 (33%)	0 (0%)	0 (0%)
Current use of asthma medication	3 (20%)	0 (0%)	0 (0%)
Post-hire physician-diagnosed asthma; or, post-hire recurrence of asthma that had been inactive for 2 years prior to hire	0 (0%)	0 (0%)	0 (0%)

[1]Flavoring Workers – workers who currently work in the starter distillate, enzymes, flavors, or spray dry rooms, QC laboratory, or maintenance.
[2]Bacterial Products Workers – workers who currently work in the animal health or human health rooms.

Spirometry Results

Of 28 current workers tested with spirometry, results for three (11%) were interpreted as abnormal; one (3.6%) had airways obstruction (mixed pattern) and two others (7%) had restriction without apparent obstruction. A spirometric interpretation of restriction can sometimes occur in the setting of obesity if the

individual being tested can not fully expand his/her lungs on inhalation; consequently, FVC is abnormally low. Defining obesity as a BMI greater than 30, two of the three workers with abnormal spirometry did not have obesity and the other had borderline obesity. Both workers with restriction currently worked in the animal health rooms and neither had ever worked in any of the flavoring production rooms. One worker with restriction reported shortness of breath on exertion, wheezing or whistling in the chest, weekly unusual tiredness or fatigue, and monthly fever, chills, or night-sweats during the past year. These symptoms, along with restriction on spirometry, can occur with hypersensitivity pneumonitis. The other worker with restriction did not report chest or systemic symptoms. The worker with airways obstruction on spirometry worked in flavoring production areas, though never in the animal or human health rooms. The airways obstruction did not fully resolve following administration of a bronchodilator, consistent with fixed airways obstruction. This worker had a history of asthma and also reported having had a cough for several days prior to spirometry testing.

Of 11 current workers with a normal initial spirometry test who completed a methacholine challenge test, one worker experienced a 20% drop in FEV_1 at a dose of 3.6 mg/mL and another experienced a 20% drop in FEV_1 at a dose of 9.2 mg/mL. Consistent with this objectively determined airways hyperreactivity, both of these workers had physician-diagnosed asthma before they came to work at the plant. One had current asthma symptoms that were not worse at work, and the other did not have current asthma symptoms. Neither was currently taking asthma medication.

All 3 former workers who were tested had normal spirometry and methacholine challenge test results.

Background on Flavoring-Related Lung Disease

NIOSH investigators have identified evidence of severe lung disease consistent with bronchiolitis obliterans in workers exposed to butter flavoring chemicals at five of six investigated microwave popcorn plants [Kanwal et al. 2003; NIOSH 2003; NIOSH 2004a; NIOSH 2004b; NIOSH 2006]. The workers at highest risk were those who prepared mixtures of butter flavorings and soybean oil in large heated tanks. Other workers near these tanks were also at risk. NIOSH is aware of similarly affected production workers at eight flavoring manufacturing plants [CDC 2007; Kanwal 2008; NIOSH 1986; NIOSH 2007; NIOSH 2008a].

Severe airways obstruction as seen in bronchiolitis obliterans is rare in the general population, affecting approximately one in a thousand people [CDC 1996]. In NIOSH medical surveys at flavoring plants and microwave popcorn plants, the workers with severe fixed airways obstruction were usually those workers with the highest exposures to flavoring chemicals from production and packaging of the product. Warehouse and office workers who had never done production work were not affected. The number of production workers at these plants is generally small (5 to 20 in most flavoring plants); finding one or more production workers with severe airways obstruction in such small groups highlights the exposure-related risk these workers can face.

Many flavoring chemicals are highly irritating to the eyes, respiratory tract, and skin. Although they are assessed as safe to consume in small amounts in food, little is known about the potential of most of these chemicals to cause lung disease if inhaled by workers [NIOSH 2004c]. Laboratory exposure studies using mice and rats have shown that the butter flavoring chemical diacetyl can cause severe injury to the lining of the respiratory tract [Hubbs et al. 2008; Morgan et al. 2008]. Rats that inhaled butter flavoring vapors had more airway damage than rats that inhaled pure diacetyl, even though the rats breathed similar diacetyl air concentrations in each study [Hubbs et al. 2002; Hubbs et al. 2008]. This indicates that some of the other chemicals used in butter flavorings may also have potential to cause lung disease.

NIOSH Findings in Flavoring Production Areas at the Chr. Hansen Plant

While we are not presently aware of severe fixed airways

obstruction among any current or former workers of the Chr. Hansen plant in New Berlin, this does not mean that there is no risk for flavoring-related lung disease at current exposure levels in the plant. Among current workers in the "flavoring worker" group (i.e., those who work in the spray dry, starter distillate, enzymes, or flavors rooms, in the QC laboratory, or in maintenance work), one worker with a past asthma history had mild fixed airways obstruction on spirometry testing. Airways obstruction due to asthma is usually reversible, either spontaneously or in response to a bronchodilator medication. Fixed airways obstruction can occur in some cases of asthma, but it can also be due to bronchiolitis obliterans caused by exposure to flavoring chemicals. Severe airways obstruction due to bronchiolitis obliterans starts as mild airways obstruction, so any fixed obstruction in a flavoring-exposed worker warrants careful and repeated medical follow-up. Additional medical tests, such as diffusing capacity of the lung for carbon monoxide (DL_{co}) and computerized tomography (CT) scans of the chest, might reveal evidence of bronchiolitis obliterans or another illness. We recommended that the Chr. Hansen worker found to have fixed airways obstruction seek additional medical evaluation; follow-up results on this worker were not available to us.

Our air sampling at the Chr. Hansen plant revealed diacetyl exposure levels comparable to levels at other plants where some of the most exposed workers developed bronchiolitis obliterans. In the past, air sampling at some of these other plants may have underestimated true diacetyl concentrations because of the effects of high humidity on NIOSH Method 2557. However, some air sampling at other plants was conducted at times when humidity was low. At a microwave popcorn plant where workers who mixed butter flavorings into heated oil ("mixers") were found to have moderate or severe fixed airways obstruction, average diacetyl exposures were approximately 1 ppm [NIOSH 2004b]; relative humidity was less than 30% during air sampling. This average exposure is comparable to average exposures we measured at the Chr. Hansen plant in the spray dry, starter distillate, and flavors rooms, and in the QC laboratory. For air sampling at the Chr. Hansen plant, we made measurements with a modified OSHA method known not to be affected by high humidity, as well as with NIOSH Method 2557.

Diacetyl exposures measured by FTIR are not known to be affected by humidity. At another microwave popcorn plant

where mixers developed severe fixed airways obstruction, peak exposures measured by FTIR were as high as 80 ppm when a mixer poured liquid butter flavoring into a tank [NIOSH 2004a]. This peak exposure is comparable to peaks exposures we measured in the spray dry room at the Chr. Hansen plant. At a flavoring plant where three workers who made powdered butter flavorings developed severe fixed airways obstruction, peak diacetyl exposures were as high as 200 ppm when workers packaged the finished product [NIOSH 2007]. (Note: Workers at that plant made powdered butter flavorings by mixing diacetyl and other liquid butter flavor ingredients into powders in a ribbon blender. They did not use a spray dryer.)

While average and peak diacetyl exposures at the Chr. Hansen plant are comparable to levels at other plants where workers developed severe lung disease, there are also important differences in production processes, work characteristics, and respirator use. These differences may lower worker risk from flavoring-related exposures at this plant compared to others. For example, workers in the spray dry room likely have far fewer opportunities for peak exposures to diacetyl compared to mixers in microwave popcorn plants. Because Chr. Hansen workers in the flavors room spend some of their time making enzyme-modified dairy flavors that do not contain diacetyl, they may be exposed less often to diacetyl than workers at some other flavoring plants where workers spend more of their time making diacetyl-containing flavorings. It is also possible that some workers at this Chr. Hansen plant have had much lower diacetyl exposures (compared to affected workers at other flavoring plants) if they have consistently used appropriate personal respiratory protection over the past several years.

There is still much that needs to be learned about how exposures to butter flavoring chemicals can cause lung disease. Some workers are likely more sensitive to these chemicals than others. At the first microwave popcorn plant studied by NIOSH investigators, where several mixers and other workers became severely ill (and where average exposures to diacetyl were among the highest that NIOSH has measured), some mixers with many years experience had no signs of lung disease [NIOSH 2006]. After some workers become ill and leave employment, the remaining workers are generally the ones more likely to better tolerate exposures to butter flavoring chemicals. At the first microwave popcorn plant studied by NIOSH, all mixers with lung disease had stopped working prior to NIOSH's first medical survey. Of the 10 Chr. Hansen former

workers with flavoring work experience that we invited for testing, the three who participated had normal spirometry results; we have little or no information on the other seven. Because flavoring-related lung disease can be severe and does not respond to medical treatment, it is important to minimize exposures to the greatest extent feasible to protect current and future workers.

