Field Study

Exposure to 4,4’-methylene bis(2-chloroaniline) (MbOCA) in New South Wales, Australia

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Abstract: Objectives: This study was conducted to determine the level of exposure of 4,4’-methylene bis(2-chloroaniline) (MbOCA) in New South Wales (NSW), Australia. Methods: An integrated occupational hygiene and biological monitoring program were used to assess the workers’ exposure to MbOCA via inhalation, ingestion and dermal contact. This was conducted by personal air monitoring, static air monitoring and surface contamination monitoring of the work environment and biological monitoring of the workers’ exposure to MbOCA at nine workplaces in NSW. Results: The air monitoring results for MbOCA gave a geometric mean (GM) of 0.06 μg/m³ and a geometric standard deviation (GSD) of 2.70 and a 95% confidence interval of 0.29 μg/m³. The surface contamination in the main work area showed the highest contamination with a GM of 74 ng/cm² and a GSD of 17 and a 95% confidence interval of 7,751 ng/cm². Biological monitoring showed a GM of 0.89 μmol/mol cr and a GSD of 11.9 and a 95% confidence interval of 52 μmol/mol cr. This indicated that 13% of the workers were over the SafeWork NSW Biological Occupational Exposure Limit of 15 μmol/mol cr. Conclusions: Workers’ exposure through inhalation was minimal; however, evidence from biological monitoring of MbOCA suggested that the main contributing factor to exposure was skin absorption. This was attributed to poor housekeeping and inadequate personal protection. Improvements in these areas were recommended, and it was also recommended to improve the awareness of the workers to the adverse effects to their health of exposure to this carcinogen.

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Introduction

The aromatic amine 4,4’-methylene bis(2-chloroaniline) (MbOCA) is a chemical curing agent used in the manufacture of polyurethane and was classified in 2010 as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC). The IARC Group 1 classification means exposure to this substance can cause cancer in humans¹. In general, occupational exposure to carcinogens has been estimated to account for around 5,000 cases of cancer (6.5% of new cases) in Australia every year².

MbOCA is usually used as a pelletized, yellow flaked solid. It chemically reacts and cross links polymer chains to form relatively stable complex polymer structures. These are tough abrasion-resistant polymers and can be used to manufacture castable urethane rubber products such as industrial tires, rollers, shock-absorption pads and conveyor belts.

The use of MbOCA in manufacturing workplaces in the state of New South Wales (NSW), Australia must be authorized by the work, health, and safety regulator of that state, SafeWork NSW. This study was undertaken to ascertain if proper workplace exposure controls were in place in NSW. It was modeled on similar studies conducted in the UK earlier by Cocker et al³ and Keen et al⁴.

Workers that handle MbOCA or work in an area where MbOCA is used can be at risk of exposure and consequently at an increased risk of adverse health effects. The acute health effects of exposure to MbOCA include irritation and a burning sensation to the skin and eyes, nausea, and gastrointestinal and renal effects⁵. Animal studies have shown that chronic exposure to MbOCA can cause...
bladder cancer.\textsuperscript{6,7} MbOCA-DNA adducts have been found in exposed workers\textsuperscript{8}; however, only a few studies have found direct evidence of bladder cancer reported in workers exposed to MbOCA.\textsuperscript{9,10} As little as two years of exposure to MbOCA has been suggested to be sufficient to increase the risk of cancer; however, due to the long latency of cancer it was found on average to occur after 11.5 years and could appear as late as after 45 years of the exposure.\textsuperscript{9,10}

A survey conducted in 2016 by the Australian national governmental agency, Safe Work Australia, found that carcinogen exposure control measures in workplaces were generally not well used in Australia.\textsuperscript{11}

The current study presented in this paper reports on an occupational hygiene survey that was conducted by the NSW state governmental agency, SafeWork NSW, and was integrated into a regulatory verification program examining compliance with the NSW legislation on carcinogens. Nine workplaces in NSW that have been authorized to store and use MbOCA were inspected for regulatory compliance and the exposure to MbOCA was measured in each workplace. The survey was used to establish the effectiveness of the control measures to reduce the workers’ exposure to MbOCA.

Methods

Polyurethane Workplace and Process Description

The study assessed nine workplaces that used and handled MbOCA. Most of the sites visited were less than 2,000 m\textsuperscript{2} in area and usually consisted of high roofs and large door entrances. The polyurethane manufacturing areas comprised of open floor areas inside the building with local exhaust ventilation. All factories had a MbOCA restricted access area marked with yellow lines on the floor and signs that were visible from the entrance of the building. The sites visited were authorized by SafeWork NSW to use MbOCA and were principally involved in the manufacturing of polyurethane products for the mining industry.

