U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
CENTER FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
CINCINNATI, OHIO 45226

HEALTH HAZARD EVALUATION DETERMINATION
REPORT HE 77-66-531

SUCRETS DEPARTMENT
MERCK, SHARP & DOHME
WEST POINT, PENNSYLVANIA

OCTOBER 1978

I. TOXICITY DETERMINATION

NIOSH has performed a combined environmental and medical evaluation of workplace conditions and the health status of employees in the Sucrets® manufacturing and packing departments of Merck, Sharp and Dohme in Westpoint, Pennsylvania. The results of employee interviews, limited physical examination, pulmonary function testing, and process evaluation disclosed that employee health complaints were associated with menthol contamination of the workroom air. Interview of employees disclosed various health complaints which they associated with menthol exposure: local irritation of the eyes, nasal passages, throat and larynx. Physical examination found large numbers of the study group with inflamed vocal chords, throats, and nasal mucosae; additionally, there appeared to be an excess of individuals with inflammation of the conjunctivae, and suspected nasal polyps unilaterally or bilaterally. Significant pulmonary function changes were found in pre- and post-exposure testing; in the total group, Forced Vital Capacity (FVC) was decreased, and Forced Expiratory Flow 75-85 percent ($FEF_{75-85\%}$), and Maximal Expiratory Flow 75 percent ($MEF_{75\%}$) were increased. Groups of individuals who had never smoked, or previously smoked and quit, showed significant decreases in FVC and Forced Expiratory Volume in one second (FEV_1) in pre- and post-exposure testing, but no significant changes in Forced Expiratory Flow (FEF). Symptomatic complaints of local irritation from menthol exposure were most prominent in those never smoking or having quit smoking; physical findings of local irritant effects were found in similar proportions in groups of those currently smoking and those not smoking. Absence of a control group and the sample size of 49 did not allow for extensive sub-group analysis or control of additional variables.

Air sampling during Regular Sucrets® production on April 22, 1977 and October 11-13, 1977 (the period during which medical testing was performed) found that menthol concentrations were highest in the candy production and cooling rooms (a range of 0.9 to 39.4 mg/M^3). Menthol concentrations in the wrapping and packing room ranged from below detectable levels to 2.3 mg/M^3. The source of menthol air contamination appears to be in the

candy room during the processing of the hot candy mass and lozenges. The contaminated air from the candy and cooling rooms appeared to be the major source of menthol air contamination in the Sucrets® wrapping and packing areas. Air sampling was not performed during the production of Mentholated Sucrets®, reported by many employees to be the situation with the most bothersome menthol air contamination.

Details of this evaluation, as well as exposure control and medical surveillance recommendations are contained in this report.

II. DISTRIBUTION AND AVAILABILITY OF DETERMINATION REPORT

Copies of this Determination Report are currently available upon request from NIOSH, Division of Technical Services, Information Resources and Dissemination Section, 4676 Columbia Parkway, Cincinnati, Ohio 45226. After 90 days the report will be available through the National Technical Information Service (NTIS), Springfield, Virginia. Information regarding its availability through NTIS can be obtained from NIOSH, Publications Office at the Cincinnati address.

Copies of this report have been sent to:

a) Merck, Sharp & Dohme, West Point, Pennsylvania
b) Authorized Representative of Employees - Local Union 886, Oil, Chemical and Atomic Workers
c) Oil, Chemical and Atomic Workers, Denver, Colorado
d) NIOSH, Region III
e) U.S. Department of Labor, Region III

For the purpose of informing the approximately 99 "affected" employees, the employers shall post the Determination Report for a period of 30 days in a prominent place(s) near where exposed employees work.

III. INTRODUCTION

Section 20(a)(6) of the Occupational Safety and Health Act of 1970, 29 U.S.C. 669(a)(6), authorizes the Secretary of Health, Education, and Welfare, following a written request by an employer or authorized representative of employees, to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found.

The National Institute for Occupational Safety and Health (NIOSH) received such a request from an authorized representative of employees concerning exposures in the Sucrets® packing area (Department 276) at Merck, Sharp & Dohme, in West Point, Pennsylvania. It was stated on the request that the employees had experienced tearing of the eyes, reddening of the nose and eyes, tightness and soreness of the throat, and loss of voice.

IV. HEALTH HAZARD EVALUATION

A. Evaluation Chronology

NIOSH industrial hygienists and medical officers under contract to NIOSH visited the Sucrets® Department on April 22, 1977 to investigate the alleged health hazards. NIOSH investigators met with representatives of Merck, Sharp & Dohme, and employees (Local Union 886, Oil, Chemical, and Atomic Workers) to discuss the request that NIOSH had received and the nature and extent of the alleged health problem. NIOSH investigators performed a walk-through survey of the Sucrets® manufacturing and packing operations to observe work activities and collect information on the materials in use. Area air sampling was performed for possible air contaminants. NIOSH medical officers individually interviewed six workers concerning the types, extent, and duration of work related health problems they had experienced. Results from the initial visit and investigation suggested the need for a more extensive follow-up investigation to include environmental monitoring and medical evaluation. Findings from the initial visit indicated that menthol, a component in some Sucrets® products, was the main air contaminant responsible for the alleged health problem. Difficulties in scheduling a follow-up visit were encountered due to the intermittent production and packing schedules.

NIOSH industrial hygienists and medical officers returned to the Sucrets® operations on October 11-13, 1977 and performed an in-depth evaluation of worker exposures to air contaminants and health effects from these exposures. Worker's exposures to air contaminants were measured during the evening work shift of October 11, 1977, and during the day and evening work shifts of October 12 and 13, 1977. NIOSH industrial hygienists investigated the sources and parameters affecting the menthol contamination of the workroom air. NIOSH medical officers interviewed and examined employee volunteers during October 11-14, 1977 to determine the types and extent of any work related health problems. Pulmonary function testing was performed before and after work periods to determine if acute (short-term) respiratory effects resulted from work exposures.

B. Process Description

Approximately 99 employees are involved in the manufacturing and packing of the Sucrets® throat lozenge products. These operations are in production for two eight-hour shifts each day, and for five to six days a week. Department 212 (Sucrets® manufacturing or "candymaking") involves about three employees per shift (a total of six). Department 276 (Sucrets® packing) employs 93 persons. There are five Sucrets® products: Regular (HMF-high menthol formula), Mentholated, Children's, Hold®, and Cough Control®. Only the Regular and Mentholated Sucrets® products have appreciable quantities of menthol. About 50 percent of the manufacturing time is spent producing the Regular Sucrets® product. The Sucrets®

products have reportedly been sold to another corporation and these Sucrets® Manufacturing operations are scheduled to stop at this location in October 1978. Employees in the Sucrets® Department are expected to transfer to other departments at Merck, Sharp & Dohme.

The candymaking operations are performed by three workers per shift. The "candy room" is separated from the packing and wrapping area by permanent walls. The candy can be made either by a continuous process method (using a Hamac-Hansella continuous cooker), or by a batch method (using a Hamac-Hansella batch cooker). At the time of this investigation, only the candy for the Childrens and Regular Sucrets® lozenges have been made by the continuous method. All products except the Childrens Sucrets® can be made by the batch method. By the batch method, a sugar solution is preheated to 240°F and cooked in a vacuum cooker to about 295°F and the steam is drawn-off to remove the water. The cooker is then opened and colorant, menthol crystals (for the Regular and Mentholated Sucrets®), and 4-hexylresorcinol is added to a "pocket" formed in the hot and viscous candy mass. The hot candy is then folded over to entrap these ingredients, and is then emptied onto a mechanical kneader and kneaded for a period of about 4-5 minutes. By the continuous method, the sugar solution is cooked and water vapor removed to produce the hot viscous candy. As the cooked candy mass flows out of the continuous cooker the 4-hexylresorcinol and flavor solution is added into the candy mass. The candy then flows into a mechanical pot where the menthol solution (about 90 percent menthol) is added and stirred mechanically. The candy then flows from the pot to the cooling band where the candy is folded several times and air is pressed out by a roller system. The candy mass (made by either the batch or continuous method) is then transferred to the spinners where the candy is rolled down to rope size, and then fed into the lozenge formers/cutters. The formed lozenges are then transferred to the cooling room where a blower is used to cool and harden the lozenges. After automatic sizing to reject over and under size lozenges, the lozenges are transferred via conveyer belts to holding bins above the wrapping machines located in the main work area. The lozenges at this point are at about 120°F.

Approximately eight employees attend the wrapping machines which wrap the individual lozenges in foil. Drums of foil wrapped lozenges are stored or transported to the adjacent packing area. Approximately 20 employees per shift are involved in packing the lozenges into tins. Approximately 10 other employees per shift operate machinery which wraps the tins in cellophane, and pack the tins in boxes for shipment. There are approximately 10 other employees per shift in the area, including supervisors and maintenance personnel. Job categories in Department 276 include: Lozenge Packer, General Worker, Cellophane Operator, Set-up Mechanic, and Group Leader.

C. Evaluation Methods

1. Medical

A cross-sectional study of possible health effects on the current employees was performed because of the absence of significant literature dealing with exposure to menthol in the workplace. The evaluation which was conducted examined for subjective symptom relationships to working menthol exposures, signs of lower and upper respiratory tract effects on physical examination, changes in values of pulmonary function, and laryngeal or vocal cord effects. A medical questionnaire detailing past medical history, smoking history, sensitivity to allergens, and recent or current symptoms was administered. Pre- and post-exposure pulmonary function testing, and a limited physical examination with indirect laryngoscopy and auscultation of the chest was performed.

