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ROBBINS & MYERS, INCORPORATED  
MOYNO PRODUCTS DIVISION  
SPRINGFIELD, OHIO

NIOSH INVESTIGATORS:  
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## I. SUMMARY

In October 1985, the National Institute for Occupational Safety and Health (NIOSH) received a request from Robbins & Myers, Inc. to investigate a possible health hazard at its Moyno Products Division plant in Springfield, Ohio. A dermatologist had previously identified a possibly work-related case of vitiligo (loss of skin pigment) in an employee of the rubber handling department. The affected employee operated a rubber injection molding machine. A second worker doing the same job was reportedly similarly affected.

On the basis of a questionnaire survey and skin examinations conducted on June 18, 1986, the NIOSH investigation identified two additional cases of vitiligo among 201 hourly employees. There was a 22 fold risk of developing vitiligo associated with the three jobs involving the most exposure to rubber, and moderate-to-severe cases of vitiligo were restricted to the most highly exposed job.

Based on the survey results, we concluded there was an increased risk of vitiligo associated with employment in the rubber handling department. Although no chemical agent likely to cause vitiligo was identified from a review of Material Safety Data Sheets relevant to operations in the rubber handling department, laboratory analysis of samples of rubber stock (purchased by Robbins & Myers from an outside supplier) identified the presence of para-tertiary butylphenol (PTBP) and 2,4-di-tertiary butylphenol (DTBP). Since PTBP has been previously associated with several outbreaks of work-related vitiligo and DTBP is structurally a closely related compound, these materials were felt to be the probable source of the vitiligo cases. The following recommendations were made with the aim of reducing the risk of further cases: 1) a laboratory testing program to ensure that rubber stock used in the plant is not contaminated with DTBP or PTBP; 2) modification of work practices to reduce the amount of skin contact with the rubber; 3) surveillance for the occurrence of further cases.

**KEYWORDS:** SIC 3561 (Pumps and Pumping equipment), rubber mixtures, occupational skin disease, vitiligo, 2,4-di-tertiarybutyl-phenol, para-tertiary-butylphenol.

## II. INTRODUCTION

In October 1985, NIOSH received a request from Robbins & Myers Inc., to investigate a possible health hazard at its Moyno Products Division in Springfield, Ohio. A dermatologist had recently identified a case of possibly work-related vitiligo in an employee of the rubber handling department. An initial site-visit was made by NIOSH staff on October 22, 1985, with two hygienists from the Ohio Industrial Commission who had previously evaluated this problem. A letter describing the initial findings of this visit was sent to the Robbins & Myers company and the United Auto Workers Local 902 on October 31, 1985.

## III. BACKGROUND

The initial plant walk-through included a review of the overall process of manufacturing the specialized cylindrical pumps known as "progressive cavity" pumps. The interior of the pump cylinder is a molded cavity made of a specialized rubber formulated (by an outside company according to specifications supplied by the Robbins & Myers chemist) to withstand corrosive industrial liquids. The majority of the production departments are occupied with either machining of the pump cylinders to appropriate specifications, or with pump assembly.

The injection molding operation takes place in the rubber handling department and is an intermediate step in the overall manufacturing process. The following sequence of operations takes place in the department: 1) preparation (degreasing and sandblasting of the "stator tubes" or pump cylinders), followed by spraying of the interior of the stator tubes with a spray adhesive compound; 2) passage of uncured rubber (purchased from an outside vendor) through a milling machine and into an injection molding machine, which forms the molded cavity in the interior of the stator tubes; 3) curing of the molded rubber at 300 degrees Fahrenheit; and 4) grinding of the excess rubber from the ends of the stator tube.

Review of the Material Safety Sheets indicated that both the spray adhesive and some of the uncured rubber formulations might contain para-substituted tertiary phenols, a class of compound associated with chemically induced vitiligo (depigmentation). No para-substituted phenols were explicitly identified on any of the Material Safety Sheets reviewed. However, a review of the historical changes in the rubber formulae with the plant chemist revealed that a formula containing the tertiary butyl phenols had been employed in the past at an unspecified date.

