

4,4'-METHYLENE BIS(2CHLOROANILINE) [MOCA]

BASELINE HEALTH MONITORING BEFORE STARTING WORK IN A MOCA PROCESS

Workers must be informed of the potential health effects associated with exposure to MOCA. In particular, workers should be made aware of potential for MOCA to be absorbed readily through the skin and the need to maintain a high standard of personal hygiene and housekeeping practices.

1. **Collection of demographic data**
2. **Work history**
3. **Medical history**
4. **Physical examination**

A physical exam will be conducted only if indicated by work and medical history.

5. **Investigation**

The following tests will be used to test the worker's baseline exposure:

- dipstick urinalysis for haematuria
- urine cytology¹ may be required depending on the medical history and previous exposure.

DURING EXPOSURE TO A MOCA PROCESS

6. **Monitoring exposure to MOCA**

The following tests will be conducted twice annually at the time of peak exposure/use:

- urinary total MOCA
- spot creatinine corrected urine for total MOCA
- dipstick urinalysis for haematuria.

Dipstick urinalysis results will be compared with the worker's baseline dipstick urinalysis. Urine cytology will also be conducted annually.

The following values should be considered when assessing exposure to MOCA:

Biological level	Source
15 µmol MOCA/mol creatinine in urine	Workcover NSW Biological Occupational Exposure Limit (BOEL) Committee.
15 µmol MOCA/mol creatinine in urine	Health and Safety Executive (UK) Biological Monitoring Guidance Value (BMGV) ²

-
- 1 See 'Biomarkers of Exposure and Effect' in Section 2- Supplementary Information on MOCA - of this Guideline for further information
 - 2 BMGVs are not health based. They are practicable, achievable levels. A BMGV represents the 90th percentile of biological monitoring results from a representative sample of workplaces with good work hygiene practices. If a result is greater than the BMGV it does not necessarily mean that ill health will occur but does indicate that control of exposure may not be adequate.

Where testing shows a level of 15 μmol MOCA or more per mol of creatinine in urine, this may indicate the worker has been exposed. In these instances:

- repeat tests should be performed at the same time of the day
- a medical examination should be conducted and the medical practitioner supervising the health monitoring should consider removing the worker from MOCA work
- the person conducting a business or undertaking should review control measures and carry out recommended remedial action
- the worker must be informed of the results of the health monitoring.

Other information

Urine samples should be collected at end of a work shift at end of the work week. Samples should be collected in plastic containers and analysed without delay.

Care should be taken to prevent contamination of the urine samples. Samples should be collected in a clean room, following the removal of contaminated clothing and washing the hands.

AT TERMINATION OF WORK IN A MOCA PROCESS

7. Final medical examination

A final medical examination will be conducted and will include:

- urine cytology for haematuria
- dipstick urinalysis
- a medical review of health monitoring records.

8. Continuing medical monitoring

The worker should be reminded of the need for continuing urine cytology and dipstick urinalysis. Where practicable, the person who is conducting a business or undertaking should provide this service and remind workers of its availability.

SUPPLEMENTARY INFORMATION ON MOCA

9. Work activities that may represent a high risk exposure

MOCA is used as a curing agent in the production of hardened isocyanate-based polyurethane products. More specifically, MOCA is utilised in the manufacturing of wear-resistant industrial products like polyurethane gears, gaskets, belts, rollers, sport boots and roller skate wheels. The compound is commonly used as a coating to set other glues, plastics and adhesives.

Examples of work activities involving MOCA which require special attention when assessing exposure include:

- dispensing MOCA powder
- processes where spattering of MOCA in the dry or molten state occurs
- manual moulding of semi-set polyurethane products.

10. Non-work sources

Not known to occur in nature therefore non-work exposure is rare. Exposure has been reported from contact with contaminated soils.

POTENTIAL HEALTH EFFECTS FOLLOWING EXPOSURE TO MOCA

11. Route of entry into the body

Skin absorption is likely to be the main route of entry in to the body and is associated with the following factors:

- poor housekeeping—visible MOCA granules on floors and work benches
- poor personal hygiene practices
- inadequate personal protection.