See Appendix I for examples of the questionnaire and physical examination form.

A Hewlett-Packard 9825A Instrument* was used, with nomogram values based on Morris.[1,2] Pulmonary function testing entailed three efforts on a forced vital capacity on this instrument, one test sequence preceeded the work shift; and a second test sequence was performed during the work hours and presumably menthol exposure. The best of three efforts is analyzed according to the Morris monogram values for forced vital capacity, forced expiratory volumes, forced expiratory flows, peak flow, and mid-expiratory flows. Testing was conducted at a location removed from production. All employees were invited to participate over both shift periods.

The information was coded, keypunched, and verified, then analyzed according to general statistical procedures: general frequency distributions, Chi-square, "t" test, Fisher's exact test, Wilcoxon matched-pairs signed-ranks test, cross tabulations, and general descriptive statistics of the sample.

Reports of physical examination findings and all pulmonary function testing were mailed to participating employees, and, with signed release of information consent, to the personal physician or corporate medical department.

2. Environmental

NIOSH industrial hygienists interviewed production employees and supervisory personnel concerning the sources, nature, and extent of air contamination in the Sucrets® Departments in relation to odor and any health effects. The ventilation systems and air movement patterns in these areas were examined using smoke tubes and visual observation.

*(Mention of commercial name does not constitute an endorsement by the National Institute for Occupational Safety and Health.)

Air Sampling and Analysis

Five area air samples were obtained during the April 22, 1977 visit and analyzed for the presence of both menthol and 4-hexylresorcinol. Air was drawn at about one liter per minute through two impingers connected in-series containing 15 ml of isopropyl alcohol. These impinger samples were analyzed for menthol and 4-hexylresorcinol by gas chromatographic methods developed by NIOSH laboratories.

Extensive air sampling for menthol was conducted during the day and evening shifts on October 11-13, 1977. Personal air sampling was performed with workers who were able to wear the sampling equipment without hindering work activities or jeopardizing the purity of the product. Otherwise, area air samples were obtained at locations which approximated breathing zone conditions. Portable air sampling pumps (MSA model G, calibrated before and after sampling) were used to draw air at about 600 ml per minute through impingers containing 12 ml of analytical grade isopropanol. Spill-proof impingers were used for the personal samples. Additional isopropanol was added to the impingers, as needed during sampling, due to evaporation. The NIOSH contract laboratory analyzed these samples for menthol using a gas chromatographic method. Drager gas detection units were used to measure several other possible air contaminants: ozone (lower limit of detection-0.05 ppm), carbon monoxide (lower limit of detection-5 ppm), oxides of nitrogen (lower limit of detection-0.5 ppm), and aldehydes (lower limit of detection-0.5 ppm). Only the measurement system for carbon monoxide is NIOSH Certified to have an accuracy of ±35 percent at 1/2 the exposure limit, and an accuracy of ±25 percent at 1 to 5 times the exposure limit.

D. Evaluation Criteria

1. Toxic Substance Medical Data

There are no reported short or long-term health effects with exposure to menthol or hexyl-resorcinol in the occupational environment. In this study the major exposure to menthol is from air contamination and the primary route of entry to the body is inhalation.

4-Hexyl-1,3-dihydroxybenzene, commonly known as hexyl-resorcinol[3] found pharmacologic use after development as an anti-helminthic. After oral ingestion, it has been found to be irritating to the oral and gastric mucosae. The dosages employed are customarily in the 1 gram range in humans[4] and both the dosage and route of administration differ from the occupational exposure under study. Oral ingestion has also been accompanied by local irritation of the stomach, with nausea and vomiting, and, in animal systems, lethargy, weight loss, and anorexia[5]. The compound is irritating to the eyes and has been associated with local skin irritation in its crystalline form[6]. The Merck Index states that hexyl-resorcinol may cause burns of the skin and mucous membranes[7]. In the murine system, concentrated forms have been reported as causing dermatitis[5].

Menthol, chemically known as hexahydrothymol, 3-p-methanol, is a principal constituent of oil of peppermint, and many isomeric forms may exist. There are no reported studies on health effects from menthol in the occupational environment. Scientific literature concentrates mainly on the oral route rather than that of inhalation as seen in the present study.

Large scale ingestion may result in abdominal pain, nausea, emesis, diarrhea, and possible central nervous system depression. In mice, a 1931 study cited an LD_{50} of 3.0 to 4.0 mg/gm, by ingestion[8]. Reports of possible interference of menthol vapors with pulmonary bacterial defense mechanisms have been published[9]; subsequent reports[10] did not substantiate this and, at concentrations meant to replicate use in a room environment of 0.13 mg/M^3 menthol, no adverse effects were reported. In two studies[12,13] menthol was compared to other potential stimulants of liver microsomal enzyme systems. No significant effects were demonstrated.

A summary of the Advisory Panel on OTC Cold, Cough, Allergy, Bronchodilator and Antiasthmatic Products[14] in 1976 concluded the following from testimony presented before it:

1) the fatal oral dose of menthol in man is approximately 2 gm

2) topical application may be irritating and repeated exposure may be sensitizing

3) in studies of vapors of menthol, no toxic or irritant effects were demonstrated

4) persistent use of lozenges with menthol or eucalyptus revealed a marginal increase of local oral mucosa and upper pharyngeal irritation over control subjects

5) aerosol studies in monkeys showed eye irritation only.

A commonly recognized effect of menthol is a "cooling" sensation on the skin. The effect derives from action on thermoreceptors in the nervous system of the skin, amplifying cold conditioned discharges[15].

Potential exposure to menthol vapors is extensive on both sides of the marketplace--cosmetics, flavoring agents, cigars, cigarettes, other tobaccos, cough lozenges, syrups--and may be significant for both manufacturing personnel and consumers.

In the current study, the Sucrets® product considered responsible for menthol exposure also contain additional compounds. Product description in Clinical Toxicology of Commercial Products lists Sucrets® products as containing dextro-methorphan, cetylpyridinium chloride, benzocaine, phenylephrin HCl, and phenylpropanolamine HCl.

2. Environmental

There are currently no standards or guidelines concerning occupational exposure limits to either menthol or 4-hexylresorcinol. A search of the available literature relating to occupational exposures failed to produce any information or reports regarding worker exposure to either menthol or 4-hexylresorcinol.

Several other possible air contaminants were measured by grab air samples (Drager method). The criteria used for these air contaminants are those exposure limits recommended by either NIOSH or the American Conference of Governmental Industrial Hygienists (ACGIH 1977 TLVs): carbon monoxide, 35 ppm 8-hour time weighted average concentration and 200 ppm ceiling (NIOSH); formaldehyde, 1 ppm for any 30 minute period (NIOSH); nitric oxide, 25 ppm 8-hour time weighted average concentration (NIOSH); nitrogen dioxide, 1 ppm ceiling concentration (NIOSH); ozone, 0.1 ppm 8-hour time weighted average concentration.

E. Evaluation Results and Discussion

1. Medical

Forty nine individuals participated in the study; 29 (59.2%) were males and 20 (40.8%) were females. Table 1 illustrates further race-sex breakdown of the sample. Forty one individuals completed both pre- and post-exposure pulmonary function testing, being composed of 23 males and 18 females, 32 (65.3%) participated from the day shift, and 17 (34.7%) from the night shift.

The range of ages for the whole group was 21 to 65 years, with a mean of 44.1 years.

Cumulative work on Sucrets® ranged from less than one year to 41 years, with a mean service of 8.4 years; 13 of the 49 participants had worked in the Sucrets® Department less than one year, to as little as one month's duration. Reported time at the present Sucrets® job ranged from one month (6 participants or 12.2%) to 41 years (1 individual); mean time at the present job was 7.7 years.

Participants were distributed among six different job categories as shown in Table 2. "Lozenge packers" accounted for 27 (55.1%) of the participants; "general workers" was the second largest group with 10 (20.4%).

Table 3 describes the smoking behavior of the sample under study. Thirteen (26.5%) individuals had never smoked cigarettes; 10 (20.4%) had smoked in the past but had quit; and 26 (53.1%) were currently actively smoking. Approximately the same proportions were represented in the group completing both pre- and post-exposure pulmonary function testing.

Table 3a further describes the degree of smoking in those currently smoking, determined by packs of cigarettes consumed daily multiplied times the number of years smoked. 57.7% of the smokers had experienced 20.1 or more maximum pack-years of smoking behavior.

Thirty four individuals (69.4%) indicated no significant previous medical history prior to employment. Twenty six (53.1%) of the participants indicated no family history of respiratory disease. Comparison of medical history prior to and after Sucrets® employment did not reveal significant change or increase in diseases reported.

Thirty five (71.4%) individuals indicated zero or one absence with a cold in the preceding year, and 49% took ten or less sick days in the preceding year.

In analyzing the data gathered, the main emphasis was placed on the relationship to menthol exposure. Employee complaints were most directly related to this, and previous environmental measurement had demonstrated less than detectable concentrations of hexyl-resorcinol.