In brief, the process for making the polyurethane product involved mechanically dispensing the pelletized, yellow flaked solid MbOCA from a hopper located within a local exhaust ventilation system into a melting pot placed underneath. At some sites the use of a hand scooper was employed to take 7-10 scoops of MbOCA pellets and transfer them into a melting pot located within the exhaust ventilation system. The weighed MbOCA was then melted on a gas burner located within the large fume hood and added into a mixture containing a prepolymer of 2, 4-toluene diisocyanate (TDI). The mixture was then degassed under vacuum at ambient temperature. It was then poured into metal molds and cured in an oven at 60°C-70°C for several minutes. The molds were allowed to cool and then removed from the oven and finished by trimming and subsequently packaged on a nearby table. The MbOCA workers wore P2 disposable masks during the whole procedure and typically used cotton gloves inside long rubber gloves during the MbOCA handling tasks.

Exposure Assessment

The occupational hygiene survey involved the assessment of nine workplaces in NSW. Seven polyurethane manufacturing sites and two MbOCA suppliers’ sites were assessed in this study by a specialist inspector and an occupational hygienist. A quantitative assessment of the exposure to MbOCA was conducted at each workplace. Inhalation exposure was assessed by performing personal and static air monitoring and potential skin exposure was assessed by detecting surface contamination. Biological monitoring was used to assess all routes of exposure.

The manufacturing locations, Sites 1-6, were assessed for air contamination; Site 7 was not assessed for air contamination as no production was occurring on the day of inspection. The seven manufacturing locations, Sites 1-7, and the two supplier locations, Sites 8 and 9, were assessed for surface contamination. The seven manufacturing locations, Sites 1-7, were also assessed for exposure to MbOCA by biological monitoring of the workers’ urine. The manufacturing and supplier numbered site identifying labels are consistent throughout the data analysis.

Process information was collected at each workplace, including the identification of workers most likely to be exposed to MbOCA and the evaluation of the exposure control measures, including local exhaust systems and personal protective equipment.

The suppliers’ sites were essentially a storage distribution center where drums of MbOCA and other chemicals were stored in warehouses. The MbOCA drums were stored in separate sections of the warehouses. The drums were 50 kg in weight and were of a fiberboard-type construction. On the days of the visits to the two suppliers, there was no activity in the handling or storing of the drums.

At all sites, worker and supervisor interviews were carried out to determine the volume of MbOCA used, if the workers were aware of any potential health effects of MbOCA exposure, what procedures were used for handling MbOCA in that workplace and what exposure controls were in place.

The employer’s health monitoring program and other relevant documents such as the workers training record, equipment maintenance records, rosters and job rotation were also reviewed.

The site visits were conducted over an eight month period and were performed midweek between Tuesday and Thursday.
Table 1. Description of tasks for exposure areas at MbOCA supplier and manufacturing workplaces

| Area   | Activity          | Task Descriptions and Sampling Locations                                                                 |
|--------|-------------------|----------------------------------------------------------------------------------------------------------|
| Area 1 | MbOCA Use         | Weighing MbOCA pellets; melting MbOCA; dispensing molten MbOCA; mixing molten MbOCA with pre-polymer.       |
| Area 2 | Production        | Casting into moulds; curing in ovens; trimming and finishing.                                            |
| Area 3 | Non-Production    | Administration; lunch and staff facilities areas.                                                        |
| Area 4 | Storage           | MbOCA drum storage areas.                                                                                 |
| Area 5 | Other             | PPE, waste bins; polyurethane product; vacuum cleaners storage areas.                                     |

*Air Monitoring*

Personal and static air monitoring was carried out at Sites 1-6 as per the US Occupational Safety & Health Administration (OSHA) Method 71\(^\text{12}\). This method involved collection of air samples on glass fiber filters that had been pretreated with sulphuric acid. The air samples were collected by drawing air at the flow rate of 1 l/min through the filter in a closed faced sampling cassette. Calibrated air sampling pumps were used for collecting the air in the breathing zone and general work atmosphere of the MbOCA workers. Sites 1-6 had \(n=3\), 1, 4, 2, 2, 4 personal air samples and \(n=2\), 1, 1, 2, 2, 0 static air samples taken respectively.