12. Target organ/effect

Blood – methaemoglobinaemia causing hypoxia and cyanosis.

Respiratory tract – irritation.

Eyes – irritation.

Kidney – haematuria, proteinuria.

Bladder – GHS Carcinogenicity Category 1B (presumed to have carcinogenic potential for humans).

13. Systemic effects

DERMAL/OCULAR EFFECTS

In a case report, a worker complained of burning face and eyes shortly after accidentally been sprayed in the face with molten MOCA [1]. In another case of accidental exposure, a worker described a burning sensation of the skin [2].

RENAL EFFECTS

In the case report [1] described above, protein was detected in the worker's urine within the first five hours after exposure, suggesting damage to the renal tubules had occurred.

In a retrospective bladder cancer incidence study conducted among 532 workers exposed to MOCA from 1968 to 1979 and 20 workers who were first employed in 1980 and 1981, 385 participated in a urine screening test [3]. Exfoliative cytology revealed 21 urine samples contained atypical cells. No cytology readings were positive for cancer. Sixteen urine samples were positive for haeme. In the course of the screening, one of the participants who had negative cytology and was negative for the presence of haeme in urine was diagnosed with a tumour of the urinary bladder.

14. Carcinogenicity

MOCA is an aromatic amine which is structurally similar to benzidine, a known human bladder carcinogen. MOCA has been shown to cause hepatomas in mice and rats, lung and mammary carcinomas in rats and bladder cancer in dogs [4,5,6].

A case study has described bladder cancer in two non-smoking males, under the age of 30, who were exposed to MOCA during its manufacture [7]. This is the only report of humans with a history of MOCA exposure developing bladder cancer.

15. Carcinogen classification³

MOCA is classified according to the GHS as Carcinogen Category 1B (May cause cancer).

16. Biomarkers of exposure and effect

EXPOSURE

The best currently available indicator of absorption of MOCA is urinary total MOCA estimations based on spot creatinine corrected urines. Although this method is not without limitations, that is unmetabolised MOCA is measured and dose-response curves are lacking, its use is a reasonable means of monitoring the effectiveness of engineering controls, personal protective equipment and work practices including education. This has been demonstrated in Western Australia where urinary monitoring showed a decrease in MOCA levels after educating the workforce on safe-handling practices of MOCA [8].

MOCA levels are usually higher at the end of the shift and reflect exposure over the preceding two to three days. The biological half-life of MOCA in urine is approximately 23 hours [2].

EFFECT

Three techniques have been used to detect bladder cancer: urinalysis for haematuria; urine cytology and cystoscopy. All three methods can be utilised for early detection of the disease. Since 1995, a latex agglutination assay for the qualitative detection of bladder tumour antigen in urine has been available. The antigen is composed of basement membrane complexes that have been isolated and characterised from the urine of patients with bladder cancer. The test, apparently has a high specificity and sensitivity in high risk groups [9,10,11]. However, it has not been trialled as a screening test in a normal population.

Dipstick urinalysis has been reported to have a sensitivity of 91 per cent to 100 per cent for haematuria, variably defined as greater than two to greater than five erythrocytes per high powered field in the sediment of spun urine [12]. Haematuria in an asymptomatic person can be an indication of bladder cancer. In current population based studies, between zero and two per cent of adults with confirmed haematuria have definite significant disease [12]. Therefore, current recommendations are not to screen the general public for haematuria because the risks of the subsequent work-up do not justify screening [10]. However, as pointed out in subsequent correspondence to this observation, individuals in high risk groups should be considered for screening since bladder cancer is potentially treatable if detected at an early stage [13]. It should be noted that haematuria may be intermittent. A person with persistent haematuria requires the cause of the haematuria to be followed up.