Exposures to Enzymes and other Organic Dusts

Enzymes of various types have been found to cause allergic diseases such as asthma, rhinitis, and conjunctivitis in many different workplace settings (e.g., food production, detergents, baking) [Baur 2005; Bernstein et al. 2006; Brant et al. 2004]. Many studies have shown that minimizing exposures to enzymes can decrease the risk that workers will develop these diseases. Even with good exposure control, a small percentage of workers may still become allergic. A *Bacillus subtilis* proteolytic enzyme is a known cause of occupational asthma. Enzymes of this type (serine proteases known as subtilisins) and/or the bacteria itself may be periodically used in this plant. NIOSH has established an REL for subtilisins. We did not assess for potential exposure to subtilisins in our industrial hygiene air sampling.

The exposures to mixed organic dust in the animal and human health rooms at the Chr. Hansen plant can also put workers at risk for respiratory disease. An animal health room worker who participated in our survey had restriction on spirometry and symptoms that can occur with the lung disease hypersensitivity pneumonitis. Such a diagnosis can only be made by a physician after additional medical evaluation, usually including a diffusing capacity test of lung function (e.g., DL_{co}), a chest x-ray, and a chest CT scan. We recommended that this worker seek additional medical evaluation to identify the cause of the symptoms and lung function abnormality. Our ventilation evaluation identified several areas in the animal health rooms where ventilation could be improved to decrease exposures (see details provided in the Results and Recommendations sections of this report). Although workers may use filtering-facepiece respirators (dust masks) in these areas, Chr. Hansen management does not require them. Mandatory respirator use would help limit the chance of these workers developing respiratory disease.

Half of all workers who worked in the animal and human

health rooms reported post-hire skin problems, a finding that warrants additional efforts to prevent skin exposures in these areas. Prevention of skin exposures may also help prevent allergic respiratory disease. Animal studies of lung disease development after exposures to beryllium and isocyanates have shown that skin exposure can lead to an allergic response (sensitization) that can later manifest as allergic respiratory disease [Bello et al. 2007; Redlich et al. 2008]. Recent evaluation of a chronic beryllium lung disease prevention program which included skin protection showed a decrease in the rate of worker sensitization to beryllium [Cummings et al. 2007].

Conclusions

Diacetyl air concentrations in flavoring production areas at the Chr. Hansen plant may be high enough to put workers at risk of developing severe lung disease. The diacetyl exposure levels measured by NIOSH in the spray dry, starter distillate, and flavors rooms and in the QC laboratory were comparable to levels at other plants where some of the most exposed workers developed bronchiolitis obliterans. Among workers with potential exposure to diacetyl and other flavoring chemicals at the Chr. Hansen plant, one worker with a past asthma history had mild fixed airways obstruction. While fixed airways obstruction can occur in some cases of asthma, it can also be due to bronchiolitis obliterans caused by exposure to flavoring chemicals. Because flavoring-related lung disease from can occur after only several months of exposure and can rapidly progress to severe irreversible disease, uncontrolled exposures should be minimized to the greatest extent feasible. NIOSH medical survey and air sampling results suggest that workers in the animal and human health rooms may have health effects from exposure to organic dust. For most symptoms that we assessed, higher proportions of animal and human health workers reported symptoms compared to warehouse and flavoring workers. One animal health worker had symptoms and spirometry test findings that can occur with hypersensitivity pneumonitis, a lung disease that can affect individuals exposed to organic dusts. Air sampling in the animal health large and intermediate packaging rooms showed intermittent peak exposures to dust during ingredient mixing and product packaging activities. For some processes, local exhaust ventilation in these rooms did not adequately control dust exposures. The recommendations below provide detailed guidance for controlling exposures through engineering controls, administrative and work practice changes, and personal protective equipment, and for medical monitoring with regularly scheduled spirometry.

1. Engineering controls:

Confirm that all local exhaust ventilation systems are operating as designed and that they are performing adequately. The following assessments should be made periodically to ensure adequate system performance: smoke visualization testing (with hoods and for room pressurization checks); hood slot/face velocity measurements; and filter differential pressure checks (for fume extraction hoods and baghouses). These evaluations should be part of a routine preventative maintenance schedule. It is also important to perform routine industrial hygiene air sampling to monitor workers' exposures and ensure that existing controls continue to effectively control exposures.

a. Starter distillate room: Reduce worker exposures from emissions from the stills. Consideration should be given to adding local exhaust near the stills to collect any fugitive vapors escaping during that process. A ventilated cabinet could be designed to partially or fully enclose the stills and reduce or eliminate their fugitive emissions. In addition, company representatives mentioned plans to implement closed transfer of starter distillate from the stills to the large tote. Management should conduct air sampling after this change to evaluate its effectiveness.

b. Flavors room: Adjust setpoints to re-balance supply and return airflow rates to maintain the room at negative pressure (a pressure differential of 0.04 ± 0.02 inches of water gauge) [ACGIH 2007] relative to the warehouse. Add local exhaust ventilation to the mixing tanks to reduce worker exposures to volatile chemicals. Install a ventilated workstation to reduce exposures for bench-top weighing and mixing tasks. This station could be based on a design from the ACGIH Ventilation Manual (see Welding Ventilation Bench Hood, VS-90-01) or could be purchased from commercial vendor [ACGIH 2007]. Engineering control evaluations at flavoring plants have shown exposure reductions of 90%–97% when performing mixing tasks using ventilated workstations [NIOSH 2008b, NIOSH 2008c].

c. Spray dry room: Add an annular/rim exhaust around the opening of the mixing tanks to reduce exposure to volatile chemicals and dust when ingredients are

added. Replace the Donaldson® Torit® fume extractor with a newer unit with two pickup hoods. This would allow placement of one hood near the discharge point and placement of the other hood near to where the worker adds/removes product to meet final weight specifications. Ensure that the local exhaust is vented outside the plant. (The current Torit® fume extractor set-up is suboptimal because filtration on these units typically does not remove VOCs (like diacetyl) and thus may recirculate the vapors into the production area while removing the powder.) Add an exhaust fan to this room to maintain the room at negative pressure relative to the warehouse. Evaluate the potential hazard related to the collection of potentially combustible dust. Refer to available OSHA references and consensus documents for information on evaluating and controlling this hazard (see Recommendation 7c).

d. Animal health large packaging room: Increase the face velocity of the bag dump station hood to at least 100 fpm (compared to the current 70 fpm) to improve dust capture. Reduce the gap between the blender discharge and the bulk tote and check the performance of the collar of the product discharge hood for the blender. Consult a qualified ventilation engineer when changing existing systems or putting new systems in place. Evaluate the potential hazard related to the collection of potentially combustible dust. Refer to available OSHA references and consensus documents for information on evaluating and controlling this hazard (see Recommendation 7c).

e. Intermediate packaging room: Install a fume extractor local exhaust system, such as a Torit® unit, to allow the collection of dust emissions during the discharge of the blender into the product packaging bags.

f. Quality control laboratory: Install a laboratory exhaust hood for performance of tests involving starter distillate, diacetyl, and other flavoring chemicals.

2. Respiratory protection:

Require mandatory respirator use by all employees who work in or enter the starter distillate, enzymes (when packaging starter distillate), flavors, spray dry, or animal or human health rooms.

This requirement should apply to contractors and temporary employees, as well as to full-time employees. Workers should use respiratory protection at all times that they are in these production work areas. An alternate approach would be to establish a system for alerting workers when diacetyl and other FEMA-designated high-priority flavoring chemicals [FEMA 2004] are being used and requiring the use of respirators by all employees in the work area during these times. Workers should also be required to use respirators when handling enzymes. Workers should also be required to use respirators when they are cleaning the spray dryer and any containers or tanks that have held flavoring chemicals.

Workers in the starter distillate, enzymes (when packaging starter distillate), flavors, and spray dry rooms should use, at a minimum, a NIOSH-approved full-face negative-pressure air-purifying respirator with combined particulate and organic vapor cartridges. (Note: Additional acid-gas cartridge protection may be necessary if there is potential for exposure to chlorine, hydrogen chloride, sulphur dioxide, or chlorine dioxide; acid-mist cartridge protection may be necessary if there is potential for exposure to ammonia, butylamine, dimethylamine, ethylamine, methylamine, or trimethylamine. Consult with the manufacturer of the respirators used for additional guidance.) A full-facepiece negative-pressure respirator will also protect the eyes from airborne dust and chemical splashes that might occur during pouring, mixing, or cleaning. A loose-fitting powered air-purifying respirator (PAPR) is an option to consider for increased worker comfort and, unlike tight-fitting respirators, does not require fit testing; follow manufacturer's recommendations for cartridge change-out schedules.

