HAZARD EVALUATION AND TECHNICAL ASSISTANCE REPORT
HETA 90-114-L2066
NATIONAL RX SERVICES, INCORPORATED
LAS VEGAS, NEVADA
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Hazard Evaluations and Technical Assistance Branch
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I. INTRODUCTION

On January 2, 1990, the National Institute for Occupational Safety and Health (NIOSH) received a request for a health hazard evaluation at National RX Services, Incorporated, Las Vegas, Nevada. The request was submitted by a representative of the Oil, Chemical, and Atomic Workers International Union, and was prompted by reports of headaches, coughs, "allergy symptoms", and chest tightness among employees at the facility. On March 21 - 22, 1990, NIOSH investigators conducted an environmental and medical survey at the facility. During this survey, employees were interviewed regarding the presence of work-related health problems. In addition, environmental samples were collected and the buildings heating, ventilation, and air conditioning (HVAC) system was examined.

II. BACKGROUND

National RX Services, Incorporated, is a mail order pharmaceutical company. The company has been at its present location in Las Vegas, Nevada, for approximately four years. During this period, the company's operations have undergone several stages of growth and expansion. The mail order operations are conducted seven days a week, with employees working staggered shifts between the hours of 6:30 am and 6:30 pm each day.

The operations taking place in the facility primarily involve clerical staff, coders, and data entry personnel who process incoming orders, and pharmacists who review the orders and fill the prescriptions. For tablets and capsules, filling of the prescriptions is done either by manual counting of the pills or by automatic dispensing machines referred to as "Baker Cell" counters. The prescriptions are then packaged for shipment to the customer. All of these operations take place in the main "pharmacy" building where the majority of the company's employees are located.

Attached to the pharmacy is an office area where supervisory and marketing staff are located. Also directly attached to the pharmacy by a set of sliding doors is a warehouse for the storage of non-pharmaceutical supplies. Attached to this warehouse is another warehouse area for the storage of pharmaceuticals. The pharmaceutical warehouse also contains a small "prepack" room where some items are prepackaged.

Approximately one year prior to the NIOSH visit, a concern had been expressed by the local union that certain symptoms and illnesses among the employees might be related to the workplace. At that time, the company hired a private consultant to evaluate the air quality within the building. Based on this evaluation, the company purchased four high-efficiency electrostatic air filtration systems, which were mounted on the ceiling in the pharmacy area. A no-smoking policy, also implemented at this time, restricted smoking to the lunchroom and outdoors. Plans were also made to re-insulate the roof of the building in order to obtain better temperature control during the summer months.

III. MATERIALS AND METHODS

A. Medical

Confidential interviews were conducted with 25 employees during the evaluation. Employees were chosen by serial selection from a general personnel list, and included 11 pharmacists, 4 coders, 4 from the clerical staff, 3 data entry personnel, and 3 others. The mean age of those interviewed was 44 years (range 26 - 71) and there was a mean of 2.3 years experience at National RX. All 25 reported working 40 hours or more per week in the building.

The interview addressed several areas, including demographic information, reported symptoms, locations and dates of an employee's work in the building, the employee's past medical history, and whether or not a physician had been consulted regarding any symptoms reported in the interview. Certain symptoms, those specifically mentioned in the health hazard evaluation request, were the main focus of the interview. These symptoms included but were not limited to nasal irritation, throat irritation, and headaches. Questions pertaining to perception of air movement, humidity, temperature, odors, and dust in the work environment were also asked.

B. Environmental

Since preliminary results of the employee interviews seemed to indicate that the majority of the complaints were related to air quality and environmental comfort parameters, the NIOSH environmental survey focused on an evaluation of the buildings ventilation system and related factors. This consisted of: (1) an examination of the building's HVAC system, (2) an examination of the building for identifiable contaminant sources, and (3) the collection of air samples designed to assess the quality of air within the building. The specific measurements and types of samples collected in the environmental survey are detailed below.

1) Instantaneous measurements of carbon dioxide (CO_2) concentrations were made at several different times and locations throughout the building and outdoors. These measurements were made using a GasTech (Model RI 411) portable direct-reading CO_2 analyzer capable of measuring CO_2 concentrations from 50 to 5000 parts per million (ppm). The instrument was calibrated before use and checked against outdoor background levels at various intervals throughout the workday.