Table 4 describes the frequency and percentage of symptomatic complaints and the subjective relationship to menthol exposure in groups of the sample who had never smoked, smoked in the past but quit, present smokers, and the total sample. In those who never smoked, complaints of runny nose, and watering of the eyes were most frequently associated with menthol exposure. Previous smokers complained of redness of the eyes associated with menthol in addition to the previous symptoms. Watering of the eyes, runny nose, and hoarseness were significant complaints that current smokers associated with menthol exposure. In the total group interviewed, more than 50% of those with specific symptoms associated runny nose, watering of the eyes, and redness of the eyes with menthol exposures. Greater percentages of non-smokers and past smokers having quit complained of the above symptoms, excluding hoarseness, than did current smokers; in general, current smokers complained of more symptoms and more frequently than the other two groups, though not related to menthol to as significant a degree.

Table 5 describes the physical examination findings in groups of menthol workers according to smoking behavior. Non-smokers showed essentially normal eye and ear examinations; on nasal examination, 4 (30.8%) demonstrated inflammation or swelling, and 2 (15.4%) demonstrated a suspected nasal polyp. Vocal cord examination showed 3 (23.1%) with inflammation; vocal cord function and chest auscultation were normal. In examination of the throat, 5 (38.5%) showed inflammatory changes.

In previous smokers, eye examination showed 2 (20%) with inflammatory changes; ear examination was essentially within normal limits; nasal examination showed 4 (40%) with inflammation or swelling, and 1 individual demonstrated a suspected nasal polyp. Two (20%) had inflamed vocal cords, and 2 (20%) had inflamed throats.

Current smokers demonstrated the following findings: essentially normal conjunctivae and eyelids; essentially normal ear examinations; 7 (26.9%) with inflammation or swelling of nasal menbranes; 4 (15.4%) with suspected nasal polyp; 9 (34.6%) with inflamed vocal cords; essentially normal vocal cord function; essentially normal chest auscultation; and 12 (46.1%) with inflamed throats.

The total group showed 6 (12.2%) with inflammation of the conjunctivae or eyelids; 14 (28.6%) had abnormalities of the ear, mainly occlusion or minor non-inflammatory abnormalities secondary to personal hygiene or previous trauma unrelated to menthol exposure; 15 (30.6%) showed inflammation or swelling of the nasal membranes; 7 (14.3%) demonstrated suspected nasal polyps; 14 (28.6%) showed inflamed vocal cords; vocal cord function and chest auscultation were essentially normal; and 19 (38.8%) demonstrated inflamed throats.

In summary, inflammatory changes in the nasal mucosae, vocal cords, and throats were found on examination of menthol workers in similar proportions in smoking as well as non-smoking individuals. The prevalence of nasal polyps in the general population is unknown; these are associated with hypersensitivity or atopic responses in nasal mucous membranes, beginning as an initial focal damage to mucosal tissue and producing the polyp as intercellular fluid collects. Seven (14.3%) of the total group demonstrated a suspected polyp, and this may represent an excess over expected occurrence.

Chronic smoking, a known cause of several irritant and inflammatory changes on the respiratory system an associated factor with long term changes in pulmonary function, can be responsible for the findings in those currently smoking. However the prominence of certain changes in the non-smoking groups suggests exposure to menthol as the cause.

Table 6 illustrates the distribution of pre-exposure pulmonary function testing in males and females in five parameters where actual values are compared to a predictive nomogram. In the total group, ten had less than 80% of the predicted $FVC_{75-85\%}$; 22 had less than 80% of predicted $FEF_{200-1200}$; 3 had less than 80% of predicted $FEF_{25-75\%}$; 35 had less than 80% of predicted $FEF_{75-85\%}$; and 38 had less than 80% of the FEV_1/FVC.

Table 7 lists the values determined by t-test on pre- and post-exposure comparative pulmonary function testing for the 41 individuals completing both tests. Four values show significance; FVC is significantly decreased; $FEF_{25-75\%}$, $FEF_{75-85\%}$, and $MEF_{75\%}$ are all significantly increased after exposure. For males only, FEV_1/FVC was significantly increased as was

$FEF_{25-75\%}$. Lozenge packers and general workers showed a significant increase in $MEF_{75\%}$. .The findings of forced expiratory flows show significant increases for the whole group as well as the groups mentioned above. Mid- and forced expiratory flows are known to be decreased in smokers, and are thought to represent degrees of small airway disease. The demonstration of significant increases in this study should be interpreted cautiously in view of variability and validity of determining predicted values, and the absence of a comparative control group.

Table 7a indicates the direction of change in several pulmonary function parameters in comparative pre- and post-menthol exposure testing, by groups according to cigarette smoking behavior. Differences in the test values for the separate groups were analyzed by the Wilcoxon matched-pairs signed ranks non-parametric test, and for the total group by the t-test. Those individuals who never smoked, or had previously smoked but quit, showed significant decreases in the forced vital capacity and the forced expiratory volume at one second (FVC and FEV_1). In those currently smoking no changes of significance were noted in pre- and post-exposure testing.

In the two groups which were not currently smoking, other causes of decrease in pre- and post-menthol exposure pulmonary function testing can be differences in effort of those examined, or possible exposure to other environmental agents which might cause bronchoconstriction. Ideally, pre-exposure testing is completed at the beginning of the work week, and post-exposure testing during the exposure period. Due to production schedules, the present study tested individuals as they became available. In some instances the post-exposure pulmonary function testing was performed during the workshift and the participants returned the next day prior to the workshift for the pre-exposure testing. Having once performed the test, a subject in further testing may perform better because of practice, or more poorly because of disinterest. Additionally, differences may arise when tests are administered by different examiners. In this study, however, these circumstances would appear to have occurred equally to the sample examined, and similar effects would be seen in each group. The absence of significant decreases in the smoking group lends support to the possibility of menthol as the cause.

Cross-sectional studies, by their design, examine only current employees. Those who have left the job because of health effects, promotion, or other reasons, are not followed or examined. The sample group in the study may represent those who for various reasons, including the interaction of health and the workplace, persist at the job. They may represent the most healthy workers; no conclusions about all individuals who have ever worked in a process can be made.

In this study, although all employees were eligible to participate, only 50% chose to do so. Results based on those motivated to participate may be biased.

Requirements of the study did not allow examination of a similar unexposed control group. Individuals did serve as their own controls in pre- and post-exposure pulmonary function testing. In the absence of documented normal values or rates of prevalence for several of the items examined in this study in the working population, firm statements about degrees of effects are difficult to make.

General workers and lozenge packers comprised 37 of 49 participants. These 2 job categories experienced the lowest measured concentration of menthol. Two candy makers participated and were exposed to the highest menthol concentration. Because the groups differed so greatly in numbers, no meaningful dose-response relationship could be determined.

Question 18 of the questionnaire (Appendix I) which was intended to examine the relationship of symptomatic complaints before and after introduction of menthol proved to have too many inconsistencies in dates recorded to be reliable.

Several employees noted that their symptoms were worse during "high menthol" production, but the testing in this study took place during Regular Sucrets® production.

2. Air Sampling

Results of area air sampling for menthol on April 22, 1977 are summarized in Table 8. Menthol levels were found to range from 0.78 to 1.69 milligrams per cubic meter (mg/M^3) of air. Analysis of the isopropyl alcohol collecting media failed to detect 4-hexylresorcinol in excess of 3.5 micrograms per sample, the lower limit of detection. No menthol or 4-hexylresorcinol was detected in the isopropyl alcohol collecting media of any of the backup impinger samples.

Table 9 summarizes NIOSH personal and area air sampling results from October 11-13, 1977. Table 10 summarizes the results of Tables 8 and 9 according to the work area of the person sampled or sample location. Menthol concentrations in the packing areas ranged from below detectable levels to 2.3 mg/M^3. Menthol concentrations in the area of the wrapping machines ranged from below detectable levels to 2.3 mg/M^3. Menthol concentrations in the cooling room ranged from 1.9 to 21.1 mg/M^3. Menthol concentrations in the candy room ranged from 4.9 to 39.4 mg/M^3. One part per million (ppm) air contamination of menthol is equivalent to 6.4 mg/M^3. (The analytic lower limit of detection was 0.1 milligram per sample and sample volumes ranged from 14.3 to 442 liters). Personal air samples were obtained for periods representing a workers' total shift period. The air sampling pumps were usually removed from workers when they went on lunch break or when participating in medical testing and interview. Regular Sucrets® were being manufactured and packed during these sampling periods. Workers and their supervisors in the various areas generally stated that the conditions were "about normal" for this type of production.

Measurement for carbon monoxide, ozone, oxides of nitrogen, and aldehydes (by the Drager unit methods) failed to detect these contaminants on October 11 and 12, 1977 at or below the accepted exposure limits. No source of these contaminants had been identified. (Measurements were taken in the interest of completeness.)

3. Discussion of Environmental Investigation

Most of the workers in the Sucrets® Department stated that the menthol contamination of the air was bothersome at times. Most of the workers stated that the amount of menthol in the air varied, and was the most noticeable and irritating during the manufacture of the "high-menthol" lozenges. Employees who were questioned about the menthol levels generally stated that they were "normal" during the NIOSH visit of October 11-13, 1977 (Regular Sucrets® were being manufactured and packed during this visit). The employees stated that menthol levels were highest in the candy room.

