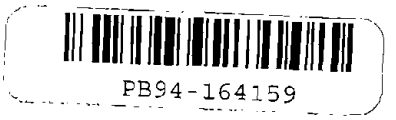

Industrial Hygiene Report
Walk-Through Survey

Final Report

Mallinckrodt Specialty Chemicals Company
16305 Swingley Ridge Drive
Chesterfield, Missouri 63017

Survey Conducted By:
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Date of Survey:
January 19, 1993

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16. Abstract (Limit: 200 words) A walk through survey was conducted at the Mallinckrodt Specialty Chemicals Company (SIC-2833) located in Chesterfield, Missouri to assess the feasibility of conducting studies on the immunotoxic effects of chemicals at this facility. The opiate refining facility at the site had been in constant operation for about 100 years. Morphine (57272), codeine (76573), thebaine (115377), noscapine (128621) and papaverine (58742) were produced. A total of 66 chemical operators, 20 salaried personnel and additional support staff were involved in the production of the opiates. Nine full time safety and health professionals were employed by the company. Urine samples were collected at scheduled periodic medical examinations and tested for opiates. Ventilation controls appeared minimal, but surfaces were free of accumulated dust. Personnel records appeared to be inadequate for retrospective mortality or morbidity studies. Because of incomplete or inconsistent data collection at various sites, it was difficult to determine if the findings at this site were comparable to those at other facilities. The authors conclude that additional exposure information may be needed to determine the feasibility of conducting a study at this facility.

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Purpose of Survey:	To meet with labor and management representatives of Mallinckrodt to describe the NIOSH Immunotoxic Study and obtain preliminary information on their industrial hygiene program, personnel records system, and medical record system. The information is being used to assess the likelihood of exposure and the feasibility of conducting a study using assays that could detect immunomodulating effects, along with the possibility of conducting a morbidity and/or mortality study.
Employer Representatives Contacted:	Mallinckrodt & Second Sts. P.O. Box 5439 St. Louis, MO 63147 (314) 530-2000 Dale Schillinger, Director, Health & Safety Christine Merli, Manager, Safety & Health Jack Frauenhoffer Director, Safety & Environmental Affairs Jon Koester, Manufacturing Director Jim Stemmler Manufacturing Superintendent Patricia Duft Senior Attorney
Employee Representatives Contacted:	Brian Wilson, Safety Representative, UAW Harry Bickford, Safety Representative, UAW
Standard Industrial Classification of Plant:	2833 - Medicinal Chemicals

INTRODUCTION

NIOSH is mandated to conduct occupational health research by the Occupational Safety and Health Act of 1970. The authority of NIOSH to conduct site visits and the procedures for such visits are described in the Code of Federal Regulations, Title 42, Part 85a.

NIOSH, with collaboration of the National Institute for Environmental Health Science (NIEHS), is interested in expanding the knowledge on immunotoxic effects of chemicals. Among the practical research questions that could be addressed include: 1) Do immunomodulating effects seen in rodent experiments correlate with effects seen in humans similarly exposed, 2) Which kinds of immunomodulating effects are seen with different chemical exposures, and 3) Are immunomodulating effects correlated with any clinically measurable or epidemiological outcomes? The literature suggests that opiate compounds are immunomodulating compounds.

PLANT AND PROCESS DESCRIPTION

The opiate refining plant has been in essentially constant production of opiate compounds for about 100 years. Other compounds that are currently produced in other buildings at the site are principly inorganic. During 1942-1957 there was a uranium processing plant on-site.

Among the alkaloids of importance that are derived from opium are morphine (10-12%), codeine (2.5-3%), thebaine, noscapine and papaverine. The opiate refining process consists of initially liquefying raw opium tar, followed by filtration, extraction and precipitation. Many of the details of this process are considered proprietary. Most high volume materials are transferred to the processing vessels via closed piping systems.

DESCRIPTION OF THE WORKFORCE

The narcotics operation is run over all three shifts. Sixty-six chemical operators, twenty salaried personnel and additional support staff are involved in the manufacture of opiate compounds. There has been a gradual increase in production and employment over the years of operation.

Job turnover is reportedly low and most new workers in this operation have been hired from other operations within the plant. Most of the operators are on a continuous rotating work week schedule. The United Auto Workers have represented the hourly workers at this site for the past 15 years.

DESCRIPTION OF MEDICAL, INDUSTRIAL HYGIENE AND SAFETY PROGRAMS

Industrial Hygiene Program

The company employs nine full-time safety and health professionals to oversee the health and safety concerns at the plant. Safety committee meetings include production and management employees. In addition to engineering controls, personal protective equipment is used as a means of preventing exposure. All operator workers are qualitatively fit tested for respirator use after they have been medically approved to wear respiratory protection at the annual physical examination. Respirators available range from simple dust masks to air-supplied full-face types. Historically, simple disposable dust masks have been used in most operations where dry opiate products might be aerosolized. More recently, HEPA cartridge respirators are being increasingly used. Respiratory protection is strongly encouraged for use during any short-term operation where release of agents into the room air are expected to occur. HEPA respirators are required for those operators where observed contamination levels exceed recommended limits. Skin protection is provided by a combination of company inititives. Company-issued cotton work clothing is washed daily. Disposable tyvek® coveralls are used during certain dusty activities. Gloves provided include butyl gloves for use with solvents. All workers are required to shower at the end of their shift. Locker facilities provide that street clothes are not in contact with soiled work clothing.