*Surface Contamination Monitoring*

Alcohol swabs were used to sample surface contamination in different locations in the workplace using 70% isopropyl alcohol Liv-Wipe\(^\text{8}\) swabs (55×65 mm) obtained from Livingstone International Pty Ltd (Sydney, Australia). The samples were collected by wiping 100 cm\(^2\) area set by a 10x10 cm template. The 100 cm\(^2\) area was wiped using gloved fingertips held together and applying firm pressure using an overlapping “S” pattern with horizontal strokes. The exposed side of the swab was folded inward and the unexposed side was used to wipe the same area using vertical “S” strokes. In the case of curved objects (containers, lids, and finished products), the area sampled was estimated. All sampling locations at each site were categorized into one of five exposure areas based on the tasks performed in relation to MbOCA at those locations. All seven manufacturers and two suppliers worksites were sampled, totaling 178 samples taken in Areas 1-5 with \(n=48\), 39, 35, 23, 33 respectively. The full description of the areas can be seen in Table 1.

*Biological Monitoring*

Biological monitoring of workers exposed to MbOCA was carried out at the seven polyurethane manufacturing workplaces, Sites 1-7. Post-shift urine samples were collected following midweek shifts from those working with MbOCA as well as from the workers whose duties did not involve the handling of MbOCA directly. The workers were informed of the purpose for collecting urines samples and personal consent was obtained from each worker. Urine samples were unable to be collected at the two supply companies as the workers declined this service. The collected workers’ urine was analyzed for total MbOCA, which comprised of the free MbOCA and the \(N\)-glucuronide conjugates of MbOCA. All urine samples were analyzed for the amount of creatinine, and the test results were normalized against this amount to account for the workers’ hydration level. Hence, the final test results were expressed as micromole MbOCA per mole of creatinine (μmol/mol cr).

*Chemical Analysis*

The chemical analysis of MbOCA involved converting the amine salts to free amines by alkaline hydrolysis with 2M sodium hydroxide at 95°C for one hour. The free amines were then extracted with toluene and derivatized with heptafluorobutyric acid anhydride. An internal standard, \(4,4’\)-(hexafluoroisopropylidene) dianiline, was added to the samples at the start of the analysis to account for the extraction efficiency and the derivatization recovery of the analysis. Samples were analyzed for MbOCA using dual column gas chromatography with dual electron capture detection in accordance with the analytical method of Skarping et al\(^\text{13}\).

*Instrumentation*

An Agilent 6890 Gas Chromatograph equipped with dual micro electron capture detectors with dual columns Agilent DB-XLB (60 m, ID 0.25 mm, Film thickness 0.25 μm), SGE BPX-35 (60 m, ID 0.25 mm, Film thickness 0.25 μm) was used to perform the analysis. Hydrogen carrier gas was used at a flow rate of 1 ml/min with nitrogen makeup gas at a flow rate of 60 ml/min. Temperature program used was started at an initial temperature of 90°C then increased at 25°C/min to 280°C and held for 8.4 mins. The total run time was 16 mins. The injection volume used was 1 μl splitless at 250°C.

*Exposure Standards*

**Airborne MbOCA**

The Australian Workplace Exposure Standard, expressed as a time weighted average (TWA) for an 8-hour shift for MbOCA, is 220 μg/m\(^3\), which is equivalent to 0.02 ppm in air\(^\text{14}\).
MbOCA in urine
The Work, Health, and Safety Regulations in NSW do not mandate a biological exposure standard. However, the SafeWork NSW Biological Occupational Exposure Limit (BOEL) Committee has recommended a BOEL of 15 μmol/mol creatinine for urinary MbOCA. This is used as a guidance value to aid in the interpretation of the biological monitoring test results and is not a mandatory exposure limit.

Surface Contamination
The Occupational Safety and Health Administration’s, USA, permissible exposure limit (PEL) for surface contamination of MbOCA recommends 1,000 ng/cm².

Data Analysis
The data analysis was performed using the statistical program IHSTAT V 1 December 01, 2007, AIHA. All calculations were verified using Microsoft Excel 2010 V 14.07015.1000. The ANOVA calculations and all graphs were generated in Microsoft Excel 2010 V 14.07015.1000.

Results
Most of the seven polyurethane manufacturing workplaces visited were small to medium sized enterprises. Two MbOCA supplier sites were also investigated using surface contamination sampling.

All sampling locations at each site were categorized into one of five exposure areas based on the tasks performed in relation to MbOCA at those locations. The full description of the areas can be seen in Table 1. Workers who worked in these areas alone could be considered a similarly exposed group. However, at some workplaces there was some cross over between the areas by some of the workers.

During inspection it was noted that empty MbOCA drums were being used as waste bins on some sites. All sites had vacuum cleaners with HEPA filters that were used to clean up spills. Workers wore long sleeved thick cotton material shirts and trousers. These clothes were washed daily. The workplace had an on site facility for laundry. The workers changed their clothes daily on site before going home. Employees at most sites working in the MbOCA areas wore leather gloves and Class A P2 half facemasks for respiratory protection. Some workplaces manually handled MbOCA on a daily basis. Other chemicals that were used at most sites included disocyanates and ethanol. The assessment of exposure to these chemicals was not undertaken as the focus of this study was to assess exposure to the carcinogens in the workplace.