NIOSH industrial hygienists probably experienced the range of potential work-exposures to menthol while conducting the air sampling. The distinctive "peppermint" odor of menthol was noticeable in all areas of the Sucrets® manufacturing and packing operations, most of the time. Menthol odor was also commonly detected in a hallway adjacent to the Sucrets® Department. The menthol in the air at the packing and wrapping areas was generally not too bothersome to the NIOSH industrial hygienists. Menthol contamination of the air in the Sucrets® manufacturing and cooling rooms was noticeably higher and quite irritating at times. When the candy making process was operating, the NIOSH industrial hygienists remained in the candy room only the time required to attend the air sampling equipment and interview the Candy Makers. The following symptoms were typically experienced in the candy room: immediate stinging and watering/tearing of the eyes was noticed upon entering, followed by moderate irritation of the nasal passages and throat. A NIOSH industrial hygienist (J.G.) hand held an air sampler for 15 minutes at the examination-port of the continuous candy cooker. This location probably has the highest exposure potential, and is one at which the Candy Maker usually spends only short periods of time. The following symptoms were experienced during this 15 minute sample: immediate stinging and tearing of the eyes, soreness and dryness in the tonsil area of the throat, a "cooling irritation" of the nose, watery nasal discharge, periodic (non-productive) coughing, and "tingling" sensations in the face and arms. "Cold sweating" occurred for about five minutes after leaving the candy room (which was hot and humid). The menthol level during this sample was 39.37 mg/M^3 (see Table 9). Menthol in the packing area air was generally not detected following time spent in the candyroom. NIOSH industrial hygienists reported experiencing dry and "chapped" lips, and mild throat soreness (when polled eight hours following their last exposure to menthol).

Interviews with the employees in the packing and wrapping areas disclosed a consistent complaint that menthol in the air was highest during the manufacture of the "mentholated" lozenges. Health and safety representatives with Merck and Company were unable to explain the worker complaints associated with the Mentholated Sucrets® since the amount of menthol in the Mentholated Sucrets® is only about ten percent above that in the Regular Sucrets®. The Mentholated Sucrets® are only manufactured by the batch method of cooking and mixing, thus suggesting that the batch vs. the continuous method of candy making was responsible for the increased employee complaints. While the candy makers agreed that their menthol exposures could be higher with the batch process (the operation of kneading the candy just after adding menthol crystals was reported to occasionally result in overwhelming exposures), the employees in the wrapping and packing areas did not agree and were uncertain as to which process resulted in their highest exposures. (The continuous cooker can produce candy at a rate 15 percent greater than by the batch method.)

The main source of menthol air contamination appeared to be from the evaporation of menthol from the hot candy and lozenges. (The boiling point of pure menthol is 212°F.) Significant menthol evaporation occurs (with the continuous cooker) while producing Regular Sucrets® once the menthol solution is added to the candy mass at the mechanical pot, and until the lozenges are cooled and hardened in the cooling room. By the batch method, menthol is released once the menthol crystals are added to the candy mass, and until the lozenges are cooled and hardened. Air samples obtained directly over the bins of unwrapped lozenges on October 13, 1977 did not indicate significant evaporation of menthol at this point in the process (see Table 9).

Evaluation of the ventilation system and air movement patterns disclosed that the menthol evaporating from the hot candy was able to escape into the candy and cooling rooms. Local exhaust ventilation systems were located above the mechanical pot (where the menthol solution is added with the continuous cooker) and at the formers. A local exhaust vent is present to control menthol vapors while mixing by the batch method. Visual inspection of these local exhaust systems using smoke tubes disclosed that evaporating menthol would be only partially captured. Effective local exhaust ventilation was not provided at the majority of the process positions where menthol evaporation occurs. A ceiling exhaust fan located above the continuous cooker was observed to noticeably reduce the accumulated menthol in the candy room air. However, this fan was reported and observed to be working only part of the time (due to apparent lack of maintenance). Air is provided to the candy room from a separate air intake on the roof above the candy room, and is distributed through several wall supply vents. The various exhaust systems (at the "mechanical pot", the formers, steam exhausts for the continuous and batch cookers, and the ceiling exhaust fan) all had separate exhaust points. The positioning of these exhaust points was

close enough so that particular wind conditions could result in contaminated make-up air provided to the candy room. The cooling room was at positive pressure relative to the candy room and wrapping area. This imbalance in the ventilation system appeared to be the major source of menthol contamination of the wrapping and packing areas during the October 11-13, 1977 visit. The ventilation in the wrapping and packing areas consists of an 80 percent recirculation of the conditioned air. The fresh air intake for the ventilation of the packing and wrapping areas appeared to be adequately distanced from any major source of exhausted contaminant. Maintenance of proper air temperature and humidity is important to prevent the lozenges from sticking.

F. Conclusions

The current study reveals that workers in the Sucrets® Department have health effects related to menthol exposure. The major symptomatic complaints associated with menthol as determined by employee interview were primarily local irritation of the eyes, nasal passages, throat, and larynx. Specifically, those who were not currently smoking complained of runny nose and redness and watering of the eyes. On physical examination, prominent findings among the non-smoking participants included inflammatory changes in the nasal mucosae, vocal cords, and throats. Seven (7) participants with suspected nasal polyps may represent an excess over expected occurrence. The occurrence of these sign and symptoms in non-smoking individuals supports the conclusion that menthol exposure is the cause.

Pre- and post-exposure pulmonary function testing showed significant decreases in FVC and FEV_1 for individuals not currently smoking; current smokers showed no significant changes; and the total sample showed a decrease in FVC and increases in $FEF_{25-75\%}$, $FEF_{75-85\%}$, and $MEF_{75\%}$.

The occurrence of these decreases in non-smoking participants may indicate a response to menthol exposure, but the sample size and means of administering the test procedure require cautious interpretation.

Dose-response relationships comparing the least and most exposed job categories were not possible due to the gross discrepancy in the number of participants in each category.

No control group was included for comparison.

No conclusion can be made as to long-term effects of exposure to menthol in this setting, but the nature of exposure seems to indicate that extended experience of local irritation can result in changes in anatomy and function. Additionally, menthol may act in an additive fashion with other agents, such as cigarette smoking, but from this study no assessment of this synergism can be made.

During a 15 minute sampling procedure at the inspection port of the continuous cooker in the candy room a NIOSH industrial hygienist experienced immediate stinging and tearing of the eyes, and irritation of the nasal passages and throat. This sample location had the highest menthol concentration measured, 39.4 mg/M^3.

Employees reported that the menthol air contamination was greatest during the manufacture of Mentholated Sucrets®. However, comparison of process activities and materials did not suggest that the production of the Mentholated vs. Regular Sucrets® would release significantly more menthol into the packing and wrapping areas (environmental conditions were not evaluated during the manufacture of the Mentholated Sucrets®). The source of menthol contamination appears to be the hot candy mass and lozenges once the menthol has been added. The release of menthol into the air occurs in the candy and cooling rooms. This contaminated air then apparently drifts into the hallway from the candy room and then possibly into the packing area, or from the cooling room to the wrapping and packing areas through door cracks or as people pass through the swinging doors. The relative positive pressure of the cooling room appeared to be the main source of drifting contaminated air on the survey dates of October 11-13, 1977.

The candy room had the highest level of menthol air contamination. A ceiling fan was observed to noticeably reduce menthol accumulations in the candy room. However, it was observed to operate only part of the time due to apparently inadequate maintenance. While there was some local exhaust ventilation at certain process points, evaporating menthol was only partially controlled at the source.

V. RECOMMENDATIONS

Industrial Hygiene

Good industrial hygiene practices dictate that worker exposures to chemicals be minimized to the greatest extent possible. Worker exposures could be reduced by a combination of engineering and process controls, administrative controls, and personal protective devices.

1. Engineering controls - The release of menthol into the candy and cooling rooms from the hot candy and lozenges should be controlled by local exhaust ventilation. Control of menthol release during the continuous cooking will require either enclosure or hooded exhaust ventilation. Hooded exhaust ventilation during batch candy making must be upgraded: containment of evaporating menthol will require flanging or exhaust hood enclosure to achieve the needed (approx.) 100 feet per minute capture velocity at the point of menthol release[16]. Ducting must be large enough to handle these increased air volumes. The candy and cooling rooms should be at negative pressure relative to the other work areas. This will require the exhausting of more air than is supplied to the candy

and cooling rooms. Maintenance of the properly designed and installed ventilation equipment is necessary for continued control of air contaminants.

2. Administrative controls - Workers should be periodically relieved from areas where excessive air contaminants are present.

3. Personal protective devices - Respirators and other personal protective devices should be used only until engineering and process controls can reduce employee exposures. NIOSH approved full-face air purifying respirators should be used when excessive menthol levels exist in the air (this would most likely occur in the candy room). Medical evaluation of the individual's ability to wear a respirator should be determined before issue is made (persons with existing lung or heart problems should not, in most cases, use respirators) Respirator usage should conform to requirements of 29 CFR 1910.134.

Medical

1. The employer should perform baseline and continued medical surveillance in the form of physical examinations with special attention to the upper airway passages and eyes. Baseline pulmonary function testing should be included. Such surveillance should apply to the most highly exposed group, and probably to the total group exposed.