The spray adhesive operation was not performed during our walk-through; customarily it was performed three to four times a week, whenever a new batch of stator tubes was required for the injection molding process. From a demonstration of the involved work procedures it appeared that there was some potential for operator exposure to secondary spray, while the interior of the stator was sprayed using a hand held nozzle. The spraying was most frequently performed by the worker designated as the "group leader", but it was sometimes performed by one of the gun and mill operators.

In the injection molding process, the amount of dermal exposure to uncured rubber depended on which of the two gun and mill machines in the work area was being operated. The older of the two machines required that the operator feed uncured stock into the rubber mill and periodically come in contact with rubber, which had been heated to approximately 120 degrees Fahrenheit during the milling process. The newer machine had an automatic feeding device for loading stock into the rubber mill and required only minimal contact with the rubber during the milling process. Operation of the gun and mill machines was usually performed by one of the gun and mill operators, but was also performed by the group leaders on occasion. Other workers from the department had less frequent opportunity for dermal contact with either cured or uncured rubber.

Medical examinations of a sample of workers from the rubber handling department showed that in addition to the index case, one additional employee had vitiligo which was possibly work-related. Both employees were employed as operators of the gun and mill injection molding machines, a job category which involved frequent skin contact with both cured and uncured rubber and occasional exposure to spray adhesives known to contain phenol formaldehyde resins. The reported onset of the first case was in 1973 and of the second case in 1975. A third gun and mill operator had loss of skin pigment more typical of cutaneous disease (discoid lupus erythematosus) than vitiligo.

In order to determine whether the finding of two cases of vitiligo in the gun and mill operators constituted a greater than expected number of cases, we compared the results of our small survey to a national survey on the prevalence of skin disorders,<sup>1</sup> employing as the denominator all eleven employees (gun and mill operators and "group leaders") with frequent exposure to spray adhesives and/or uncured rubber during the injection molding operation. Based on an estimated 0.05 expected cases, there was less than a 1% probability of the two cases occurring by chance alone. If the comparison was made excluding the index case, the probability of finding one additional case among the remaining ten employees was 4%. Based on the results of this comparison, we determined that there was sufficient cause to carry out 1) a medical survey to determine the prevalence of vitiligo within the plant population, and 2) laboratory investigations to determine the source of possible exposures to para-substituted phenol compounds.

#### IV. EVALUATION METHODS

##### A. Environmental

Because it was not possible to quantitatively evaluate the degree of skin exposure to chemical agents in the rubber handling department, a job-exposure ranking system, which listed each job in the rubber handling department, was employed. The criterion for ranking was the amount of time employees in each category spent handling either cured

or uncured rubber, based on observation of employees at various workstations in the rubber handling department, and a review of employees' job duties with the department foreman.

A bulk sample of spray adhesive and two bulk samples - one cured and the other uncured - of the most commonly used formulation of rubber were qualitatively analyzed for the presence of tertiary phenols by two separate methods. In the first method, the rubber samples were individually treated by heating the bulk sample to 150 degrees Celsius in a tube furnace for 30 minutes. Air was continually passed through the oven during heating and the effluent passed through a silica gel tube. The generated silica sample was then desorbed with ethanol and analyzed with a gas-chromatography/mass spectrometry (GC/MS) unit. The same bulk rubber sample was also analyzed in the following manner. A cotton swab soaked in ethanol was used to wipe a small portion of the rubber's surface. The swab was then put into a vial containing more ethanol and extracted in a sonic bath. A blank swab was treated in the same manner. The ethanol extracts were then analyzed using the GC/MS unit.

Quantitative analysis was performed by extracting the bulk rubber using 10 mL of carbon disulfide in an ultrasonic bath. The solution was then analysed by gas chromatography and compared to a weighed standard.

#### B. Medical

On June 18, 1986, a survey of the production workforce was carried out in order to determine the overall prevalence of vitiligo in the plant population. The survey was carried out using a self-administered questionnaire filled out by all participating workers. The questionnaire included work history information and questions regarding specific symptoms of vitiligo and related illnesses such as alopecia areata (areas of hair loss). Complete examination of the skin was carried out on all workers who reported any depigmentation or "white spots" on the skin, and on all workers who were currently employed in the rubber handling department. A 10% systematic sample of workers from outside the rubber handling department with negative screening questionnaires was also examined.