2) Measurements of dry bulb and aspirated wet bulb temperatures were made at several different times and locations throughout the building and outdoors using a Stortz sling psychrometer. These data were used to determine relative humidity using a psycometric chart.

3) Concentrations of carbon monoxide, nitrogen dioxide, nitrous fumes, and sulfur dioxide were measured using Draeger direct reading colorimetric indicator tubes. These samples were collected using a Draeger hand pump according to the manufacturers instructions.

4) Air flow patterns through the building were determined by observation of smoke generated by smoke tubes.

IV. EVALUATION CRITERIA

As a guide to the evaluation of the hazards posed by workplace exposures, NIOSH field staff employ environmental evaluation criteria for assessment of a number of chemical and physical agents. These criteria are intended to suggest levels of exposure to which most workers may be exposed up to 10 hours per day, 40 hours per week, for a working lifetime without experiencing adverse health effects. It is, however, important to note that not all workers will be protected from adverse health effects if their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a preexisting medical condition, and/or a hypersensitivity (allergy).

In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the worker to produce health effects even if the occupational exposures are controlled at the level set by the evaluation criterion. These combined effects are often not considered in the evaluation criteria. Also, some substances are absorbed by direct contact with the skin and mucous membranes, and thus, such contact may increase the overall exposure. Finally, evaluation criteria may change over the years as new information on the toxic effects of an agent becomes available.

The primary sources of air contamination criteria generally consulted include: (1) NIOSH Criteria Documents and Recommended Exposure Limits (RELs), (2) the American Conference of Governmental Industrial Hygienist's (ACGIH) Threshold Limit Values (TLVs), (3) the U.S. Department of Labor (OSHA) federal occupational health standards, and (4) the indoor air quality standards published by the American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE). The first three sources provide environmental limits based on airborne concentrations of substances to which workers may be occupationally exposed in the workplace environment for 8 to 10 hours per day, 40 hours per week for a working lifetime without adverse health effects. The ASHRAE guidelines specify recommended outside air ventilation rates needed to maintain acceptable indoor air quality for the majority (at least 80%) of a building's occupants. Indoor air should not contain concentrations of contaminants sufficient to impair health, or to cause discomfort to a majority of the occupants. For application to the general population, ASHRAE often recommends lower evaluation criteria than those used in industry.

A time-weighted average (TWA) exposure refers to the average airborne concentration of a substance during a normal 8- to 10-hour workday. Some substances have recommended short-term exposure limits (STELs) or ceiling values which are intended to supplement the TWA where there are recognized toxic effects from high, short-term exposures. A discussion of the substances evaluated in this survey and the ASHRAE comfort and ventilation guidelines is presented below.

A. Carbon Dioxide

Carbon dioxide is a normal constituent of exhaled breath that can often be used as an indication of whether adequate quantities of fresh outdoor air are being introduced into a building or work area. The outdoor, ambient concentration of CO_2 is about 350 ppm. Typically the CO_2 level is higher inside than outside (even in buildings with few complaints about indoor air quality). However, if indoor CO_2 concentrations are more than 1000 ppm (3 to 4 times the outside level), the building may be receiving inadequate outside air, or the air may be poorly distributed by the HVAC system. Although the CO_2, at these levels, is not responsible for these complaints such as headache, fatigue and eye and throat irritation, a high level of CO_2 does indicate that other contaminants in the building may also be increased and could be contributing to the symptoms among building occupants.[1]

B. Temperature and Relative Humidity

The majority of references addressing temperature and humidity levels as they pertain to human health frequently appear in the context of assessing conditions in hot environments. Development of a "comfort" chart by ASHRAE presents a comfort zone considered to be both comfortable and healthful. This zone lies between 73° and 77°F (23° and 25°C) and 20 to 60 percent relative humidity.[2]

C. Ventilation

Neither NIOSH nor OSHA have developed ventilation criteria for general ventilation. Criteria often used by design engineers are the guidelines published by ASHRAE. Until recently, the ASHRAE Ventilation Standard 62-73 (1973) was utilized, but recommendations were based on studies performed before the more modern, air-tight buildings became common. These older buildings permitted more air infiltration through leaks and cracks around windows and doors, and through floors and walls. Modern buildings are usually much more airtight and permit less air infiltration. Due to the reduced infiltration, ASHRAE questioned whether the 1973 minimum ventilation values assured adequate outdoor air supply in modern, air-tight buildings.