Limited industrial hygiene air monitoring has been performed at the plant for solvents and dusts. Analysis of opiate air monitoring samples was initiated about a year ago. Recent sampling has used GC-MS analysis for specifically characterizing the air concentrations of opiate compounds. All of these samples are personal 8-hour TWA determinations. The limit of detection is about 0.01 mg/m^3. Full-shift monitoring has been performed during jobs involving conversion, drying, finishing and packaging. Air sampling results ranged from non-detectable to 1.1 mg/m^3 as an 8-hour TWA.

Urine analysis summary results for narcotics, primarily codeine and morphine, indicate elevated positive results (>200 ng/mL) occurring among 6 of the samples collected from about 115 employees in the screening program. The urine samples are collected during scheduled periodic medical examinations. Neither work schedules nor environmental monitoring have been

correlated with the urine results to ascertain the relationship of work exposures to elevated results. Therefore, it is not known when the last workplace exposure occurred when elevated urine results are received. About 60% of the morphine dose is eliminated via the urine in 8 hours and 90% is eliminated in 24 hours. For the purpose of determining extent of exposure, not knowing the duration since last exposure makes an interpretation of this data difficult. If the elapsed time from last exposure was known, the urine concentration could be used to back-calculate the exposure dose. However, specific urine results were not obtained during this visit.

Medical Program

Mallinckrodt has an on-site dispensary staffed full-time with a nurse and an Emergency Medical Technician. Two physicians from Barnes Care Corporate Health Sevices staff the dispensary on 2 half-days. Baseline and periodic physical examinations are performed on-site for all production workers. Periodic medical evaluations include pulmonary function testing, blood chemistry, complete blood counts, urinalysis, and chest X-rays. Additionally, drug testing for opiates and other illicit drugs is completed for narcotics production workers. Medical records are kept on-site.

Over the period of 1988 - 1992, Mallinckrodt's OSHA log for medical conditions referable to opiate exposure contains entries for bronchospasm, rash, and sinusitis. There were 2 cases of bronchospasm in 1989, 1 case in 1990, but no cases in 1991 or 1992. The company credits improved exposure control and work practices for the absence of bronchospasm in the past 2 years. During this interval (1988-92), the number of cases of rash ranges from 2 to 8 without an apparent trend either up or down.

Mallinckrodt provides a medical benefits package to the production workers. Health insurance is administered by a benefits administration company. Mallinckrodt describes itself as self-insured. Mallinckrodt subscribes to an insurance carrier for workers compensation insurance.

DESCRIPTION OF THE PERSONNEL RECORDS SYSTEM

Personnel records are probably inadequate to perform retrospective mortality or morbidity studies. Work assignment records are maintained at the level of the production group foreman. There is no standardization in the production group records and old records are often discarded. Information regarding job and department changes is not always found for the records which have been maintained.

INSPECTION OF THE PLANT

The visual inspection of the drug manufacturing areas left an impression of extraodinary hygiene. All surfaces within these departments appeared virtually free of accumulated dust. This observation, however, was inconsistent with the general lack of local ventilation controls and the manual transfer of dry materials at several processing points. Either the product material is of such consistency that it does not readily become aerosolized, or regular clean-up is responsible for the hygienic conditions in this facility. Solvents and aqueous bulk processing chemicals were all pumped via permanent piping to closed vessels. Thus, little or no odor of these chemicals was detected during the walk-through survey. The operations appeared to require only occasional attention and activity by employees, an aspect that would reduce the likelihood of exposure.

CONCLUSIONS

Based upon the information that is presently available, it is difficult to determine whether current exposures to opiates at this site are comparable to those at other plants because of incomplete and inconsistent data collection at each site.

At Mallinckrodt, elevated drug screening results from narcotics production workers were obtained in approximately 5% of the urine samples collected in 1992. Full-shift air monitoring data indicate that air concentrations to opiates in some areas of Mallinckrodt are as high or higher than at another company that produced opiates and where there was evidence of immunomodulating effects. However, such airborne exposures are limited to only about 36 employees. How much of the measured exposure is due to short-term activities while the workers are presumably wearing respiratory protection and how well they are being protected is not well characterized. Historical exposure data to opiates is reportedly scarce. Ventilation controls to remove residual contaminants appeared minimal. However, the nature of the material may preclude appreciable aerosolization since there were few visual indications of dust accumulations throughout the work areas (although excellent housekeeping may also partly account for this). Union representatives did not believe that workers in the opiate production departments perceived excess health problems associated with opiate production. Data from the OSHA log on work-related illnesses, as well as sick leave time taken among opiate workers, would suggest no excess in morbidity in general or to bronchospasm specifically.

Personnel record systems may be incomplete and not allow the performace of a retrospective epidemiological study. This problem should not preclude performance of a epidemiological morbidity study, if desired, although the number of exposed workers is small.

In conclusion, additional information on the level of exposure may be needed to determine the feasibility and desirability of conducting a study at this site. A joint decision by NIOSH and NIEHS staff regarding further activities should be made subsequent to this report.