For workers in the animal and human health rooms, the minimum level of protection should be a NIOSH-approved N-95 filtering-facepiece respirator. Half- and full-facepiece respirators may provide a more consistent seal and hence a higher level of protection so long as they are fitted with N-95 or more protective filters.

A formal respiratory protection program that adheres to the requirements of the OSHA Respiratory Protection Standard (29 CFR 1910.134) is required. The administrator for the program must have adequate training and experience to run it and regularly evaluate its effectiveness. The respiratory protection program must include a written policy, change-out schedule for canisters

and cartridges, pre-use medical evaluation, pre-use and annual fit-testing and training, and the establishment and implementation of procedures for proper respirator use (such as prohibiting use with facial hair, ensuring a user seal check, inspection of respirators prior to each use, and ensuring proper storage of respirators to protect them from damage, contamination, dust, sunlight, and extreme temperatures). Details on the Respiratory Protection Standard and on how a company can set up a respiratory protection program are available on the OSHA website (http://www.osha.gov/SLTC/respiratoryprotection/index.html).

3. Medical surveillance with spirometry:

Monitor all maintenance workers and workers who work in or enter the starter distillate, enzymes, flavors, or spray dry rooms or the QC laboratory with regularly-scheduled spirometry tests; obtain baseline tests before workers are allowed to work in these areas and retest every six months. Obtain baseline tests and repeat tests annually for workers in the animal and human health rooms. Some workers may require more frequent testing if test results are abnormal.

Use a spirometry provider who follows ATS guidelines for high quality testing; the provider should be able to document that spirometry technicians have attended a NIOSH-approved spirometry course and utilize proper testing technique. The physician who reviews the tests should be familiar with the ATS guidelines [ATS/ERS 2005] and with the nature of the lung disease that can occur from exposures to flavoring-related chemicals. Provide the physician with a copy of this report and the NIOSH Alert, *Preventing Lung Disease in Workers Who Use or Make Flavorings* (available on the internet at http://www.cdc.gov/niosh/docs/2004-110/). The physician should evaluate workers' sequential spirometry tests for abnormalities and for excessive declines in FEV_1 (i.e., declines in FEV_1 that are greater than what would be expected due to normal aging and normal variability in the test measurement). The California Department of Public Health has produced detailed guidance on medical surveillance for flavoring-related lung disease on the internet at http://www.cdph.ca.gov/programs/ohb/Documents/flavor-guidelines.pdf.

4. Work practices:

a. Whenever possible, avoid open pouring, measuring,

and transfer of FEMA-designated high-priority flavoring chemicals [FEMA 2004].

b. Add diacetyl and other FEMA-designated high-priority chemicals into a tank last, when possible, to minimize the time during which vapors can enter the room air when the tank is open. Structure tasks to minimize the time workers spend in proximity to FEMA-designated high-priority chemicals and related production processes.

c. Train employees on how to properly use local exhaust hoods.

d. Keep containers of flavoring chemicals/ingredients sealed when not in use.

e. Minimize the potential for nearby workers to be exposed to flavoring chemicals; notify nearby workers when flavoring chemicals will be used and, where feasible, isolate processes and/or shorten process durations.

f. Clearly label containers containing FEMA-designated high-priority flavoring chemicals and post signs in areas where these chemicals will be used.

g. When feasible, use cold water to wash containers and tanks that have held flavoring chemicals, and refrigerate FEMA-designated high-priority flavoring chemicals.

h. Clean spills promptly to minimize emissions of chemical vapors. Wear personal protection equipment, including respirators (with organic vapor cartridges and particulate filters) and eye and skin protection, when cleaning up spills or when washing empty containers or plant equipment that has been in contact with flavoring chemicals or ingredients. If any flavoring chemicals are disposed of via floor or sink drains, flush the drains immediately with water to minimize the potential for any chemical vapors to be released back into production rooms. Clean powder spills using vacuum cleaners equipped with HEPA filters. Instead of using compressed air or dry-brushing or dry-sweeping, use vacuum cleaners equipped with HEPA filters as much as possible to clean residual powders from equipment.

i. If hands or other body areas contact flavoring chemicals, promptly wash with soap and water.

j. Specific recommendations:

i. Spray dry room: If possible, change the production process for powdered butter flavoring and encapsulated starter distillate so that diacetyl and starter distillate are added last to the mixing tank.

ii. Animal health large packaging room: Do not allow workers to enter the blender to sweep out remaining powder material. Without proper lockout/tagout procedures, entry into the blender could result in serious injury or death. This process should be done, if possible, with HEPA vacuuming instead of dry-sweeping. If dry-sweeping is absolutely necessary, have the worker use a long-handled broom so that the worker does not need to enter the blender.

iii. Animal health small packaging room: Discontinue the use of compressed air to clean off product containers; instead, use wet rags to wipe outer surfaces of packages.

5. Skin protection:

Provide workers in the starter distillate, enzymes, flavors, spray dry, and animal health rooms with appropriate protective clothing and gloves to prevent skin contact with flavoring chemicals, powder materials, and cleaning agents in these work areas. Warehouse and QC laboratory workers at risk for skin contact with flavorings or other chemicals may also require similar skin protection.

6. Eye protection:

Provide appropriate eye protection for all workers in all production rooms, and for all other workers who may be at risk for hazardous exposures to their eyes in other plant areas (e.g., QC laboratory).

7. Administrative controls:

Limit entry into production rooms to production workers and supervisory staff only (i.e., eliminate the necessity for QC laboratory or office workers to enter production rooms).

8. Other issues:

a. We observed a worker who entered the large blender in the animal health large packaging room to push out residual powder material. It was not apparent that lockout/tagout procedures on the blending machine had been followed. Because of unguarded machinery within the blender, the blender qualifies as a permit-required confined space.

i. Lockout/tagout: Facility safety procedures should be reviewed for a proper lockout/tagout program for all machines in the plant. A formal lockout/tagout program that adheres to the requirements of the OSHA Standard (29 CFR 1910.147) is required. This program must identify all hazardous energy sources, establish a program for lockout/tagout, be reviewed with all workers in affected areas, and be strictly enforced. Details on the Lockout/Tagout Standard are available on the OSHA website (http://www.osha.gov/SLTC/controlhazardousenergy/standards.html). The NIOSH Alert *Preventing Worker Deaths from Uncontrolled Release of Electrical, Mechanical, and Other Types of Hazardous Energy* (available on the internet at: http://www.cdc.gov/niosh/99-110.html) provides additional information.

ii. Confined spaces: All work areas should be evaluated to identify permit-required confined spaces. Procedures for activities in these spaces need to adhere to the OSHA Permit-Required Confined Spaces Standard (29 CFR 1910.146). This standard requires: worker training; the posting of danger signs; a written permit space program; testing, monitoring, and controlling environmental conditions for safe entry operations; use of permits signed by the entry supervisor for each entry operation; an attendant outside of permit space during entry operations; and use of harnesses with a retrieval line and procedures for summoning rescue and emergency services. Details on the Confined Spaces Standard are available on the OSHA website (http://www.osha.gov/Publications/osha3138.html).

b. Evaluate fork-lift safety and ensure that workers have training on the best safety practices for fork-lift operation and load handling. Ensure that workers have training on proper techniques for manual lifting of materials / containers.

c. Evaluate potential fire safety concerns of powders used and produced at the plant. National Fire Protection Association (NFPA) 654, Standard for the Prevention of Fire and Dust Explosions from the Manufacturing, Processing, and Handling of Combustible Particulate Solids, contains comprehensive guidance on the control of dusts to prevent explosions [NFPA 2006]. In addition, OSHA has issued a Safety and Health Information Bulletin (SHIB 07-31-2005) entitled, Combustible Dust in Industry: Preventing and Mitigating the Effects of Fire and Explosions [OSHA 2005].

d. Ensure compliance with all applicable environmental protection regulations when disposing of residual flavoring chemicals such as diacetyl.

e. Ensure that exposures to subtilisins are below the NIOSH recommended exposure limit (REL) of 0.00006 mg/m^3 of air (60-minute short-term exposure limit (STEL)) if *B. subtilis* bacteria or subtilisins are being used.