The minimum rate of outside air permitted under ASHRAE Standard 62-1989 is 20 cfm/person for general office areas, and 15 cfm/person for commercial pharmacies.[3] Where concentrated smoking occurs, such as smoking lounges, ASHRAE Standard 62-1989 recommends an outside air supply rate of at least 60 cfm/person. The basis of the outside air supply rates recommended by ASHRAE is for maintaining an indoor air quality that is considered acceptable by at least 80% of the building's occupants. However, unless referenced or specified by local building codes, building owners are not legally required to comply with these ASHRAE Standards. Most building codes refer to an earlier version of this standard (ASHRAE Standard 62-73) which was intended to conserve energy rather than promote adequate indoor air quality.

V. RESULTS

A. Medical

The most common problem identified in the interviews was "poor air quality", reported by 10 persons, followed by problems with stuffiness in the work area, reported by 9 persons. Seven employees complained about wide fluctuations in temperature at different locations in the warehouse. Five persons identified specific symptoms, such as nasal stuffiness, eye irritation, scratchy throat, or headaches which worsened while in the workplace, and improved when away from work. Employees attributed most symptoms to a variety of causes including: the ventilation system, the uneven temperatures in the building, the lack of fresh air, and dust in the workplace. Most workers said that the problems had begun occurring in the year previous to our visit.

There were no complaints or symptoms mentioned that were suggestive of exposure to any specific drug or therapeutic substance in the workplace. All 11 pharmacists denied handling specific drug products on a routine basis. Most pharmaceutical drugs to be packaged were transferred directly from pill hoppers to bottles, and direct skin contact by the pharmacists was minimal. However, several pharmacists mentioned that certain drugs, especially certain generic compounds, were more prone to breakage and generated an excess amount dust when the pills fell from the hoppers through the automated counters into the holding areas. The dust was usually contained by the hoppers, but at times it was released when the pills were transferred into the bottles by the pharmacists.

B. Environmental

1. HVAC System Inspection

Ventilation for the National RX Services building is provided through 18 rooftop air handling units (AHUs). Ventilation to the areas of the main pharmacy building is provided by eight 5-ton AHUs which distribute the air through 42 supply registers. During an inspection of the AHUs, it was noted that no intake vents were present which would allow for introduction of outside air into these systems. This finding was verified by the ventilation system contractor who indicated that, by original design, these units were set up for recirculation only. While there were cracks and small openings around the housings of the AHUs which would allow for the infiltration of outside air, it was not possible to determine how much air was introduced in this manner.

Each of the AHUs were equipped with pleated fabric filters in the air supply ducts. These filters were reportedly changed twice a year, and did not appear to be overloaded at the time of the survey. All drip pans were equipped with drains, and no slime or microbial growth was noted in the pans on any of the eight units examined.

The non-pharmaceutical warehouse area is supplied with fresh air through four evaporative air cooling units which utilize 100% outside air. These systems are reportedly used during the months of March through August.

While these units had reportedly been serviced recently for their Spring start-up, visual inspection revealed a substantial accumulation of dirt and scale on the filter material and in the recirculating reservoirs of the evaporative coolers. However, no slime or microbial growth was noted in any of these units.

2. Air Monitoring Results

Table 1 presents the results of the air samples collected for carbon dioxide (CO_2). During the period of the survey, outdoor CO_2 levels ranged from 300 to 325 ppm. CO_2 concentrations measured in the the non-pharmaceutical warehouse also ranged from 300 to 325 ppm, which would be expected due to the low occupancy of this area and the fact that the evaporative cooling units supply this area with 100% outside air. Concentrations of CO_2 in the adjacent pharmaceutical warehouse ranged from 325 to 350 ppm in the general warehouse area, and 700 to 800 ppm in the enclosed prepack room located within the warehouse.

In the main pharmacy building, CO_2 measurements were taken at several different locations, including, the mail sorting area, the review/coding area, the baker cell area, the prepack area, and the vertical shelf area. The average of the readings in these areas ranged from 650 ppm to 1050 ppm. Four measurements taken in the pharmacy building were at or above the guideline of 1000 ppm CO_2 used by NIOSH investigators in indoor air quality investigations to indicate problems caused by insufficient amounts of outside air.[1]

The average concentration of CO_2 in the pharmacy building in the morning was 700 ppm, then increased dramatically to 1050 ppm by late morning. The early afternoon readings then show a slight decrease to 900 ppm, which was possibly due to the fact that there was less occupancy over this period due to lunch breaks. The late afternoon readings (collected the previous day) show an average of 650 ppm; however, during this period the sliding doors between the pharmacy building and the non-pharmaceutical warehouse were fully opened for repairs. Since the smoke tube results indicated strong airflow from the non-pharmaceutical warehouse where CO_2 values were essentially the same as the outside air, this last value would be expected to be substantially lower than normal.