2. Further investigation of exposure to menthol in the workplace utilizing sufficient sample size and control groups for the determination of short and long-term effects should be pursued. Such investigation may be conducted by NIOSH, manufacturing firms, or independently.

3. Basic research into aspects of menthol toxicity or effects by inhalation in human and animal systems should be conducted, especially in view of the widespread exposure to the consuming public as well as workers.

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Table 1

Distribution of Study Participants by Race and Sex
Sucrets® Department, Merck, Sharp, & Dohme

Race/Sex	Frequency	Percentage
White Males	13	26.5
Black Males	16	32.7
White Females	16	32.7
Black Females	4	8.2
TOTAL	49	100.1*

*(Adds to greater than 100 percent due to rounding)

Table 2

Job Categories of Study Participants
Sucrets® Department, Merck, Sharp, & Dohme

Category	Frequency	Percent of Total
Lozenge Packer	27	55.1
General Worker	10	20.4
Cellophane Operator	4	8.2
Set-up Mechanic	4	8.2
Group Leader	2	4.1
Candy Maker	2	4.1
TOTAL	49	100.1*

*(Adds to greater than 100 percent due to rounding)

Table 3

Cigarette Smoking Behavior
of Participants
and Completion of Pulmonary Function Testing

Smoking Behavior Category	Number	Per Cent of Total (n=49)	Completion Before and After Testing	Per Cent of Total (n=41)
Never Smoked	13	26.5	10	24.3
Previous smokers having quit	10	20.4	9	21.9
Current Smokers	26	53.1	22	53.7
TOTAL	49	100.0	41	99.9

Table 3a

Maximum Pack-Years Smoking Behavior
(Packs/Day X Years Smoked)
among Current Smokers

Maximum Pack-Years	Number	Per Cent of Total (n=26)
0.1-20	11	42.3
20.1-40	10	38.5
40.1 or more	5	19.2
TOTAL	26	100.0

Table 4 (page 1)

Symptomatic Complaints and Subjective Relationship to Menthol Exposure
in Groups of Menthol Workers According to Smoking Behavior

Never Smoked (n=13)

	Complained of symptom		Previous individuals subjectively relating symptom to menthol exposure	
Symptomatic Complaint	Number	% of those never smoking	Number	% of those complaining
Wheezing	0	0	0	0
Shortness of breath	4	30.8	0	0
Tightness in chest	3	23.1	1	33
Pain in chest	1	7.7	0	0
Cough	0	0	0	0
Sore throat	2	15.4	1	50
Hoarseness	2	15.4	0	0
Dry throat or mouth	5	38.5	3	60
Numbness of tongue or mouth	0	0	0	0
Difficulty swallowing	0	0	0	0
Runny nose	7	53.8	5	71.4
Sneezing	5	38.5	2	40
Nosebleeds	1	7.7	0	0
Congestion in nose	5	38.5	2	40
Watering of eyes	7	53.8	7	100
Itching of eyes	4	30.8	2	50
Redness of eyes	4	30.8	2	50
Swollen eyelids	2	15.4	1	50
Headache	4	30.8	2	50
Skin rash or irritation	2	15.4	0	0
Nausea	0	0	0	0

Table 4 (page 2)

Symptomatic Complaints and Subjective Relationship to Menthol Exposure in Groups of Menthol Workers According to Smoking Behavior

Previous Smokers (n=10)

Symptomatic Complaint	Complained of symptom		Previous individuals subjectively relating symptom to menthol exposure	
	Number	% of those previously smoking	Number	% of those complaining
Wheezing	0	0	0	0
Shortness of breath	1	10	0	0
Tightness in chest	0	0	0	0
Pain in chest	1	10	0	0
Cough	1	10	0	0
Sore throat	1	10	1	100
Hoarseness	2	20	1	50
Dry throat	1	10	1	100
Difficulty swallowing	1	10	0	0
Numbness of tongue or mouth	0	0	0	0
Runny nose	6	60	4	67
Sneezing	2	20	1	50
Nosebleeds	1	10	1	100
Congestion in nose	4	40	1	25
Watering of eyes	4	40	4	100
Itching of eyes	1	10	1	100
Redness of eyes	4	40	4	100
Swollen eyelids	0	0	0	0
Headache	1	10	0	0
Skin rash	0	0	0	0
Nausea	0	0	0	0

Table 4 (page 3)

Symptomatic Complaints and Subjective Relationship to Menthol Exposure
in Groups of Menthol Workers According to Smoking Behavior

Current Smokers (n= 26)

Symptomatic Complaint	Complained of symptom		Previous individuals subjectively relating symptom to menthol exposure	
	Number	% of those currently smoking	Number	% of those complaining
Wheezing	6	23.1	0	0
Shortness of breath	8	30.8	2	33
Tightness in chest	6	23.1	2	33
Pain in chest	5	19.2	0	0
Cough	14	53.8	1	7.1
Sore throat	6	23.1	1	16.7
Hoarseness	6	23.1	4	67
Dry throat	9	34.6	1	11.1
Difficulty swallowing	3	11.5	0	0
Numbness of tongue or mouth	0	0	0	0
Runny nose	11	42.3	6	54.5
Sneezing	10	38.5	2	20
Nosebleeds	3	11.5	1	33
Congestion in nose	7	26.9	2	28.6
Watering of eyes	15	57.7	9	60
Itching of eyes	5	19.2	2	40
Redness of eyes	7	26.9	2	28.6
Swollen eyelids	2	7.7	1	50
Headache	5	19.2	1	20
Skin rash	5	19.2	0	0
Nausea	2	7.7	1	50

Table 5 (page 1)

Physical Examination Findings in Groups of Menthol Workers According to Smoking Behavior

Examination Area and Findings	Never Smoked (n=13)		Previous Smokers (n=10)		Current Smokers (n=26)		Total Group (n=49)	
	Number	%	Number	%	Number	%	Number	%
Conjunctiva/Eyelids								
Normal bilaterally	12	92.3	5	50	22	84.6	39	79.6
Inflammatory changes	1	7.7	2	20	3	11.5	6	12.2
Miscellaneous abnormalities or no response	0	0	3	30	1	3.8	4	8.2
TOTAL	13	100.0	10	100.0	26	99.9	49	100.0
Ear Drums								
Normal bilaterally	11	84.6	7	70	17	65.4	35	71.4
Miscellaneous abnormalities or no repsonse	2	15.4	3	30	9	34.6	14	28.6
TOTAL	13	100.0	10	100.0	26	100.0	49	100.0
Nasal Membranes								
Normal bilaterally	5	38.5	2	20	11	42.3	18	36.7
Inflammation or swelling	4	30.8	4	40	7	26.9	15	30.6
Suspected polyp on right and/or left side	2	15.4	1	10	4	15.4	7	14.3
Miscellaneous abnormalities or no response	2	15.4	3	30	4	15.4	9	18.4
TOTAL	13	100.1	10	100.0	26	100.0	49	100.0

Table 5 (continued page 2)

Physical Examination Findings in Groups of Menthol Workers According to Smoking Behavior

Examination Area and Findings	Never Smoked (n=13)		Previous Smokers (n=10)		Current Smokers (n=26)		Total Group (n=49)	
	Number	%	Number	%	Number	%	Number	%
Vocal Cords								
Normal bilaterally	10	76.9	8	80	15	57.7	33	67.3
Inflamed	3	23.1	2	20	9	34.6	14	28.6
Miscellaneous abnormalities or no response	0	0	0	0	2	7.7	2	4.1
TOTAL	13	100.0	10	100.0	26	100.0	49	100.0
Vocal Cord Function								
Normal bilaterally	13	100	10	100	23	88.5	46	93.9
Miscellaneous abnormalities or no response	0	0	0	0	3	11.5	3	6.1
TOTAL	13	100.0	10	100.0	26	100.0	3	100.0
Lungs								
Normal auscultation bilaterally	13	100	10	100	24	92.3	47	95.9
Miscellaneous abnormalities or no response	0	0	0	0	2	7.7	2	4.1
TOTAL	13	100.0	10	100.0	26	100.0	49	100.0

Table 5 (continued page 3)

Physical Examination Findings in Groups of Menthol Workers According to Smoking Behavior

Examination Area and Findings	Never Smoked (n=13)		Previous Smokers (n=10)		Current Smokers (n=26)		Total Group (n=49)	
	Number	%	Number	%	Number	%	Number	%
Throat								
Normal	8	61.5	7	70	13	50	28	57.1
Inflamed	5	38.5	2	20	12	46.1	19	38.8
Miscellaneous abnormalities or no response	0	0	1	10	1	3.9	2	4.1
TOTAL	13	100.0	10	100.0	26	100.0	49	100.0

Table 6

Distribution of Pre-exposure Pulmonary Function Values as Percentage of Predicted Normals by Sex

Sucrets® Department
Merck, Sharp & Dohme
West Point, Pennsylvania

MALES (n=24)

% of Normal	FVC		FEV_1/FVC		$FEF_{200-1200}$		$FEF_{25-75\%}$		$FEF_{75-85\%}$	
	#	%	#	%	#	%	#	%	#	%
Over 80%	19	79.2	4	16.7	13	54.2	7	29.2	6	25.0
65-79%	3	12.5	15	62.5	6	25.0	4	16.7	0	0
50-64%	2	8.3	4	16.7	1	4.2	5	20.8	3	12.5
Less than 50%	0	0	1	4.2	4	16.7	8	33.3	15	62.5
Total	24	100.0	24	100.1	24	100.0	24	100.0	24	100.0