Workers were considered to be probable cases of work-related vitiligo if they 1) gave a positive response to screening questions regarding the loss of skin pigment since beginning employment at Robbins & Myers, and 2) on examination, had depigmented areas of skin that fluoresced under a Wood's lamp. The relationship of vitiligo to dermal rubber exposure was analysed by comparing the prevalence of vitiligo in hourly workers currently or formerly employed in the rubber handling department to other workers in the plant, and by comparing the most highly exposed job categories within the rubber department with the remainder of survey participants.

Alopecia areata was diagnosed on the basis of the appearance of patchy hair loss on the scalp or beard in the absence of visible scarring. If the condition was reported to have begun after the beginning of employment at the plant, it was considered possibly work-related. Epidemiologic analyses were performed on the cases of alopecia in a fashion similar to that described above for the cases of vitiligo.

## V. EVALUATION CRITERIA

Precise estimates of dose-response relationships in occupational vitiligo have to date been impossible, since it has not been feasible to quantify skin exposure to depigmenting chemicals.<sup>2</sup> Exposures can be evaluated qualitatively by observation of work practices, and knowledge of the concentration of depigmenting agents present in the process materials. However, it is not possible to clearly establish what concentration of a depigmenting agent may be considered "safe" or too low to be a significant hazard.

In an epidemiologic investigation, establishing which component of a chemical mixture is responsible for the depigmenting effects observed in the workplace may not be possible, but data from other studies document a relationship between depigmentation and para-substituted catechols and phenols<sup>3</sup>. These chemicals are structurally similar to the amino acid tyrosine, which is the starting point in the synthesis of melanin and other skin pigments. Specific compounds which have been implicated in outbreaks of occupational vitiligo include monobenzyl ether of hydroquinone (MBEH), monomethyl ether of hydroquinone (MMEH), para-tertiary butyl catechol (PTBC), para-tertiary butyl phenol (PTBP), para-tertiary amyl phenol (PTAP), and a variety of para-substituted alkyl phenols.<sup>3</sup>

## VI. RESULTS AND DISCUSSION

### A. Environmental

The ranking of jobs within the rubber department indicated that the jobs which involved the highest degree of skin contact with either cured or uncured rubber were 1) gun and mill operator, 2) group leader, and 3) mold assembler. Rankings for all jobs in the department are presented in Table 1.

Analysis of the uncured bulk rubber sample in a tube furnace showed the presence of a di-tertiary butyl phenol (DTBP) compound, molecular weight 206, and para-tertiary butyl phenol (PTBP) compound, molecular weight 150. The same compounds were also identified from alcohol wipe samples of both uncured and cured rubber stock. Quantitative analyses performed on extracts of both cured and uncured rubber showed DTBP to be present in the extracts in concentrations ranging from 0.01% to 0.03%. The PTBP was present in concentrations too low to be quantified by the analytic technique used. No para-substituted phenol of any type could be detected in the bulk sample of spray adhesive.

### B. Medical

#### 1. Participation

Two hundred and one employees participated in the medical survey conducted on June 18, representing a 73% sample of the 272 employees in the entire hourly workforce. Of the 72 non-participants, 50 were estimated to have been absent from work at the time of the survey due to vacations or sickness. Twenty-two refused participation.

Of those participating, 86 were current or former employees of the rubber handling area; 115 had no history of employment in that plant department.

## 2. Vitiligo

Fifteen (7%) of the survey participants reported the onset of depigmented skin lesions since beginning employment at the Robbins & Myers plant. Of these fifteen employees four were found to have vitiligo on examination. One of these four also had alopecia areata. One additional case of vitiligo was observed in an employee who also had alopecia areata. Because this employee first noted the onset of depigmentation more than 10 years before beginning work at Robbins & Myers, he was excluded from the analysis of the survey data.