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Appendix A: Industrial Hygiene Air Sampling Methods

Analytes	Media/sampler	Flow (lpm)	Analytical methods
Respirable dust in air	37-mm PVC filter with cyclone	1.7	Gravimetric analysis by NMAM Method 0600 [NIOSH 2003]
Real-time respirable dust in air	Photometric meter, PersonalDataRAM, model pDR-1000AN/1200 or HazDust IV	-	Direct-reading instrument [ACGIH 2001] (Thermo Electron Corporation, Franklin, MA), Environmental Devices Corp., Plaistow, NH
Volatile organic compounds (VOCs) in air (screening for identification)	Thermal desorption tube	0.02	Gas chromatography / mass spectrometry by NMAM Method 2549 [NIOSH 2003]
Real-time VOCs in air	Photoionization meter, ppbRAE	-	Direct-reading instrument [ACGIH 2001] (ToxiRAE, Rae Systems, Inc., Sunnyvale, CA)
Total VOCs (quantitative for total mass)	Coconut shell charcoal (CSC) tubes, SKC# 226-01	0.10	Gas chromatography by NMAM Method 1550 [NIOSH 2003]
Ketone compounds in air (diacetyl and acetoin)	1) Anasorb tube (Diacetyl and acetoin), SKC# 226-121	0.05	Gas chromatography by NMAM Methods 2557 and 2558 [NIOSH 2003]
	2) Silica gel tube (Diacetyl only), SKC# 226-10-03	0.05	Gas chromatography by modified OSHA Method PV 2118 [2007].
Real-time diacetyl, concentrations in air	Fourier transform infrared (FTIR) gas analyzer	-	Direct-reading instrument [ACGIH 2001] (Gasmet DX-4010,™ Temet Instruments Oy, Helsinki, Finland)
Aldehydes in air (acetaldehyde and benzaldehyde)	Sorbent tube (silica gel treated with 2,4 dinitrophenylhydrazine), SKC# 226-119	0.1 or 0.5	High performance liquid chromatography (HPLC) by NMAM Method 2016 [NIOSH 2003]
Organic acids in air (acetic, butyric, caprioc, caprylic, lactic, and propionic acids)	Sorbent tube (silica gel) – ORBO 53 tubes, SKC# 226-10-3	0.1 or 0.5	HPLC methods by NIOSH In-house Method. [NIOSH 2003]
Inorganic acids in air (nitric and phosphoric)	Sorbent tube (silica gel) SKC# 226-10-03	0.2	Ion chromatography by NIOSH Method 7903. [NIOSH 2003]
Air temperature and % relative humidity	Psychrometer	-	Direct-reading meter [ACGIH 2001]

lpm – liters per minute; PVC – polyvinylchloride; NMAM – NIOSH Manual of Analytical Methods; VOCs – volatile organic compounds.

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ID:_____

RDHETA 2007 – 0327 Chr. Hansen: CURRENT WORKERS

Interviewer: _____ Interview Date: __ __ / __ __ / __ __ __ __
(Month) (Day) (Year)

Section I: Identification and Demographic Information

Name: _____ _____ ____
(Last name) (First name) (MI)

Address:_____
(Number, Street, and/or Rural Route)

_____ _____ _____
(City) (State) (Zip Code)

Home Telephone Number: ( ) _____ - _____

If you were to move, is there someone who would know how to contact you?

Name: _____ _____ ____
(Last name) (First name) (MI)

Relationship to you:_____

Address:_____
(Number, Street, and/or Rural Route)

_____ _____ _____
(City) (State) (Zip Code)

Home Telephone Number: ( ) _____ - _____

~~~~~~

1. Date of Birth: __ __ / __ __ / __ __ __ __
(Month) (Day) (Year)

2. Sex: 1. ____ Male 2. ____ Female

3. Are you Spanish, Hispanic, or Latino? 1.____Yes 2.____No.

4. Select <u>one or more</u> of the following categories to describe your race:
1. ___ American Indian or Alaska Native
2. ___ Asian
3. ___ African-American or Black
4. ___ Native Hawaiian or Other Pacific Islander
5. ___ White

5. When did you begin to work at the Chr. Hansen plant in New Berlin? __ __ / __ __ __ __
(Month) (Year)
~~~~~~

ID:_____

Section II: Health Information

I'm going to ask you some questions about your health. The answer to many of these questions will be "Yes" or "No." If you are in doubt about whether to answer "Yes" or "No," then please answer "No." I am also going to refer to "this plant". We understand that there are two Chr. Hansen plants in the Milwaukee area, but these questions refer to only the New Berlin plant.

6. Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill? 1. ___ Yes 0. ___ No

IF YES:

a) Do you get short of breath walking with people of your own age on level ground? 1. ___ Yes 0. ___ No

b) Do you ever have to stop for breath when walking at your own pace on level ground? 1. ___ Yes 0. ___ No

c) Do you ever have to stop for breath after walking about 100 yards (or after a few minutes) on level ground? 1. ___ Yes 0. ___ No

d) In what month and year did this breathlessness start? __ __ / __ __ __ __ (Month) (Year)

7. Do you usually have a cough? 1. ___ Yes 0. ___ No
(Count cough with first smoke or on first going out-of-doors. Exclude clearing of throat.)

IF YES:

a) Do you usually cough on most days for 3 consecutive months or more during the year? 1. ___ Yes 0. ___ No

b) In what month and year did this cough begin? __ __ / __ __ __ __ (Month) (Year)

8. During the last 12 months, have you had any trouble with your breathing? 1.____Yes 0. ____No

IF YES:

a) Which of the following statements best describes your breathing?
1. ___ I only rarely have trouble with my breathing
2. ___ I have regular trouble with my breathing but it always gets completely better
3. ___ My breathing is never quite right

ID:_____

9. Have you had wheezing or whistling in your chest at any time in the last 12 months? 1. ___ Yes 0. ___ No

IF YES:

a) In what month and year did this wheezing or whistling first begin? *(Not limited to the last 12 months)*
__ __ / __ __ __ __
(Month) (Year)
(optional answer: childhood)

b) Have you had this wheezing or whistling when you did not have a cold?
1. ___ Yes 0. ___ No

c) Have you been at all breathless when the wheezing noise was present? 1. ___ Yes 0. ___ No

d) When you are away from this plant on days off or on vacation, is this wheezing or whistling
1. ___ Better
2. ___ The same
3. ___ Worse
4. ___ N/A

10. Have you woken up with a feeling of tightness in your chest at any time in the last 12 months? 1. ___ Yes 0. ___ No

IF YES:

a) In what month and year did this feeling of tightness in you chest first begin? (*Not limited to the last 12 months*)
__ __ / __ __ __ __
(Month) (Year)

b) When you are away from this plant, on days off or on vacation, is this problem
1. ___ Better
2. ___ The same
3. ___ Worse
4. ___ N/A

ID:_____

11. Have you been woken by an attack of shortness of breath at any time in the last 12 months? 1. ___ Yes 0. ___ No

IF YES:

a) In what month and year did these attacks of shortness of breath first begin? (*Not limited to the last 12 months*) __ __ / __ __ __ __ (Month) (Year)

b) When you are away from this plant, on days off or on vacation, is this problem
1. ___ Better
2. ___ The same
3. ___ Worse
4. ____ N/A

12. Have you had an attack of asthma in the last 12 months? 1. ___ Yes 0. ___ No

IF YES:

a) When you are away from this plant, on days off or on vacation, is this problem
1. ___ Better
2. ___ The same
3. ___ Worse
4. ____ N/A

13. During the last 12 months did you see a doctor for chest symptoms, such as cough, shortness of breath, chest tightness or wheezing? 1. ___ Yes 0. ___ No

IF YES:

a) What did the doctor tell you that you had?

Drop down menu for interviewer to select from:
1. ___ allergies
2. ___ asthma
3. ___ bronchitis
4. ___ chronic bronchitis
5. ___ emphysema
6. ___ pneumonia
7. ___ sinusitis
8. ___ other
Describe "other" _____
_____

ID:_____

14. During the last 12 months, have you had any episodes of stuffy, itchy, or runny nose? 1. ___ Yes 0. ___ No

IF YES:

a) Is there an exposure at work that brings on these nasal symptoms? 1. ___ Yes 0. ___ No 9. ____ Don't Know

IF YES:

b) Describe exposure(s):

_____

_____

15. During the last 12 months, have you had any episodes of burning or stinging nose? 1. ___ Yes 0. ___ No

IF YES :

a) Is there an exposure at work that brings on these nasal symptoms? 1. ___ Yes 0. ___ No 9. ____ Don't Know

IF YES:

b) Describe exposure(s):

_____

_____

16. During the last 12 months, have you had episodes of watery, itchy eyes? 1. ___ Yes 0. ___ No

IF YES:

a) Is there an exposure at work that brings on these eye symptoms? 1. ___ Yes 0. ___ No 9. _____ Don't Know

IF YES:

b) Describe exposure(s):

_____

_____

ID:_____

17. During the last 12 months, have you had any episodes of burning or stinging eyes? 1. ___ Yes 0. ___ No

IF YES:

a) Is there an exposure at work that brings on these eye symptoms? 1. ___ Yes 0. ___ No 9. _____ Don't Know

IF YES:

b) Describe exposure(s):

_____

_____

18. During the last 12 months, have you had fever, chills or night-sweats? 1. ___ Yes 0. ___ No

IF YES:

a) How often have you had the fever, chills, or night-sweats?