A total of 24 personal and static air monitoring samples were taken from Area 1 at six of the seven polyurethane manufacturing sites. The test results for each site are shown in Fig. 1. Unfortunately, no air samples were obtained from the seventh site as no production was occurring on the day of the assessment.
Fig. 2. MbOCA surface contamination of the areas defined in Table 1 for seven polyurethane manufacturers and two MbOCA supply company workplaces in NSW, Australia. The maximum value whisker of Area 1 is plotted on a broken scale and had a value of 11,040 ng/cm². Area 1 to 5 n=48, 39, 35, 23, 33 respectively. Dashed line shows OSHA PEL at 1,000 ng/cm². Box represents 25-75% confidence interval; horizontal line in the box is the median; black diamond point is the arithmetic mean and vertical lines are the ranges of the data.

The air monitoring results showed very low levels of airborne MbOCA. Of the 24 air samples taken 8 (30%) gave levels below the Limit of Quantitation (LOQ) of 0.01 μg/filter sample equivalent to 0.03-0.05 μg/m³, depending on the air volume. These values that were less than the LOQ were included in the statistical analysis as a value half the LOQ. Across all sites, the data gave a geometric mean (GM) of 0.08 μg/m³ and a geometric standard deviation (GSD) of 2.70 and a 95% percentile of the lognormal distribution of 0.29 μg/m³. This is approximately three orders of magnitude below the Safe Work Australia Time Weighted Average exposure limit of 220 μg/m³.

A total of 178 surface contamination samples were collected from the nine sites. Statistical analysis using ANOVA was performed on the distributions of results between the five areas and showed that Area 1 was significantly different from the other areas (p<0.001). Area 1 showed the highest contamination with a GM of 74 ng/cm² and a GSD of 17 and a 95% percentile of 7,751 ng/cm². This illustrates the wide range of contamination levels on the surfaces in the workplaces. The MbOCA storage locations of Area 4 showed surprising contamination levels with a GM of 34 ng/cm² and a GSD of 11.01 and a 95% percentile of 1,760 ng/cm². The results for all areas are displayed in Fig. 2.

Biological monitoring was performed by collecting post-shift urine samples at seven of the workplaces from 24 workers who may be at significant risk of exposure to MbOCA. The distribution of results gave a GM of 0.89 μmol/mol cr with a GSD of 11.9 and a 95% percentile of 52 μmol/mol cr. The statistical analysis showed that 13% of the distribution could possibly be over the BOEL of 15 μmol/mol cr. The test results are presented in Fig. 3.

Discussion

All personal air monitoring samples were less than 10% of the Australian TWA exposure limit of 220 μg/m³ for airborne MbOCA. This indicates that the workers are not at risk of significant exposure to MbOCA through inhalation. This is not surprising due to MbOCA having the chemical properties of low volatility and a high melting point inhibiting the amount present in the workplace air. In the light of such low airborne exposures and considering the genotoxic properties of MbOCA, regulatory bodies could easily lower this exposure standard without imposing any challenge for industry to comply. The low exposures also demonstrated that the controls of airborne exposure are adequate; however, it was reiterated to the employer and workers that the melting and mixing tasks should always be conducted under a fume hood extraction and to have adequate natural ventilation in MbOCA work areas to maintain such low exposures. Maintenance of
Surface contamination with MbOCA was evident in all workplaces with high levels found at locations within two exposure group categories. The highest contamination was found in the Area 1 location where MbOCA was directly handled. MbOCA levels as high as 11,040 ng/cm$^2$ were detected. Surface contamination sampling is an easy and convenient tool for workplace assessments but requires sufficient samples to address the variability of the contamination to be able to properly interpret the potential exposure\textsuperscript{16}.

The tasks at the Area 1 location in the different workplaces involved the filling of hoppers with MbOCA pellets, transferring MbOCA pellets into the melting pots, dispensing molten MbOCA manually into mixing vessels, and mixing MbOCA with prepolymer on an open bench. Most contamination was detected on melting area surfaces, mixing benches, and on MbOCA weighing scales.

It appears that unsafe work practices, such as spilling the MbOCA during weighing or melting and the subsequent inadequate cleaning of the surfaces would have largely contributed to this contamination. Good housekeeping and regular decontamination of the surfaces to prevent exposure was suggested to the employers and workers.