Measurements of temperature and relative humidity revealed that the dry bulb temperatures in the pharmacy building ranged from 73° to 77° Fahrenheit (F), with the relative humidity ranging from 38% to 46%. These values fall within the guidelines of 73° and 77°F temperature range and the 20 to 60 percent relative humidity range recommended by ASHRAE.[4]

The detector tube samples which were collected in the pharmacy area indicated that carbon monoxide, nitrogen dioxide, nitrous fumes, and sulfur dioxide were all below their limits of detection of 5 ppm, 2 ppm, 0.5 ppm, and 0.5 ppm, respectively.

VI. DISCUSSION AND CONCLUSIONS

NIOSH has carried out several studies involving pharmaceuticals companies.[4,5] However, these investigations have dealt with pharmaceutical production and manufacturing workers, and have not specifically dealt with pharmaceutical packaging workers. Pharmaceutical production and manufacturing workers are likely to have a greater potential for exposure to drugs than workers with controlled administration and packaging of pharmaceutical drugs.[6] Exposure in manufacturing plants occurs in the handling of the finely divided chemical solids and granules which are ground, granulated, and compressed into pill form. Most manufacturing workers are involved in batch processing of drugs, have repeated contact with the same drug, and thus have a greater chance for heavier exposure to one drug. Packaging workers, on the other hand, deal with multiple drugs that are already in pill form, and are unlikely to be exposed to the finely divided solids or pill dust on a continuous basis.[6]

The complaints reported by the employees at National RX concerned the air quality and temperature control of the warehouse. The reported symptoms were common and non-specific. They are not suggestive of any specific biologic, environmental, or pharmaceutical contaminant.

Building-related illness episodes have been reported more frequently in recent years as buildings have been made more air-tight to conserve energy and to reduce air conditioning expenses. Modern office buildings are constructed primarily of steel, glass, and concrete, with windows that cannot be opened, thus making the building totally dependent on mechanical systems for air conditioning. Contaminants may be present in make-up air or may be introduced from indoor activities, furnishings, building materials, surface coatings, air handling systems, and the building occupants. Symptoms often reported are eye, nose, and throat irritation, headache, fatigue, and sinus congestion. Occasionally, upper respiratory irritation and skin rashes are reported. In some cases, the cause of the symptoms has been ascribed to an airborne contaminant, such as formaldehyde, tobacco smoke, or insulation particles, but most commonly a single cause cannot be pinpointed. In the majority of studies of these buildings, NIOSH has attributed the problems to inadequate ventilation.[1]

During the course of this survey, no single environmental agent was identified in the building that would be directly responsible for the symptoms reported by the employees. However, measurements of CO_2, the parameter used to assess the amount of outside air introduced into the building, were found to exceed the NIOSH and ASHRAE "guideline" of 1000 ppm in some instances during the period of this survey. Since CO_2 levels above 1000 ppm in buildings can be associated with increased complaints of headaches, tiredness, and eye, nose and throat irritation, it is possible that the lack of outside air contributing to this situation has a bearing on the health effects being experienced by the employees. Furthermore, the evaporative coolers were operating in the warehouse area during the period of this survey. Since a strong airflow pattern was present from the warehouse into the pharmacy building, it is

probable that CO_2 levels were somewhat lower than would be present during times when this system is not operating, i.e., winter months. Therefore, efforts to increase the amount of outside air into the work area would be a prudent step to help to alleviate the employees health complaints.

VII. RECOMMENDATIONS

1) Steps should be taken to ensure that appropriate amounts of outside air are introduced into the building to conform to ASHRAE guidelines. Air should also be properly tempered to ensure that it meets minimum ASHRAE guidelines for comfort (i.e., temperature and relative humidity).[2,3]

2) Although the types and pattern of symptoms did not indicate the employees' complaints to be related to exposure to pharmaceutical products, care should be taken to reduce employee exposure to the dust generated from these products as much as possible. Where certain pharmaceutical products create excessive dust, these areas and/or individual Baker Cell units should be frequently cleaned to prevent the possibility of the introduction of these dusts into the work environment.