In two cases, the vitiligo was confined to the genital area, and in the other, two (both identified at the time of the initial survey), extensive areas of depigmentation were present on the trunk, as well as on the upper and lower extremities.

The employees with the most extensive depigmentation both reported onset of the lesions more than ten years prior to the date of the survey (1973 and 1975). One of the two remaining cases reported onset of depigmentation in 1984, and the other employee reported the first occurrence of depigmentation in May 1986. No additional cases of vitiligo were detected in any of the 43 employees who were examined but had negative screening questionnaires. The sensitivity, specificity, and predictive value of the screening questionnaire based on these results are given in Table 2.

Comparison of the survey results with those of a national examination survey<sup>1</sup> revealed that a statistically significant excess of vitiligo was present among the survey participants (Table 3). Further analysis, based on comparison of groups of employees within the plant, showed an approximately fourfold risk of vitiligo associated with employment in the rubber handling department (Table 4), although the 95% confidence interval for this risk estimate included one. When former and current workers in the three most highly exposed jobs in the rubber department were compared to the remainder of the survey participants, there was a 22-fold difference in the risk (95 % confidence interval: 4.7-102.7) (Table 5). Furthermore, when the analysis was repeated limiting the cases (hereafter referred as moderate-to-severe cases) to those which involved at least three of the following anatomical regions: trunk, genital region, upper extremities, lower extremities, and the head and neck, no cases were found outside the most highly exposed job category (Table 6).

The survey performed in June of 1986 thus confirmed the initial impression of an increased risk of vitiligo associated with employment in the rubber handling department of the Moyno Products division. The risk appears to be directly associated with jobs involved in handling rubber. Within the rubber handling department, no cases were found in employees who had not previously been employed in one of the following job categories: gun and mill operator, group leader, and mold assembler.

The two most severe cases of vitiligo in employees of the rubber handling department appeared in 1973 and 1975, more than 10 years prior to the date of our initial visit (October 1985). From the results of our process review, it is unclear whether exposures similar to those which led to the appearance of these two cases were similar to those currently taking place in the rubber handling department. At the time of our survey, no product expected to contain a known vitiligo-causing substance could be identified in our review of rubber formulae and material safety data sheets. DTBP was nevertheless

detected in quantifiable amounts in samples of both cured and uncured rubber. We surmise that the DTBP found in the rubber stocks used at Robbins & Myers may arise from contamination in the formulation process.

### 3. Alopecia Areata

Two cases of alopecia were noted in workers who also had vitiligo. There was no difference in the prevalence of alopecia between workers currently or formerly employed in the rubber handling department, and the remainder of the survey participants. There is thus no evidence that the occurrence of alopecia was related to exposure to rubber chemicals.

## VII. CONCLUSIONS

On the basis of the epidemiologic evidence associating the cases of vitiligo with employment in the rubber handling department and the laboratory identification of DTBP in bulk rubber samples from the department, we conclude that DTBP is the probable cause of the vitiligo cases identified in the plant.

## VIII. RECOMMENDATIONS

The goal of the preventive measures listed below is the prevention of further cases of work-related vitiligo in the Robbins & Myers workforce, specifically by eliminating exposure to rubber contaminated with para-substituted phenol compounds. Measures for accomplishing this goal are discussed below.

### A. Laboratory Testing Program

Since the DTBP presumptively identified as the cause of the vitiligo cases at Robbins & Myers is not deliberately added to the product formulation, it will be necessary to periodically perform chemical analyses in order to ascertain the presence of this contaminant in rubber stock purchased from outside vendors. To the degree that the contaminant cannot be completely eliminated from the rubber formulation, the following additional measures should be instituted.

### B. Modification of Workpractices

Eliminating use of the old injection-molding equipment has the potential for significantly reducing the time of operator contact with rubber stock, since the newer equipment does not require the gun and mill operator to handle the rubber as it is being milled.