FEMALES (n=18)

Over 80%	13	72.2	0	0	7	38.9	3	16.7	1	5.6
65-79%	4	22.2	11	61.1	2	11.1	5	27.8	0	0
50-64%	1	5.6	6	33.3	5	27.8	3	16.7	5	27.8
Less than 50%	0	0	1	5.6	4	22.2	7	38.9	12	66.7
Total	18	100.0	18	100.0	18	100.0	18	100.1	18	100.0

Table 7

Pre- and Post-exposure Pulmonary Function Mean Values
Total Group (n=41)
Sucrets® Department
Merck, Sharp & Dohme
West Point, Pennsylvania

	MEAN VALUE		
	Pre-exposure	Post-exposure	Difference
FVC(L[a])	3.6832	3.6198	-0.0634*(L)
$FEV_{0.5}$(L)	1.8027	1.7612	-0.0415(L)
$FEV1_{actual}$(L)	2.5890	2.5851	-0.0039(L)
FEV1/FVC(%) predicted	69.7645	70.9430	+1.1785%
$FEF_{.2-1.2}$(L/S[b])	4.9075	4.9385	+0.0310(L/S)
$FEF_{25-75\%}$(L/S)	2.1961	2.3485	+0.1524**(L/S)
$FEF_{75-85\%}$(L/S)	0.4737	0.5577	+0.0840***(L/S)
PF(L/S)	6.0046	6.0154	+0.0107(L/S)
$MEF_{50\%}$(L/S)	2.9915	3.0810	+0.0895(L/S)
$MEF_{75\%}$(L/S)	0.7855	0.9072	+0.1218****(L/S)

*p = .032

**p = .024

***p = .019

****p = .024

All values in one tailed t-test.

a - (L) liters
b - (L/S) liters per second

Table 7a

Significance and Direction of Change
in Pre-and Post-Exposure
Pulmonary Function Testing
of Menthol Workers by Groups

Category	Pulmonary Function Parameter					
	FVC	FEV1	FEV1 / FVC	FEF .2-1.2	FEF 25-75%	FEF 75-85%
Never Smoked (n=10)*	decreased#	decreased#	NS	NS	NS	NS
Previous Smokers (n=9)*	decreased#	decreased#	NS	NS	NS	NS
Current Smokers (n=22)*	NS	NS	NS	NS	NS	NS
Total group (n=41)**	decreased#	NS	NS	NS	increased#	increased#

*Wilcoxon Matched-Pairs Signed Ranks Test

**Student's t-test

NS=not significant

significant at p=0.05

Table 8

Summary of Air Sampling Results for Menthol in the Sucrets® Department
April 22, 1977

Sucrets® Department
Merck, Sharp & Dohme
West Point, Pennsylvania

Sample #	Location	Sample Period	Menthol Concentration mg/M^3
1	Upper level of bins for wrapping machines	12:23 pm-2:28 pm	0.8
2	Concurrent to Sample #1	12:23 pm-2:28 pm	1.1
3	On top of pallets between packing machines 4 and 5	12:25 pm-2:28 pm	1.7
4	Concurrent to Sample #3	12:25 pm-2:28 pm	0.7
5	On top of Esterline Recorder in candy room	12:27 pm-2:28 pm	0.9

Table 9

SUMMARY OF PERSONAL AND AREA AIR SAMPLING FOR MENTHOL

MERCK & CO. - SUCRETS DEPARTMENTS
WEST POINT, PENNSYLVANIA

October 11-13, 1977

Person or Location Sampled	Sample Period	Concentration of Menthol mg/M3*
	10/11/77	
Packing Area	8:36 a.m. - 3:25 p.m.	1.6
Wrapping Area	8:39 a.m. - 3:26 p.m.	0.7
Candy Cooling Room	8:44 a.m. - 3:27 p.m.	12.4
Packer	9:16 a.m. - 12:24 p.m. 1:10 p.m. - 2:11 p.m. 2:47 p.m. - 3:19 p.m.	N.D.**
Adjacent to Candy Machine	9:39 a.m. - 3:29 p.m.	9.3
Wrapping Machine Operator	9:18 a.m. - 12:24 p.m. 2:11 p.m. - 3:18 p.m.	N.D.
Wrapping Machine Operator	9:30 a.m. - 12:25 p.m. 1:12 p.m. - 2:10 p.m.	N.D.
Celophane Wrapping Machine Operator	9:16 a.m. - 12:24 p.m. 1:10 p.m. - 2:11 p.m. 2:47 p.m. - 3:19 p.m.	N.D.
Wrapping Machine Operator	9:27 a.m. - 12:22 p.m. 1:09 p.m. - 2:24 p.m.	N.D.
Adjacent to Batch Mixer in Candy Room	4:53 p.m. - 9:45 p.m.	6.2
Adjacent to Wrapping Machine #11	5:18 p.m. - 10:00 p.m.	1.7
Packer on Packing Machine #4	5:07 p.m. - 8:23 p.m. 8:50 p.m. - 10:40 p.m.	2.3
On Upper Walkway Adjacent to Candy Machine	4:50 p.m. - 10:07 p.m.	18.2
Breathing zone of NIOSH industrial hygienist at highest level of candy machine	10:15 p.m. - 10:30 p.m.	39.4
Candy Maker during "Normal" Activities (Breathing zone measurement)	10:15 p.m. - 10:30 p.m.	12.2
	10/12/77	
Wrapping Machine Operator	8:21 a.m. - 12:22 p.m. 2:43 p.m. - 3:29 p.m. 8:14 a.m. - 12:25 p.m. 2:45 p.m. - 3:30 p.m.	N.D. N.D.
Packer on Packing Machine #2	8:43 a.m. - 12:25 p.m. 1:12 p.m. - 2:55 p.m.	N.D.

Table 9 (con'd)

Person or Location Sampled	Sample Period	Concentration of Menthol mg/M^3*
	10/12/77 (Cont'd.)	
Packer on Packing Machine #4	8:40 a.m. - 12:23 p.m. 1:15 p.m. - 3:22 p.m.	N.D.
Wrapping Area	9:05 a.m. - 2:45 p.m.	0.6
Adjacent to Candy Machine	8:59 a.m. - 3:38 p.m.	8.8
Adjacent to Conveyor out of Candy Machine	8:58 a.m. - 3:38 p.m.	12.9
Packing Area	9:06 a.m. - 3:40 p.m.	0.7
Cooling Room	9:02 a.m. - 3:39 p.m.	12.2
By the Formers in Candy Room	4:15 p.m. - 10:20 p.m.	7.9
Candy Room	4:30 p.m. - 11:32 p.m.	9.5
Adjacent to Water Fountain in Candy Room	4:23 p.m. - 11:35 p.m.	6.2
Adjacent to Wrapping Machine #15	4:27 p.m. - 11:25 p.m.	1.2
Cooling Room	4:33 p.m. - 11:33 p.m.	1.9
Wrapping Machine Operator	5:30 p.m. - 8:05 p.m. 8:59 p.m. - 11:47 p.m.	2.3
Celophane Wrapping Machine Operator	5:27 p.m. - 8:09 p.m.	N.D.
Wrapping Machine #9 Operator	5:35 p.m. - 8:02 p.m. 8:53 p.m. - 11:38 p.m.	1.1
Packer	5:40 p.m. - 8:10 p.m.	N.D.
Candy Maker during "Normal" Activities	11:02 p.m. - 11:17 p.m.	25.6
	10/13/77	
Wrapping Area	9:26 a.m. - 3:25 p.m.	1.0
Hallway Outside Sucrets Department	9:43 a.m. - 3:41 p.m.	2.7
Adjacent to Candy Machine	9:04 a.m. - 3:34 p.m.	11.8
Adjacent to Formers in Candy Room	9:11 a.m. - 3:37 p.m.	11.1
Over Bins of Unwrapped Sucretes	9:23 a.m. - 3:30 p.m.	1.0
Cooling Room	9:16 a.m. - 3:32 p.m.	21.1
Adjacent to Packing Machine #3	9:46 a.m. - 2:40 p.m.	N.D.
Wrapping Machine Operator	10:13 a.m. - 12:25 p.m. 2:17 p.m. - 3:26 p.m.	N.D.
Over Bins of Unwrapped Sucretes	5:15 p.m. - 7:39 p.m.	1.2
Adjacent to Wrapping Machine #4	5:10 p.m. - 7:39 p.m.	1.1
Packing Area	4:53 p.m. - 9:03 p.m.	1.7
Cooling Room	4:58 p.m. - 9:00 p.m.	12.2
Adjacent to Spinners in Candy Room	5:01 p.m. - 9:00 p.m.	9.4
Adjacent to Candy Machine	5:05 p.m. - 9:01 p.m.	4.9

* mg/M^3 - milligrams of menthol per cubic meter of air.

** N.D. - None detected where the analytic lower limit of detection is about 0.1 milligram per sample and sample volumes ranged from 14.3 to 442.8 liters.