1. ___ Rarely
2. ___ Monthly
3. ___ Weekly
4. ___ Daily

19. During the last 12 months, have you had unusual tiredness or fatigue? 1. ___ Yes 0. ___ No

IF YES:

a) How often have you had the unusual tiredness or fatigue?

1. ___ Rarely
2. ___ Monthly
3. ___ Weekly
4. ___ Daily

20. Has a doctor ever told you that you had chronic bronchitis? 1. ___ Yes 0. ___ No

IF YES:

a) How old were you when it began? _____ Years old

ID:_____

21. Have you ever had asthma? 1. ___ Yes 0. ___ No

IF YES:

a) Do you still have it? 1. ___ Yes 0. ___ No

b) How old were you when your asthma began? _____ Years old
option: childhood

c) Was it confirmed by a doctor? 1. ___ Yes 0. ___ No

d) Did you have asthma before you began working at this plant? 1. ___ Yes 0. ___ No

IF B or D INDICATE PRE-HIRE ONSET:

e) During the two years immediately before you started to work at the New Berlin plant, were you having asthma symptoms or were you taking asthma medication? 1. ___ Yes 0. ___ No

IF YES TO E: *go on to Question #22*

IF NO TO E:
f) After you began working at the New Berlin plant, did your asthma symptoms return? 1. ___ Yes 0. ___ No

IFYES TO F:
g) In what month and year did your asthma come back _____month _____year

22. Are you currently taking any medicine (including inhalers, aerosols, or tablets) for asthma? 1. ___ Yes 0. ___ No

23. Do you have any nasal allergies including hay fever? 1. ___ Yes 0. ___ No

24. Since you began working at this plant, have you developed any new skin rash or skin problems? 1. ___ Yes 0. ___ No

IF YES:

a) Is there an exposure at work that brings on this skin rash or skin problem?
1. ___ Yes 0. ___ No 9. _____ Don't Know

IF YES:
b) Describe exposure(s) and symptoms:
_____

ID:_____

25. Have you ever had to change your job, job duties, or work area at this plant because of breathing difficulties? 1. ___ Yes 0. ___ No

IF YES:

a) What month and year did you change your job, job duties, or work area? __ __ / __ __ __ __ (Month) (Year)

b) What was your job, job duties, and/or work area before the change?

Describe: _____

c) How did your job, job duties, and/or work area differ after the change?

Describe:_____

d) Were your breathing problems after the change:

1. ___ Better
2. ___ The Same
3. ___ Worse

Section III. Work Information

I'm now going to ask you questions about your work history at this plant.

26. During an average work week, how many hours do you work? _____ Hours per week

27. Are there any chemicals or substances in this plant that bring on chest symptoms, such as cough, shortness of breath, chest tightness, or wheezing? 1.___ Yes 0.___ No

IF YES:

a) What chemicals or substances caused these chest symptoms?

_____

ID:_____

28. Have you ever been exposed to an unusual chemical spill or release in this plant? 1.___ Yes 0.___ No

IF YES:

What was the chemical?	What was the date of the spill or release? (mm/yyyy)	Did you have any symptoms from it?	If Yes, What were your symptoms?
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	
		1.___ Yes 0.___ No	

ID:_____

29. I'm now going to ask you some questions about all the jobs that you have had while at this plant. We will start with your current job and work back through time.

Job Number	Major Work Area	Job Title	Start Date (MM/YYYY)	End Date (MM/YYYY)	Additional Questions
	Starter Distillate	Process Operator Helper Other			
	Enzymes	Process Operator Helper Other			Did you do afternoon transfers in Starter Distillate? 1.___ Yes 0.___ No
	Flavors	Process Operator Helper Lead Operator Other			Did you handle diacetyl? 1.___ Yes 0.___ No If YES: How often did you handle diacetyl? [choose the closest answer] 1. ___Daily 2. ___At least once per week 3. ___At least once per month 4. ___< one time per month Did you handle lipase or other enzymes? 1.___ Yes 0.___ No
	Spray Dry	Spray Drier Operator Lead Spray Dryer Operator Helper Other			Did you make powdered starter distillate? 1.___ Yes 0.___ No If YES: How often did you make powdered starter distillate? [choose the closest answer] 1. ___Daily 2. ___At least once per week 3. ___At least once per month 4. ___< one time per month Did you make powdered carmine? 1.___ Yes 0.___ No

ID:_____

					Did you make powdered enzyme modified dairy products? Yes/no
	Animal Health	Process Operator Helper Other			
	Human Health	Process Operator Helper Other			
	Maintenance	Mechanic Other			
	Quality Control	Senior Quality Systems Specialist Other			
	Animal and Human Health	Production Supervisor Replacement Specialist Other			
	All Flavors	Production Supervisor Other			
	Other	Other			
	Warehouse	Material Handler Lead Material Handler Warehouse Manager Warehouse Coordinator Material Handler-Culture			

For each Job Number:
When you worked in this job, did you use a respirator or mask? 1.___ Yes 0.___ No

Which type(s) of respirator or mask did you wear?

Dust mask (N-95) 1.___ Yes 0.___ No
If YES: Were you fit-tested for this respirator? 1.___ Yes 0.___ No

Half-face piece 1.___ Yes 0.___ No
If YES: Were you fit-tested for this respirator? 1.___ Yes 0.___ No

Full-face piece 1.___ Yes 0.___ No
If YES: Were you fit-tested for this respirator? 1.___ Yes 0.___ No

ID:_____

30. Have you ever worked at any other flavoring plants? 1. ___Yes 0. ___No

IF YES:

a) Describe what you did and for how many years

_____

_____

_____

Section IV: Tobacco Use Information

I'm now going to ask you a few questions about tobacco use.

31. Have you ever smoked cigarettes? (*NO if less than 20 packs of cigarettes in a lifetime or less than 1 cigarette a day for 1 year.*) 1. ___ Yes 0. ___ No

IF YES:

a) How old were you when you first started smoking regularly? _____ Years old

b) Over the entire time that you have smoked, what is the average number of cigarettes that you smoked per day? _____ Cigarettes/day

c) Do you still smoke cigarettes? 1. ___ Yes 0. ___ No

IF NO:

d) How old were you when you stopped smoking cigarettes regularly? _____ Years old

Thank you for participating in this survey!

Appendix C: Tables

Table C1. Predominant volatile organic compounds in air (measured with thermal desorption tubes)

Location	Date	Predominant Compounds[1]	Activities / Note	Diacetyl Used[2]
Starter Distillate	Monday 12/3/07	1) diacetyl, 2) acetic acid, 3) diethylphthalate*, 4) dimethylphthalate*	Producing starter distillate. Seven units operating·	Yes
	Tuesday 12/4/07	1) diacetyl, 2) diethylphthalate*, 3) dimethylphthalate*, 4) phthalic anhydride, 5) acetic acid	Producing starter distillate. Seven units operating.	Yes
Enzymes	Thursday 12/6/07	1) ethyl ether, 2) pentane, 3) diacetyl, 4) isopentane	Bottling starter distillate (1X).	Yes
Flavors	Monday 12/3/07	1) butyric acid, 2) ethyl butyrate, 3) butyl butyrate, 4) iethylphthalate*, 5) hexanoic acid, 6) methyl amyl ketone, 7) dimethylphthalate*	Natural cheddar flavor produced. Dumped cheese in hopper and poured butyric acid.	No
	Tuesday 12/4/07	1) butyric acid, 2) isovaleraldehyde, 3) hexanoic (caproic) acid, 4) 2-methylbutanal, 5) butyl butyrate, 6) acetic acid, 7) diacetyl	Natural parmesan flavor and natural butter flavor produced.	No
	Wednesday 12/5/07	1) butyric acid, 2) diacetyl, 3) hexanoic (caproic) acid, 4) methyl hexanoate (caproate), 5) acetic acid, 6) diethylphthalate*, 7) butyl butyrate, 8) isovaleraldehyde	Natural sour cream, manchego cheese flavor, natural parmesan flavor, natural butter flavor.	Yes
Spray Dry	Monday 12/3/07 Shift 1	1) diacetyl, 2) methyl ethyl ketone, 3) furfuryl alcohol, 4) aliphatic oxy-compound, 5) acetic acid, 6) diethylphthalate*	Powder flavor from starter distillate (50X) produced and packaged.	Yes
	Monday 12/3/07 Shift 2	1) acetic acid, 2) diacetyl, 3) furfuryl alcohol, 4) glycolaldehyde, 5) aliphatic oxy-compound, 6) acetoin, 7) 5-(hydroxymethyl) furfural	Powder flavor from starter distillate (45X) produced and packaged.	Yes
	Tuesday 12/4/07 Shift 1	1) diacetyl, 2) acetic acid, 3) cyclohexanone, 4) furfuryl alcohol, 5) glyoxal, 6) furfural, 7) aliphatic oxy- compound, 8) 2-methyl furan	Powder flavor from starter distillate (50X) produced and packaged.	Yes

[1]Based on the largest peaks in each sample chromatogram.
[2]Diacetyl or starter distillate reported or observed in use during process.
*Also present on some field and/or media blanks.