Surface contamination samples from the MbOCA storage areas of the polyurethane manufacturers (Area 4) surprisingly also had high contamination, mostly on the lids or rims of the MbOCA drums as well as the door handles of cabinets where the drums were stored. Samples taken at the MbOCA suppliers’ work sites also showed significant contamination on the lids and rims of MbOCA drums that were stored for delivery to its customers. This contamination appeared to have occurred in the MbOCA manufacturing process, which remained on the exterior of the drums. It was recommended that appropriate PPE, such as thick rubber gloves, should be worn to prevent exposure even while moving unopened drums. It was also suggested that empty MbOCA drums should not be used for any other purpose such as waste bins.

Some surface contamination samples taken in the non-MbOCA use areas (Area 2, 3, and 5) showed detectable amounts of MbOCA. This indicated that contamination from MbOCA use areas may have been transferred due to poor personal hygiene, possibly in combination with inadequate housekeeping practices.

Biological monitoring results showed that three (12.5%) out of 24 workers had MbOCA in urine levels exceeding the SafeWork NSW BOEL of 15 μmol/mol cr. Twenty one of the workers were below the MbOCA BOEL with twelve workers (50%) being below 10% of the BOEL. More than half of those tested (63%) had detectable amounts of MbOCA in their urine.

It was noted that some workers had higher urinary MbOCA results than their coworkers at the same workplace, despite doing similar work activities under com-
mon exposure controls. This is particularly evident at Sites 2, 3, and 5 where the test result was above the acceptable BOEL. This suggests that individual hygiene and work practices may be different, hence resulting in higher exposures than their colleagues. Some workers may be exposed due to inadvertent ingestion by habitual nail biting or repeatedly touching their mouths, both of which will increase the chance of ingesting contaminants on their hands. In such instances, improving the overall engineering controls at these workplaces would not necessarily reduce personal exposure. Training on how to correctly remove and dispose of contaminated gloves and clothing, along with training on personal behavior and hygiene, and adequate supervision could potentially reduce exposures for those workers with higher urinary MbOCA results.

As shown in Fig. 1, no evidence of adverse airborne exposures to MbOCA at any of the workplaces was found. The biological monitoring test results indicate that a number of workers are exposed to MbOCA by poor work practices probably through direct contact or via handling and/or surface contamination. This type of exposure was evident at all workplaces and suggests that dermal exposure to MbOCA is the most common route of exposure.

During the study it was noted that all workers who handled MbOCA wore overalls, half face mask respirators, and various types of gloves to prevent skin exposure. It appears that the high contamination on some surfaces may be transferred to workers through either incorrect choice or use of gloves and/or generally poor hygiene practices. Better training and more awareness of the hazards of MbOCA and its potential health effects was emphasized.

This study confirms the conclusions of similar surveys conducted in the UK that concluded that skin absorption is the most likely route of exposure to MbOCA at the polyurethane manufacturing sites.

Conclusions

This hygiene survey was conducted as part of a regulatory program to verify the safe use of an authorized carcinogen in a small to medium manufacturing industry sector. The results demonstrated the importance of surface contamination sampling and biological monitoring as useful tools to determine the workers’ potential and actual exposure to MbOCA.

Exposure of workers to airborne MbOCA were not evident in the personal and static air samples with air concentrations well below the occupational limit. Control measures to prevent airborne exposures appear to be effective at each workplace.

Surface contamination monitoring suggested workers’ exposure could have occurred through contact with the skin. Although there are no guidance limits on unsafe levels, the surface contamination detected in the MbOCA work areas and in some storage locations were excessive and perhaps demonstrated a less than appropriate approach to the handling of this chemical. From observation of tasks and the exposure control measures in place, it was concluded that improving work practices, housekeeping and surface decontamination would appear to have a significant effect on reducing exposure to MbOCA.

It was suggested that training, particularly on how to correctly remove and dispose of contaminated gloves and clothing, would improve individual work practices and reduce workers’ exposure to MbOCA. Employers must select suitable impervious gloves for MbOCA work and provide adequate supervision to reduce exposures for those workers with higher urinary MbOCA results.

The study clearly showed that biological monitoring was an effective tool to monitor the actual exposure of the workers to MbOCA. It showed that some workers exceeded the SafeWork NSW recommended BOEL. This highlights the need for a regular monitoring program that would provide assurance that the controls are continuing to be effective in protecting the workers. Biological monitoring in urine can highlight an individual worker’s personal work practices and is an easy, convenient, non-invasive method to monitor exposure and can be undertaken by the employers to give a cost effective assessment of the exposures in their workplaces.

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Conflicts of Interest: The authors declare that there are no conflicts of interest.

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