Table 10

Summary of Personal and Area Air Sampling for Menthol by Location

Merck & Co. - Sucrets® Departments
West Point, Pennsylvania

April 22, 1977
October 11-13, 1977

Area of Sample or Person Sampled	Sample Period	Menthol Concentration mg/M^3*
Wrapping		
Upper level of bins for wrapping machines (2 samplers)	4/22/77, 12:23 pm-2:28 pm	0.8 1.1
Wrapping area	10/11/77, 8:39 am-3:26 pm	0.7
Wrapping machine operator	10/11/77, 9:18 am-12:24 pm 2:11 pm-3:18 pm	N.D.**
Wrapping machine operator	10/11/77, 9:30 am-12:25 pm 1:12 pm-2:10 pm	N.D.
Wrapping machine operator	10/11/77, 9:27 am-12:22 pm 1:09 pm-2:24 pm	N.D.
Adjacent to wrapping machine #11	10/11/77, 5:18 pm-10:00 pm	1.7
Wrapping machine operator	10/12/77, 8:21 am-12:22 pm 2:43 pm-3:29 pm	N.D.
Wrapping machine operator	10/12/77, 8:14 am-12:25 pm 2:45 pm-3:30 pm	N.D.
Wrapping area	10/12/77, 9:05 am-2:45 pm	0.6
Adjacent to wrapping machine #15	10/12/77, 4:27 pm-11:25 pm	1.2

Table 10 (con'd)

Area of Sample or Person Sampled	Sample Period	Menthol Concentration mg/M^3*
Wrapping (con'd)		
Wrapping machine operator	10/12/77, 5:30 pm-8:05 pm 8:59 pm-11:47 pm	2.3
Wrapping machine #9 operator	10/12/77, 5:35 pm-8:02 pm 8:53 pm-11:38 pm	1.1
Wrapping area	10/13/77 9:26 am-3:25 pm	1.0
Over bins of unwrapped Sucrets®	10/13/77, 9:23 am-3:30 pm	1.0
Wrapping machine operator	10/13/77, 10:13 am-12:25 pm 2:17 pm-3:26 pm	N.D.
Over bins of unwrapped Sucrets®	10/13/77, 5:15 pm-7:39 pm	1.2
Adjacent to wrapping machine #4	10/13/77, 5:10 pm-7:39 pm	1.1
Packing		
On top of pallets between packing machines 4 and 5	4/22/77, 12:25 pm-2:28 pm	1.7 0.7
Packing area	10/11/77, 8:36 am-3:25 pm	1.6
Packer	10/11/77, 9:16 am-12:24 pm 1:10 pm-2:11 pm 2:47 pm-3:19 pm	N.D.
Celophane wrapping machine operator	10/11/77, 9:16 am-12:24 pm 1:10 pm-2:11 pm 2:47 pm-3:19 pm	N.D.

Table 10 (con'd)

Area of Sample or Person Sampled	Sample Period	Menthol Concentration mg/M^3*
Packing (con'd)		
Packer on packing machine #4	10/11/77, 5:07 pm-8:23 pm 8:50 pm-10:40 pm	2.3
Operator on packing machine #2	10/12/77, 8:43 am-12:25 pm 1:12 pm-2:55 pm	N.D.
Packer on packing machine #4	10/12/77 8:40 am-12:23 pm 1:15 pm-3:22 pm	N.D.
Packing area	10/12/77 9:06 am-3:40 pm	0.7
Celophane wrapping machine operator	10/12/77, 5:27 pm-8:09 pm	N.D.
Packer	10/12/77, 5:40 pm-8:10 pm	N.D.
Adjacent to packing machine #3	10/13/77, 9:46 am-2:40 pm	N.D.
Packing area	10/13/77, 4:53 pm-9:03 pm	1.7
Candy Room		
On top of Esterline recorder	4/22/77, 12:27 pm-2:28 pm	0.9
Cooling room	10/11/77, 8:44 am-3:27 pm	12.4
Adjacent to candy machine	10/11/77, 9:39 am-3:29 pm	9.3
Adjacent to batch mixer	10/11/77, 4:53 pm-9:45 pm	6.2
On upper walkway adjacent to candy machine	10/11/77, 4:50 pm-10:07 pm	18.2
Breathing zone of NIOSH industrial hygienist at highest level of candy machine	10:15 pm-10:30 pm	39.4

Table 10 (con'd)

Area of Sample or Person Sampled	Sample Period	Menthol Concentration mg/M3*
Candy Room (con'd)		
Candy Maker during "Normal" activities (Breathing zone measurement)	10/11/77, 10:15 pm-10:30 pm	12.2
Adjacent to candy machine	10/12/77, 8:59 am-3:38 pm	8.8
Adjacent to conveyor out of candy machine	10/12/77, 8:58 am-3:38 pm	12.9
Cooling room	10/12/77, 9:02 am-3:39 pm	12.2
By the formers	10/12/77, 4:15 pm-10:20 pm	7.9
Candy room	10/12/77, 4:30 pm-11:32 pm	9.5
Adjacent to water fountain	10/12/77, 4:23 pm-11:35 pm	6.2
Cooling room	10/12/77, 4:33 pm-11:33 pm	1.9
Breathing zone measurement of Candy Maker during "Normal" activities	10/12/77, 11:02 pm-11:17 pm	25.6
Adjacent to candy machine	10/13/77, 9:04 am-3:34 pm	11.8
Adjacent to formers	10/13/77, 9:11 am-3:37 pm	11.1
Cooling room	10/13/77, 9:16 am-3:32 pm	21.1
Cooling room	10/13/77, 4:58 pm-9:00 pm	12.2
Adjacent to spinners	10/13/77, 5:01 pm-9:00 pm	9.4
Adjacent to candy machine	10/13/77, 5:05 pm-9:01 pm	4.9

Table 10 (con'd)

Area of Sample or Person Sampled	Sample Period	Menthol Concentration mg/M^3*
Other		
Hallway outside Sucrets® department	10/13/77, 9:43 am-3:41 pm	2.7

*mg/M^3 - milligrams of menthol per cubic meter of air
**N.D. - None detected where the analytic lower limit of detection is 0.1 milligram per sample and sample volumes ranged from 14.3 to 442.8 liters.

REQUEST AND AUTHORIZATION FOR RELEASE OF INFORMATION

I,_____, hereby request and authorize the project director to inform the following physicians whose names and addresses I have entered below of any significant findings from the above named study concerning me. (Do not leave blank. Write "no" where you do not wish to give a name and address)

PLEASE PRINT

1. My personal physician(s):

   Dr._____

   Street_____

   City/State_____Zip_____

2. Company or other physician:

   Dr._____

   Street_____

   City/State_____Zip_____

_____ _____
(Signature) (Date)

CONSENT FORM FOR MERCK, SHARPE, & DOME

I,_____, voluntarily agree to participate in a health hazard evaluation at Merck, Sharpe, & Dome, at West Point, Pennsylvania, conducted by the Division of Occupational Medicine, Cook County Hospital, Chicago, Illinois. for the National Institute for Occupational Safety and Health (NIOSH). This evaluation is conducted under the authority of Section 20 (a) (6) of the Occupational Safety and Health Act and in accordance with federal regulations (42 Code of Federal Regulations Part 85).

I understand that I will be asked questions about my current and past health and that I will be requested to undergo a limited physical examination by a physician. I understand that I will be asked, on two occasions, to have my lung function tested by blowing through a machine which will cause me little or no discomfort and involves no risk to my health. The results will be sent to me and, if I wish, to my doctor (see below). I understand that at any time during the study I have the right to ask questions of NIOSH and that I am free to withdraw my consent and to discontinue participation in the study at any time without prejudice to myself.

Any information gathered in this evaluation will not be disclosed in a manner which will identify me except with my written permission (see below) or except as required by law. The information will be used by NIOSH primarily for purposes of the health hazard evaluation and also for occupational health research.

SIGNATURE_____ DATE_____
(Subject)

INVESTIGATOR_____ DATE_____

I.D.# _ _ _ _ 1-4

DOB _ _/_ _/_ _
Mo. Day Yr.

5/Blank
6-11

PHYSICAL EXAMINATION FOR MERCK, SHARPE, & DOME

INSTRUCTIONS: If a finding is present on the right side, circle "R", if on the left side, circle "L", if both sides, circle "B". If you see an abnormality that is not listed, circle the appropriate letter in the "other" category and write out what you found. If you have extensive comments, put them in the "comments" section at the end.

Note: If you circle "normal", you cannot circle any other category in that column.

1. Conjunctiva and lids are/have:

Normal.....	R	L	B		12
Swollen.....	R	L	B		13
Inflamed.....	R	L	B		14
Tearing	R	L	B		15
Blepharitis.....	R	L	B		16
Other (list).....	R	L	B	_____	17-19

_____

2. Ear drums are:

Normal.....	R	L	B		20
Bulging.....	R	L	B		21
Retracted.....	R	L	B		22
Bluish (fluid behind)...	R	L	B		23
Perforated	R	L	B		24
Other (list).....	R	L	B	_____	25-27

(If canal is occluded, list here)_____

_____

I.D. #__ __ __ __

DOB __ __/__ __/__ __
Mo. Day Yr.