Table C2. Full-shift TWA diacetyl and acetoin air concentrations[1] by sample type and area using NIOSH Methods 2557[2] and 2558

Plant Area	Type	N	Mean	SD	GM	GSD	Min	Max
Starter Distillate	Diacetyl (Personal)	3	1.43	0.626	1.35	1.51	0.963	2.14
	Diacetyl (Area)	15	0.723	0.318	0.661	1.55	0.328	1.41
	Acetoin (Personal)	3	0.064	0.023	0.062	1.44	0.043	0.089
	Acetoin (Area)	15	0.034	0.011	0.031	1.49	0.015	0.050
Enzymes[3]	Diacetyl (Personal)	2	0.099	0.002	0.099	1.01	0.098	0.100
	Diacetyl (Area)	2	0.045	0.045	0.032	3.46	0.013	0.077
	Acetoin (Personal)	2	ND	-	ND	-	ND	ND
	Acetoin (Area)	2	ND	-	ND	-	ND	ND
Flavors	Diacetyl (Personal)	5	0.298	0.306	0.079	12.2	ND	0.692
	Diacetyl (Area)	4	0.126	0.186	0.024	12.5	ND	0.396
	Acetoin (Personal)	5	0.009	0.006	0.008	2.11	ND	0.018
	Acetoin (Area)	4	0.013	0.011	0.010	2.66	ND	0.026
Spray Dry	Diacetyl (Personal)	7	0.764	0.706	0.301	9.18	0.003	1.86
	Diacetyl (Area)	5	0.826	0.623	0.515	4.06	0.046	1.78
	Acetoin (Personal)	7	0.015	0.011	0.011	2.43	ND	0.031
	Acetoin (Area)	5	0.023	0.024	0.014	3.02	ND	0.059
Quality Control	Diacetyl (Personal)	2	0.014	0.010	0.012	2.14	0.007	0.021
	Acetoin (Personal)	2	ND	-	ND	-	ND	ND
Animal Health	Diacetyl (Area)	2	ND	-	ND	-	ND	ND
	Acetoin (Area)	2	ND	-	ND	-	ND	ND
Warehouse	Diacetyl (Personal)	2	0.010	0.007	0.009	1.97	0.006	0.015
	Diacetyl (Area)	1	0.121	-	0.121	-	0.121	0.121
	Acetoin (Personal)	2	ND	-	ND	-	ND	ND
	Acetoin (Area)	1	ND	-	ND	-	ND	ND

[1] Concentrations in parts per million parts air (ppm).
[2] Recent investigations indicate that Method 2557 for diacetyl is affected by absolute humidity; these measurements are presented for reference only considering this situation.
[3] On day that workers packaged 1X starter distillate.
TWA – Time-weighted average; GM – geometric mean; GSD – geometric standard deviation; STD – standard deviation; Min – minimum; Max – maximum; ND – below detectable limits in air (approximately 0.005 ppm for diacetyl and 0.007 ppm for acetoin, depending on sample volume).

Table C3. Average temperature, relative humidity (RH), and absolute humidity (AH) measurements by date and work area

Plant Area	Date	N	Temperature (^{0}F)	RH (%)	AH (mg/l)
Starter Distillate	12/3/07	3	71.7	22.7	4.40
	12/4/07	4	70.0	22.0	4.05
	12/5/07	6	73.9	26.0	5.38
Enzymes[1]	12/6/07	4	61.3	28.2	3.92
Flavors	12/3/07	3	68.0	33.7	5.81
	12/4/07	2	66.5	33.5	5.83
	12/5/07	4	68.5	33.5	5.87
	12/6/07	4	67.8	35.8	6.15
Spray Dry	12/3/07	2	70.8	28.5	5.37
	12/3/07[2]	3	75.7	25.7	5.63
	12/4/07	5	73.5	30.4	6.21
	12/4/07[2]	3	76.7	24.7	5.60
	12/5/07	3	72.0	29.7	5.82
Animal Health	12/3/07	3	67.3	29.3	4.97
	12/4/07	3	64.7	23.7	3.66
	12/5/07	3	66.3	28.3	4.62
	12/6/07	4	65.4	22.5	3.56
Human Health	12/5/07	3	68.0	23.0	3.97
Quality Control	12/4/07	2	72.0	22.5	4.42
	12/6/07	2	73.0	21.5	4.36
Warehouse	12/4/07	4	69.8	25.0	4.56
	12/12/07	5	73.7	22.8	4.73

[1]On day that workers packaged 1X starter distillate.
[2]Indicates measurements taken during a second shift.
N – number of measurements taken; RH – percent relative humidity; AH – absolute humidity in milligrams water per liter of air (mg/l).

Table C4. Currently available OSHA standards or recommended exposure limits for the chemicals that NIOSH measured with air sampling

Analyte	OSHA PEL		NIOSH REL		ACGIH TLV®	
	TWA	STEL / C	TWA	STEL / C	TWA	STEL / C
Acetaldehyde	200 ppm	-	CA	-	-	C – 25 ppm, A3
Benzaldehyde	-	-	-	-	-	-
Diacetyl	-	-	-	-	-	-
Acetoin	-	-	-	-	-	-
Acetic acid	10 ppm	-	10 ppm	STEL – 15 ppm	10 ppm	STEL – 15 ppm
Lactic acid	-	-	-	-	-	-
Propionic acid	-	-	10 ppm	STEL – 15 ppm	10 ppm	-
Butyric acid	-	-	-	-	-	-
Caproic acid	-	-	-	-	-	-
Caprylic acid	-	-	-	-	-	-
Nitric Acid	2 ppm	-	2 ppm	STEL – 4 ppm	2 ppm	STEL – 4 ppm
Phosphoric Acid	1 mg/m^3	-	1 mg/m^3	STEL – 3 mg/m^3	1 mg/m^3	STEL – 3 mg/m^3

- – no available OSHA standard or other recommended exposure limit.
A3 – A3 level carcinogen (Confirmed animal carcinogen w/ unknown relevance to humans).
C – ceiling exposure limit.
CA – carcinogen (NIOSH recommends lowest feasible exposure).
mg/m^3 – milligrams per cubic meter of air.
PEL – permissible exposure limit.
ppm – parts per million parts air.
REL – recommended exposure limit.
STEL – short-term exposure limit.
TLV® – Threshold Limit Value.
TWA - time-weighted average

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

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November 8, 2007
HETA 2007-0327
Interim Letter I

Robert Brill
Director of Legal and Regulatory Affairs
Chr. Hansen, Inc.
9015 West Maple Street
Milwaukee, WI 53214

Dear Mr. Brill:

The National Institute for Occupational Safety and Health (NIOSH) received a confidential Health Hazard Evaluation request from workers at the Chr. Hansen facility in New Berlin, Wisconsin on August 10, 2007. Health hazards listed in the request included diacetyl, butter flavoring, cleaning agents, colors, cultures, enzymes, and cheese flavors. Possible related health effects listed included eye and breathing problems.

NIOSH responded by sending a team of three physicians, two industrial hygienists, and a mechanical engineer to complete a walkthrough visit of the facility from September 24-26, 2007. During our visit, we observed processes and work practices in the Starter Distillate, Enzymes, Flavors, and Animal Health work areas and we interviewed a number of workers. This letter provides our observations from the visit and our recommendations as were discussed during our closing meeting on September 26, 2007.

We observed several instances of improper respirator use: 1) workers using N-95 filtering face pieces without prior medical clearance or fit-testing; 2) workers with beards wearing respirators; and 3) workers not properly wearing respirators. The current work practice is to minimize exposure of temporary workers by having them leave the work area when hazardous chemicals are used, this may not always be possible. We recommend the following actions:

- Medically clear and fit-test all workers who use respirators.
- Ensure that workers are trained in the proper use of these respirators, including the necessity of using both straps and no beard growth. According to 29 CFR 1910.134 (g)(1)(i)(A) facial hair that comes between the sealing surface of the facepiece and face is not permitted.
- A formal respiratory protection program that adheres to the requirements of the OSHA Respiratory Protection Standard (29 CFR 1910.134) is required. The administrator for the program must have adequate training and experience to run it and regularly evaluate its

effectiveness. The Respiratory Protection Program must include a written policy, change schedule for canisters and cartridges, pre-use medical evaluation, pre-use and annual fit-testing and training, and the establishment and implementation of procedures for proper respirator use (such as, prohibiting use with facial hair, ensuring user seal check and inspection of respirators prior to each use, and ensuring proper storage of respirators to protect respirators from damage, contamination, dust, sunlight, and extreme temperatures). Details on the Respiratory Protection Standard and on how a company can set up a respiratory protection program are available on the OSHA website (http://www.osha.gov/SLTC/respiratoryprotection/index.html).