3) Drip pans for the cooling coils and the evaporative coolers should be regularly inspected to ensure that no microbial growth accumulates on these systems.

VIII. REFERENCES

1. National Institute for Occupational Safety and Health. Guidance for Indoor Air Quality Investigations. Cincinnati, Ohio: Hazard Evaluations and Technical Assistance Branch, National Institute for Occupational Safety and Health, 1987.

2. American Society of Heating, Refrigerating and Air-Conditioning Engineers, Inc. ASHRAE Standard 55-1981, Thermal Environmental Conditions for Human Occupancy. Atlanta, Georgia: ASHRAE, 1981.

3. American Society of Heating, Refrigerating and Air-Conditioning Engineers, Inc. ASHRAE Standard 62-1989, Ventilation For Acceptable Indoor Air Quality. Atlanta, Georgia: ASHRAE, 1989.

4. National Institute for Occupational Safety and Health, Health Hazard Evaluation, Mylan Pharmaceuticals, Morgantown, West Virginia; November 1982, Report 81-322-1228

5. National Institute for Occupational Safety and Health, Health Hazard Evaluation, Rexall Drug Company, St. Louis, Missouri; September 1982, Report 80-79-1189

6. Teichman RF, Fallon LF, Brandt-Rauf Pw. Health Effects on Workers in the Pharmaceutical Industry: a Review; Journal of the Society of Occupational Medicine 1988. 38, 55-57.

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TABLE 1
ENVIRONMENTAL MEASUREMENTS OF INDOOR AIR QUALITY PARAMETERS
NATIONAL RX SERVICES INCORPORATED
LAS VEGAS, NEVADA

Sample Time	Sample Location	Dry Bulb Temperature °F	Relative Humidity (Percent)	Carbon Dioxide (ppm)
Samples collected March 21, 1990				
3:45 pm	Outdoors	86	24	325
3:55 pm	Non-Pharmaceutical Warehouse	71	56	325
4:05 pm	Mail Sorting Area - Pharmacy	75	44	575*
4:10 pm	Baker Cells 9 - 10 - Pharmacy	**	**	725*
Samples Collected March 22, 1990				
7:45 am	Outdoors	74	28	325
7:48 am	Non-Pharmaceutical Warehouse	62	62	325
7:50 am	Pharmaceutical Warehouse	67	50	350
7:52 am	Prepack - Pharm. Warehouse	72	46	725
7:55 am	Mail Sorting Area - Pharmacy	75	38	625
7:58 am	Review/Coding - Pharmacy	75	38	700
8:00 am	Baker Cells 9 - 10 - Pharmacy	75	41	775
8:02 am	Prepack 1 & 2 - Pharmacy	75	38	725
8:05 am	Vertical 6 - Pharmacy	**	**	**
10:40 am	Outdoors	74	40	300
10:43 am	Non-Pharmaceutical Warehouse	67	54	350
10:45 am	Pharmaceutical Warehouse	70	48	375
10:46 am	Prepack - Pharm. Warehouse	75	38	800
10:48 am	Mail Sorting Area - Pharmacy	74	40	975
10:50 am	Review/Coding - Pharmacy	74	40	1000
10:53 am	Baker Cells 9 & 10 - Pharmacy	74	41	1075
10:55 am	Prepack 1 & 2 - Pharmacy	74	40	1075
10:58 am	Vertical 6 - Pharmacy	73	40	1075
1:00 pm	Outdoors	83	30	300
1:03 pm	Non-Pharmaceutical Warehouse	69	55	300
1:05 pm	Pharmaceutical Warehouse	71	52	350
1:08 pm	Prepack - Pharm. Warehouse	74	47	700
1:10 pm	Mail Sorting Area - Pharmacy	77	39	900
1:12 pm	Review/Coding - Pharmacy	76	42	900
1:15 pm	Baker Cells 9 & 10 - Pharmacy	75	44	950
1:17 pm	Prepack 1 & 2 - Pharmacy	75	44	925
1:20 pm	Vertical 6 - Pharmacy	73	46	900

Evaluation Criteria - Refer to Section IV of Report

Abbreviations and Key
* - Door between Non-Drug Warehouse and production area opened for repair.
** - No reading taken
ppm - parts of contaminant per million parts of air