3. Nasal membranes and septum are/have:

Normal.....	R	L	B		28
Pale	R	L	B		29
Inflamed.....	R	L	B		30
Polyp.....	R	L	B		31
Swollen.....	R	L	B		32
Dry	R	L	B		33
Bleeding	R	L	B		34
Thick Discharge.....	R	L	B		35
Thin Discharge.....	R	L	B		36
Perforated.....	R	L	B		37
Other (list).....	R	L	B	_____	38-40

_____

4. Throat is:

Normal .....Yes	No			41
Inflamed.....Yes	No			42
Pale.....Yes	No			43
Swollen.....Yes	No			44
Other (list)			_____	45-46

_____

I.D. #__ __ __ __

DOB__ __/__ __/__ __
Mo. Day Year

5. Vocal chords are/have:

Normal in anatomy.....R	L	B		47
Polyp.....R	L	B		48
Inflamed.....R	L	B		49
Pale.....R	L	B		50
Thickened.....R	L	B		51
Other (list).....R	L	B	_____	52-54
_____				
Normal in function.....R	L	B		55
Paralysis on.....R	L	B		56
Other (list).....R	L	B	_____	57-59
_____				

6. Lungs are/have:

Normal..... R	L	B		60
Wheezing..... R	L	B		61
Rales..... R	L	B		62
Decreased breath sounds.... R	L	B		63
Prolonged expiratory phase..R	L	B		64
Rhonchi.....R	L	B		65
Other (list).....R	L	B	_____	66-68
_____				

7. Height in inches __ __ . __ 69-72

COMMENTS:_____ 73

_____

EXAMINERS INITIALS_____ DATE OF EXAM__ __/__ __/__ __ 74-75

76-79 bla

80/4

QUESTIONNAIRE FOR MERCK, SHARPE & DOME

*(INTERVIEWER'S INITIALS*_____

NAME_____
(first) (last)

I.D. NUMBER ___ ___ ___ ___
1-4

ADDRESS_____

CITY_____ZIP_____

1. Which shift are you now working?

Days.....1

Nights.....2 5

2. When were you born? 6-7 8-9 10-11

___ ___/ ___ ___/ ___ ___
Month Day Year

3. What is your racial background?

White.....1

Black.....2

Oriental.....3

Other_____..4 12
(specify)

4. (Sex)

Male.....1

Female.....2 13

Now I'm going to ask you a few questions about your work experience within this company.....

WORK HISTORY

5. When did you first begin working at Merck? 14-15 16-17

___ ___/ ___ ___
Month Year

I.D. NUMBER ___ ___ ___ ___

6. When did you start to work with Sucrets?

__ __/__ __ (Mo. / Year) 18-19 20-21

7a. What job title do you now have?

_____ 22-24

7b. What kind of work do you do; that is, what are your duties on the job?

_____

_____

7c. How long have you worked as a _____? *(insert job title from 7a)*

___ __ __Months 25-27

8a. What was the title of your job at this company immediately before your present job? _____. 28-30
(if none, skip to Q.10a)

8b. What kind of work did you do; that is, what were your duties on the job?

_____

8c. How long did you work at that job?

___ ___Months 31-33

9a. What was the title of the job, within this company, that you had immediately before that job? *(if none, skip to Q. 10a)* 34-36

_____

9b. What kind of work did you do; that is, what were your duties on the job?_____

_____

9c. How long did you work at that job?

___ ___ ___Months 37-39

10a. Do you now or have you ever smoked cigarettes?

Yes.....1

No.....2 40
(skip to Q. 11)

10b. *(if yes....)*
At what age did you start smoking?

___ ___Years 41-42

10c. How many packs per day do you or did you smoke?

Less than ½ pack.....1

½ pack.....2

1.....3 43

2.....4

3 or more.....5

10d. Do you smoke cigarettes now?

Yes.....1
(skip to Q. 11)

No.....2 44

10e. *(if no...)*
When did you quit?

Month___ ___ 45-46

Year ___ ___ 47-48

11. Do you now or have you within the last 12 months smoked a pipe or cigar regularly?

Yes.....1 49

No.....2

Occasionally.....3

Now I'm going to ask you a few questions about your health...

MEDICAL HISTORY

12. Have you ever been told by a doctor, a nurse, or other health worker that you have:

	YES	NO	*(if yes...)* WHEN WERE YOU FIRST TOLD? MONTH	YEAR	
a. Asthma	1	2	____	____	50-52
b. Bronchitis	1	2	____	____	53-55
c. Hay fever	1	2	____	____	56-58
d. Allergies	1	2	____	____	59-61
e. Sinus condition	1	2	____	____	62-64
f. Polyps, nodule, or growth on vocal cords	1	2	____	____	65-67
g. Polyps, nodule, or growth in nose	1	2	____	____	68-70
h. Emphysema	1	2	____	____	71-73

I.D. NUMBER ___ ___ ___ ___

	YES	NO	MONTH	YEAR	
i. Other lung disease	1	2	____	____	74-76
j. Conjunctivitis or "pink eye"	1	2	____	____	77-79
					80/1
					1-4/DUP.
k. Laryngitis	1	2	____	____	5-7
l. Pharyngitis	1	2	____	____	8-10

13. How many times during the past 12 months have you had a cold or other respiratory infection that required staying home for more than one day?

None.....0

1.....1

2.....2

3.....3 11

4.....4

More than 4.....5

14. How many days were you off work in the past 12 months because you were sick? (excluding trauma)

___ ___ ___ 12-14

15. Does anyone in your immediate family, that is, parents, grandparents, brothers, or sisters have:

	YES	NO	
HAY FEVER	1	2	15
ASTHMA	1	2	16
SINUS TROUBLE	1	2	17
ALLERGIES	1	2	18

I.D. NUMBER__ __ __ __

16. Do you experience breathing difficulties, sneezing or nasal congestion when you smell perfume, cooking odors, or cigarette smoke?

YES.....1

NO.....2 19

17. Are you allergic to aspirin?

YES.....1

NO.....2 20

18. ON ANY OCCASION OR DURING ANY ACTIVITY, ARE YOU BOTHERED OR IN ANY WAY LIMITED BY: I.D.# __ __ __ __

(If YES, ask a..... ask b..... ask c.....)

	YES	NO	a. DOES THIS OCCUR: AT WORK ONLY	AT HOME ONLY	ALL THE TIME	b. WHEN DID YOU NOTICE THIS?	c. CAN YOU RELATE THIS TO ANY SITUATION OR PARTICULAR PRODUCT YOU HANDLE?	
a. WHEEZING	1	2	3	4	5	__MO.__YR.		21-2
b. SHORTNESS OF BREATH	1	2	3	4	5	__MO.__YR.		27-3
c. TIGHTNESS IN CHEST	1	2	3	4	5	__MO.__YR.		33-3
d. PAIN IN CHEST	1	2	3	4	5	__MO.__YR.		39-4
e. COUGH	1	2	3	4	5	__MO.__YR.		45-5
f. SORE THROAT	1	2	3	4	5	__MO.__YR.		51-5
g. HOARSENESS	1	2	3	4	5	__MO.__YR.		57-6
h. DRY THROAT OR MOUTH	1	2	3	4	5	__MO.__YR.		63-6
i. DIFFICULTY SWALLOWING	1	2	3	4	5	__MO.__YR.		69-7
								75-79 Blan
								80-2 Dup.
								1-4 Dup.
j. NUMBNESS OF TONGUE OR MOUTH	1	2	3	4	5	__MO.__YR.		5-1
k. RUNNY NOSE	1	2	3	4	5	__MO.__YR.		11-1
l. SNEEZING	1	2	3	4	5	__MO.__YR.		17-2
m. NOSE BLEEDS	1	2	3	4	5	__MO.__YR.		23-2
n. CONGESTION IN NOSE	1	2	3	4	5	__MO.__YR.		29-3
o. WATERING OF EYES	1	2	3	4	5	__MO.__YR.		35-4
p. ITCHING OF EYES	1	2	3	4	5	__MO.__YR.		41-4
q. REDNESS OF EYES	1	2	3	4	5	__MO.__YR.		47-5
r. SWOLLEN EYELIDS	1	2	3	4	5	__MO.__YR.		53-5
s. HEADACHE	1	2	3	4	5	__MO.__YR.		59-6
t. SKIN RASH OR IRRITATION	1	2	3	4	5	__MO.__YR.		65-7

I.D. #_____

18. On any occasion or during any activity, are you bothered or in any way limited by:

			Menthol related?	
	Yes	No	Yes	No
a. Wheezing	1	2	1	2
b. Shortness of breath	1	2	1	2
c. Tightness in chest	1	2	1	2
d. Pain in chest	1	2	1	2
e. Cough	1	2	1	2
f. Sore throat	1	2	1	2
g. Hoarseness	1	2	1	2
h. Dry throat or mouth	1	2	1	2
i. Difficulty swallowing	1	2	1	2
j. Numbness of tongue or mouth	1	2	1	2
k. Runny nose	1	2	1	2
l. Sneezing	1	2	1	2
m. Nosebleeds	1	2	1	2
n. Congestion in nose	1	2	1	2
o. Watering of eyes	1	2	1	2
p. Itching of eyes	1	2	1	2
q. Redness of eyes	1	2	1	2
r. Swollen eyelids	1	2	1	2
s. Headache	1	2	1	2
t. Skin rash or irritation	1	2	1	2
u. Nausea				

	Yes	No
19. Only one PFT performed?	1	2