We observed a worker who entered the large blender in the Animal Health production room to push out the remaining powder material. It was not apparent that lockout/tagout procedures on the blending machine had been followed. Because of unguarded machinery within the blender, the blender qualifies as a permit-required confined space.

- We recommend that facility safety procedures be reviewed for a proper lockout/tagout program for all machines in the facility. A formal lockout/tagout program that adheres to the requirements of the OSHA Standard (29 CFR 1910.147) is required. This program must identify all hazardous energy sources, establish a program for lockout/tagout, be reviewed with all workers in affected areas, and be strictly enforced. Details on the Lockout/Tagout Standard are available on the OSHA website (http://www.osha.gov/SLTC/controlhazardousenergy/ standards.html). The NIOSH Alert *Preventing Worker Deaths from Uncontrolled Release of Electrical, Mechanical, and Other Types of Hazardous Energy* at URL: http://www.cdc.gov/niosh/99-110.html provides additional information.
- We recommend that all workplaces to be evaluated to identify permit-required confined spaces. Procedures for activities in these spaces need to adhere to the OSHA Permit-Required Confined Spaces Standard (29 CFR 1910.146). This standard requires: worker training; the posting of danger signs; a written permit space program; testing, monitoring, and controlling environmental conditions for safe entry operations; use of permits signed by the entry supervisor for each entry operation; an attendant outside of permit space during entry operations; and use of harnesses with a retrieval line and procedures for summoning rescue and emergency services. Details on the Confined Spaces Standard are available on the OSHA website (http://www.osha.gov/Publications/osha3138.html).
- Another option for this particular blender is to have the worker use a long-handled broom to allow the worker to remain outside of the blender when sweeping out its contents.

The worker in Starter Distillate wore a full facepiece respirator with organic vapor cartridges while transferring starter distillate. Following the transfer, the worker removed the respirator. However, we measured high total volatile organic compound levels for approximately 20 minutes after this procedure.

- We recommend the transfer of starter distillate be mechanized to a closed operation to minimize exposures.
- In the interim, workers in Starter Distillate should use respiratory protection while working in this room.

The worker in Enzymes may have potential for diacetyl exposure when diluted starter distillate is packaged. Respiratory protection is advised for this worker during this process until exposures

are evaluated.

The hazardous chemicals list that is used to direct workers when to use respiratory, skin, and eye protection listed acetoin as requiring only eye and skin protection and did not list benzaldehyde at all.

- We recommend that the list be updated to include both acetoin and benzaldehyde as requiring use of a full facepiece respirator with organic vapor cartridges and gloves.
- We also recommend that a comprehensive toxicological review of the hazardous chemicals list be done to help ensure that it includes appropriate chemicals and personal protective equipment requirements.

We appreciate the assistance of the management and employees of Chr. Hansen during our walkthrough visit and hope that these recommendations are helpful. If you have any questions, please do not hesitate to contact us at (304) 285-6383 (Dr. Sahakian) or (304) 285-5959 (Dr. Kullman).

At present, we are planning a return visit for assessing exposures and worker health at the facility. Within the next several weeks we will be contacting you to discuss our plans concerning our visit scheduled for December 3-14, 2007.

Sincerely,

Nancy Sahakian, MD, MPH
CDR, USPHS
Medical Officer

Gregory Kullman, PhD, CIH
CAPT, USPHS
Industrial Hygienist
Field Studies Branch
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Mailed 1-28-08

January 28, 2008
HETA 2007-0327
Interim Letter II

Robert Brill
Director of Legal and Regulatory Affairs
Chr. Hansen, Inc.
9015 West Maple Street
Milwaukee, WI 53214

Dear Mr. Brill:

The National Institute for Occupational Safety and Health (NIOSH) received a confidential Health Hazard Evaluation request from workers at the Chr. Hansen facility in New Berlin, Wisconsin on August 10, 2007. Health hazards listed in the request included diacetyl, butter flavoring, cleaning agents, colors, cultures, enzymes, and cheese flavors. Possible related health effects listed included eye and breathing problems.

As part of our response to this Health Hazard Evaluation request, NIOSH requested from the Concentra Clinic copies of spirometry tests of workers of the Chr. Hansen, Inc. New Berlin facility. We received results for 23 spirometry tests. Workers included current workers in the facility's spirometry surveillance program and workers who had worked at the facility in the past 5 years in the Starter Distillate, Enzymes, Flavors, and/or Spray Drying work areas. A NIOSH medical officer and spirometry technician reviewed the reports. I also met with staff at the Concentra Clinic on December 13, 2007 to learn about their procedures for spirometry testing and to discuss with them our recommendations.

Background Information:

Many test characteristics enter into achieving a quality spirometry test. Reproducibility of measured lung volumes from repeated maneuvers helps to confirm that the worker provided maximal effort during the test. Having three or more acceptable curves helps to ensure that faulty starts, coughs, or obstruction of the mouthpiece did not occur. Spirometry test quality should be evaluated to ensure accuracy of the result and validity of the interpretation and to allow optimal comparison of sequential tests over time. The proper interpretation of a spirometry test (whether the test is "normal" or "abnormal") depends on a number of factors. In their guidance document (Miller et al., 2005b), the American Thoracic Society (ATS) suggests that Hankinson prediction equations (Hankinson et al., 1999) be used to determine lower limit of normal values for lung volumes based on the height, age, gender, and race of the individual tested. Hankinson prediction equations are available for Caucasians, Blacks, and Hispanics, but

not for Asians; however, a factor of 0.94 can be applied to Caucasian values to obtain expected values for Asians (Pellegrino et al., 2005). Compared to other available prediction equations, Hankinson equations are the most current and are based on test results from a much larger number of individuals that are representative of the U.S. adult population.

ATS suggests that spirometers display flow-volume and volume-time curves to optimize quality control of the test and that test operators visually inspect the performance of each maneuver for quality before proceeding to another maneuver. ATS recommends daily calibration of spirometers, use of a nose-clip, and the standing position for test subjects during testing. The standing position allows individuals to more fully fill and empty their lungs. If a worker is unable to perform the test in the standing position, then the sitting position should be used and all follow-up tests should be performed in this position to allow for comparison. To facilitate this comparison, the worker's position (whether standing or seated) should be recorded on the spirometry test print-out.

Spirometry test quality depends on the ability of the spirometry technician to effectively coach the worker, to identify problems with the tracings and with the worker's effort, and to know when more than three maneuvers are needed. By recording the technician's name (or identification number) on the test print-out and by systematically evaluating the quality of tests conducted by individual technicians, targeted instruction and training can be provided to correct technician shortcomings. One such measure of quality is to grade the tests from A to F (see Appendix A for an example of the quality scoring mechanism used by NIOSH).

Results:

Only 52% of the reviewed spirometry tests achieved a quality score of A or B based on reproducibility of results and quality of the maneuvers (Table 1 and Appendix A). A realistic goal is that 85% of tests should be of A or B quality. This is based on a review of 18,000 spirometry tests from a large outpatient pulmonary function laboratory which showed that 90% of tests achieved reproducibility of FEV_1 within 120 mL, and reproducibility of FVC within 150 mL (Enright et al., 2004).

The spirometer used by the Concentra Clinic provided print-outs with flow-volume and volume-time curves of the three best maneuvers; however, lung volumes for the three maneuvers and lower limit of normal values were not included. The spirometer is able to provide real-time flow-volume and volume-time curves if results are printed out after each maneuver; however, the practice is to have the worker blow several "good" blows as determined by the equipment and then to print out the results all at once. The spirometer uses the 1983 Knudson and not the 1999 Hankinson prediction values, and the logic used by the spirometer to decide whether a test is abnormal is not known. All tests indicated that calibration of the spirometer had been performed on the test day (Table 2).

Nose clips were not used during spirometry maneuvers. None of the tests reviewed had the position of the worker recorded (Table 2). However, on speaking with the staff at the clinic, workers are tested in the standing position. Based on reported height and race for the same individual tested multiple times, and use of first names to identify the gender, we identified 3

recording errors in these individual characteristics. None of the tests had the name of the spirometry technician recorded to help assess quality of tests of individual spirometry technicians (Table 2).

Conclusion and Recommendations:

Spirometry quality is essential when spirometry tests are being used for medical surveillance. In medical surveillance, the baseline test obtained at hire is used as a comparison for subsequent tests. Both abnormal tests and substantial declines in forced expiratory volume in one second (FEV_1) over more than one test are important. For example, an individual with an above average baseline FEV_1 who later has a spirometry test showing a significant drop in FEV_1 within the normal range may have early bronchiolitis obliterans.