### C. Medical Surveillance of Exposed Workers

Medical surveillance should be instituted as a means of insuring the effectiveness of other preventive measures. This form of control can at best serve to reverse the course of vitiligo in affected workers and can only be regarded as a form of secondary prevention. We would suggest that surveillance - consisting of a screening questionnaire and skin examination - be carried out as workers rotate through the most highly exposed jobs in the rubber handling department. Possible vitiligo cases should be confirmed by referring the affected individuals to a

physician. Workers with confirmed cases of vitiligo should be informed that continued exposure to DTBP or PTBP may prolong or exacerbate the course of their illness.

IX. REFERENCES

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XI. DISTRIBUTION AND AVAILABILITY OF REPORT

Copies of this report are currently available upon request from NIOSH, Division of Standards Development and Technology Transfer, 4676 Columbia Parkway, Cincinnati, Ohio 45226. After 90 days, the report will be available through the National Technical Information Service (NTIS), 5285 Port Royal, Springfield, Virginia 22161. 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:

1. ROBBINS & MYERS, INCORPORATED
2. UNITED AUTO WORKERS, LOCAL 902
3. OSHA, Region V

For the purpose of informing affected employees, copies of this report shall be posted by the employer in a prominent place accessible to the employees for a period of 30 calendar days.

Table 1  
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Ranking of Rubber Handling Department Job  
Categories by Degree of Exposure to Cured and Uncured Rubber Exposure

<u>Rank</u>	<u>Job Title</u>
1	Gun and Mill Operator
2	Group Leader
3	Mold Assembler
4	Trucker
5	Sandblaster
6	Inspection
7	Thread Set-up
8	Screw Machine Operator
9	Sizing Lathe Operator

Table 2  
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Sensitivity and Specificity of Screening Questionnaire\* in  
Detecting Work-Related\*\* Cases of Vitiligo

Dermatologic Examination with Wood's Lamp

<u>Questionnaire:</u>	Positive	Negative	Total
Positive	4	11	15
Negative	0	43	43
TOTAL	4	54	58

Sensitivity=100%; specificity= 80%

Predictive value of a positive=29%; predictive value of a negative test=100%.

- \* Questions on both Alopecia and Vitiligo were used to screen survey participants. An employee who gave a positive response indicating the presence of either vitiligo or alopecia was subsequently examined.
- \*\* This table excludes one case of vitiligo which began prior to employment at the Robbins & Myers company.

Table 3  
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Observed versus Expected Number\*  
of Vitiligo Cases Among Survey Participants  
Based on Comparison to Results from the  
Health and Nutrition Examination Survey-HANES)

Cases Observed in 198 Participants of <u>Robbins &amp; Myers Vitiligo Survey</u>	Expected Number <u>of Cases</u>
4	1.1

\* Age specific data on the prevalence of vitiligo were used to calculate the expected number of cases among the survey participants

Standardized Morbidity Ratio = 3.6,  $p=0.02$  based on Poisson probability distribution.

Table 4  
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Prevalence of Vitiligo in Current and Former  
Employees of the Rubber Handling Department Compared to  
Remainder of the Survey Participants

	<u>Current and Former Employees of Rubber Handling Department</u>	<u>Other Survey Participant</u>
Vitiligo	3	1
Non-case	<u>83</u>	<u>113</u>
	86	114

Prevalence Ratio = 3.98; 95 % confidence interval = 0.5 - 31.7

p=0.21 using one-tailed Fisher's exact test

Table 5  
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Prevalence of Vitiligo in Three Most Highly Exposed  
Job Categories\* Compared to Remainder of Survey Participants

	<u>Current and Former Gun and Mill Op, Group Leader, or Mold Assembler</u>	<u>Other Survey Participant</u>
Vitiligo	3	1
Non-case	21	175
TOTAL 24	176	

Prevalence Ratio = 22.0, 95% Confidence Interval = 4.7 - 103.7

p=0.006 using Fisher's Exact test

Table 6  
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Prevalence of Moderate-Severe Vitiligo\* in Gun  
and Mill Operators Compared to Remainder of Survey Participants

	<u>Current or Former Gun and Mill Operator</u>	<u>Other Survey Participant</u>
Vitiligo	2	17
Non-case	<u>0</u>	<u>181</u>
	2	198

Prevalence Ratio is undefined

p=0.009 using Fisher's Exact test