We recommend that testing be done with a spirometer that: 1) prints out the values and flow-volume and volume-time curves of at least the 3 best maneuvers; 2) uses Hankinson prediction formulas; 3) uses the lower of limit of normal values to determine whether lung volumes and/or the spirometry test are abnormal; 4) uses the largest FEV_1 and the largest forced vital capacity (FVC) of all acceptable maneuvers to determine whether these lung volumes are below the lower limit of normal; and 5) uses the acceptable maneuver with the largest sum of FEV_1 and FVC to determine the FEV_1/FVC ratio and other indices (Miller et al., 2005b). A display with both flow-volume and volume-time curves following each maneuver is useful. A nose clip should be used. The spirometry technician's name (or identification number) and the position of the worker should be recorded on the test print-out. Spirometry technicians should attend a NIOSH-approved initial spirometry training course (See http://www.cdc.gov/niosh/topics/spirometry/ for information on NIOSH-approved spirometry training courses); ATS recommends periodic retraining (Miller et al., 2005a). One specific problem noted was that workers frequently did not take a maximal inhalation. This indicates a need for better coaching by the spirometry technician and more maneuvers by the worker until an acceptable test is achieved.

Because rapid decline in FEV_1 may indicate the onset of lung disease, it is important to follow FEV_1 over time. One way to accomplish this is to have a sheet in the worker's medical record that records: 1) the highest FEV_1 test result (which would serve as the baseline); and 2) the mL difference and percent decline of FEV_1 values of follow-up tests from that highest FEV_1 value. Workers with a 15% drop in their FEV_1 value compared to their highest FEV_1 value should have the spirometry test repeated 2 to 4 weeks later (to allow for recovery from a possible viral respiratory infection). If the decline persists, the worker should be referred to a pulmonologist for evaluation. During this time period the worker should be restricted from further exposures to flavoring chemicals at work.

The reason for using the worker's highest FEV_1 test result as a baseline is that, due to a learning effect, the FEV_1 from the subsequent periodic screening tests may be higher. Additionally, if a worker has asthma, there may be a temporary decline in FEV_1 on some days. In this case, the best FEV_1 would serve as a preferred baseline for monitoring the possible development of early bronchiolitis obliterans.

Workers whose tests show airways obstruction should have 4 puffs of a bronchodilator administered and their spirometry test should be repeated. If the airways obstruction persists despite the administration of bronchodilator, the airways obstruction is likely to be "fixed"; if the airways obstruction substantially improves (FEV_1 increases 12% and 200 mL), the airways obstruction is "reversible." Results should be recorded in the chart and they should be referred to a pulmonologist. Workers with fixed airways obstruction should be removed from further exposure to flavoring chemicals. Workers with reversible airways obstruction may have asthma and should likewise be medically evaluated by a pulmonologist.

Chr. Hansen, Inc. should provide the spirometry program director (at present, Concentra Clinic) with information for each worker in their medical surveillance program. This information should include a list and description of current and previous job assignments, hazardous exposures, exposures measurements, personal protective equipment provided or used, relevant Material Safety Data Sheets (MSDSs), and applicable occupational safety and health standards. When workers are referred to pulmonologists for further evaluation, this information should be included with the referral. Physicians providing medical surveillance and referral pulmonologists should provide individual workers with: 1) results of any medical tests performed; 2) their opinion whether exposure to flavoring chemicals would increase risk of impairment due to medical condition(s) that they may have; 3) recommended restriction of exposure to flavoring chemicals; 4) recommended restriction of use of respiratory protective devices due to medical condition(s); and 5) recommended further evaluation and treatment of detected medical condition(s). Pulmonologists should provide to Chr. Hansen, Inc.: 1) recommended restrictions of worker exposure to flavoring chemicals; 2) recommended use of respiratory protective equipment; and 3) a statement that the worker was informed about the results of their medical examination and about medical condition(s) that should have further evaluation or treatment.

During our December 13 visit with Concentra Clinic, we made recommendations on how the quality of their spirometry tests could be improved. Our review of spirometry tests indicated that 52% of tests were of A or B quality. For workers in the medical surveillance program who do not yet have an A or B quality test, we suggest that another spirometry test be achieved with attention to spirometry test quality. Since our visit, Concentra Clinic has begun checking the quality of their spirometry tests. We suggest that at a minimum of 85% of spirometry tests should be A or B quality.

Sincerely,

Nancy Sahakian

Nancy Sahakian, MD, MPH
Medical Officer
Field Studies Branch

cc:
Michael Kulbacki, Production Manager
Worker representative
Confidential requestors
OSHA Region 5
Wisconsin State Health Department
Maja Jurisic, Regional Medical Director, Concentra Clinics

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Table 1. Test Scores Based on Quality of Forced Expiratory Volume in One Second and Forced Vital Capacity (see Appendix A)

Test Score	Number	Percent
A	8	35
B	4	17
C	6	26
D	5	22
F	0	0
Total	23	100

Table 2. Other Test Errors or Deficiencies

Type of Test Error	Number	Percent
Height error[a]	2	9
Race error – Black[b]	1	4
Possible gender error	0	0
No weight recorded	2	9
Plateau not achieved	1	4
Only 2 of 3 curves acceptable	1	4
Spirometer not calibrated on the same day as the test	0	0
Spirometry technician's name not recorded	23	100
Hankinson's prediction equations not used	23	100
Lower limit of normal values not recorded	23	100
Position of worker (sitting or standing) not recorded	23	100

[a]Some individuals had more than one test. If two tests on the same individual had different heights, we assumed that one test had the correct height, and counted this as only one case of error in height.
[b]Some individuals had more than one test. If two tests on the same individual had different a different race, we assumed that one test had the correct race, and counted this as only one case of error in race. Tests only recorded whether the worker was Black or non-Black. Since the software did not correct for Hispanic and Asian race/ethnicities, this was not recorded.

Appendix A: Scoring Criteria for Spirometry Test Quality

Test scores are based on the lowest grade for either FEV_1 or FVC. For example, if the FVC grade is B and FEV_1 grade is C, then the spirometry test quality score is C.

FVC Grades

Grade A: At least 3 acceptable curves (Miller et al, 2005),
- If best FVC is derived from the last curve, repeatability within 50 mL; otherwise, FVC repeatable within 100 mL*
- FVC acceptable curve demonstrates
  - > 6-second exhalation
  - Achievement of exhalation volume plateau

Grade B: At least 2 acceptable curves,
- FVC acceptable curve requirements
  - > 6-second exhalation
  - Achievement of exhalation volume plateau
- FVC repeatability within 150 mL

Grade C: At least 2 acceptable curves,
- FVC acceptable curve requirements are > 6-second exhalation ONLY. (Plateau is not required.)
- FVC repeatability within 250 mL

Grade D: Only one acceptable curve

Grade F: No acceptable curves

FEV_1 Grades

Grade A: At least 3 acceptable curves, repeatable within
- If best FEV_1 is derived from the last curve, repeatability within 50 mL; otherwise, FEV_1 repeatable within 100 mL*

Grade B: At least 2 acceptable curves, repeatable within 150 mL

Grade C: At least 2 acceptable curves, repeatable within 250 mL

Grade D: Only one acceptable curve

Grade F: No acceptable curve

* For the assessment of spirometry quality of Concentra Clinic spirometry tests, we used the 100 mL cut-off for Grade A for FEV_1 and FVC because individual information for each maneuver and the order of the maneuvers were not provided on the reports.

Acknowledgements and Availability of Report

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This report was prepared by Nancy Sahakian, Greg Kullman, and Richard Kanwal of RDHETAP, Division of Respiratory Disease Studies, and Kevin Dunn, of Division of Applied Research and Technology. Field assistance was provided by Randy Boylstein, Chris Piacitelli, Mike Beaty, Thomas Jefferson, Yulia Iossifova, James Couch, Dave Spainhour, Brian Tift, and Nicole Edwards. Statistical programming was provided by Nicole Edwards. Analytical support was provided by Clayton Environmental Services, Inc. Desktop publishing was performed by Tia McClelland.

Copies of this report have been sent to employee and management representatives at Chr. Hansen, Inc., the Wisconsin Department of Health and Family Services, and OSHA Region 5. This report is not copyrighted and may be freely reproduced. The report may be viewed and printed from the following internet address: http://www.cdc.gov/niosh/hee. Copies may be purchased from the National Technical Information Service (NTIS) at 5825 Port Royal Road, Springfield, Virginia 22161. Information regarding the NTIS stock number may be obtained from the NIOSH Publications Office at the Cincinnati address.

Below is a recommended citation for this report:
NIOSH [2009]. Health Hazard Evaluation Report: Title of report, City, State. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institutute for Occupational Safety and Health, NIOSH HETA No. 2007-0327-3083.

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