Urine cytology has been used as a screening technique for work-related bladder cancer in the U.K. since the 1950's [14]. It is a technique which is easily reproducible when the laboratory personnel are adequately trained in preparation and interpretation of smears. Among fourteen groups of investigators the correlation of positive cytology with clinical findings ranged from 100 per cent to 26 per cent with a mean sensitivity of 71.6 per cent [14]. The false positive rates ranged from 11.3 per cent to 11.9 per cent. In both MOCA exposed bladder cancer cases reported by Ward et al 1988, urine cytology was negative. Urinary cytology screening is felt to be of little value in detecting low-grade papillary neoplasms [15]. However, urine cytology has had a favourable impact on patients whose disease is uncovered by this method with screened cases living 3.6 years longer than unscreened cases [16]. Therefore, screening urine cytology for groups at high risk for bladder cancer may provide early detection of the disease.

■ 3 This classification information is provided on an advisory basis and is taken from the European Union's Annex VI to Regulation (EC) No 1272/2008, updated by the 1st Adaption to Technical Progress to the Regulation. Other hazard classes and categories may apply - see <http://esis.jrc.ec.europa.eu/index.php?PGM=cla>. These classifications are legally binding within the European Union.

4,4'-METHYLENE BIS(2-CHLOROANILINE) [MOCA]

Finally, cystoscopy is another method which may be employed for bladder cancer screening. Cystoscopy is an invasive procedure which allows visualisation of the urinary bladder along with the ability to perform biopsies. However, this procedure lends itself to significant risk including the risks of anaesthesia. Therefore, cystoscopy will not be utilised as a screening procedure. The general population would reject having this test performed on a routine basis. However, if urinalysis for haematuria or urine cytology indicate a result where bladder cancer is considered then cystoscopy should be utilised to confirm the diagnosis.

Urinary measurement of total MOCA and the urinary bladder cancer detection technique of urinalysis for haematuria are the methods best suited for health monitoring of MOCA. Urine cytology, the antigen test and cystoscopy are useful as case management tools but not as routine screening tests. Cystoscopy has too many risks to consider as a mass screening procedure.

REFERENCED DOCUMENTS

1. Hossein HR and Van Roosmalen PB, 'Acute Exposure to Methylene-bis-ortho chloroaniline (MOCA)', *American Industrial Hygiene Association Journal*, vol 39(6), pp 496-497, 1978.
2. Osorio AM, Clapp D, Ward, E, Wilson HK and Cocker J, 'Biological Monitoring of a Worker Acutely Exposed to MBOCA', *American Journal of Industrial Medicine*, vol 18(5), pp 577-589, 1990.
3. Ward E, Halperin W, Thun, M, Grossman HB, Funk B, Koss L, Osorio AN and Schulte P, 'Screening Workers Exposed to 4,4'-Methylene-(2-chloroaniline) for Bladder Cancer by Cystoscopy. In: International Conference on Bladder Cancer Screening in High-Risk Groups, September 13-14, 1989', *Journal of Occupational Medicine*, vol 32(9), pp 865-868, 1990.
4. Russfield AG, Homburger F, Boger E, Van Dongen CG, Weisburger EK and Weisburger JH, 'The Carcinogenic Effect of 4,4' - Methylene bis (2 - chloroaniline) in Mice and Rats', *Toxicology and Applied Pharmacology*, vol 31, pp 47-54, 1975.
5. Stula EF, Barnes JR, Sherman H, Reinhardt CF and Zapp JA, 'Urinary Bladder Tumors in Dogs from 4,4' - Methylene bis (2 - chloroaniline)', *Journal of Environmental Pathology and Toxicology*, vol 1, pp 31-50, 1977.
6. Ward E, Blair Smith A and Halperin W, '4,4' - Methylene bis (2 - chloroaniline): An Unregulated Carcinogen', *American Journal of Industrial Medicine*, vol 12, pp 537-549, 1987.
7. Ward E, Halperin W, Thun M, Grossman HB, Fink B, Koss L, Osorio AM and Schulte P, 'Bladder Tumours in Two Young Males Occupationally Exposed to MOCA', *American Journal of Industrial Medicine*, vol 14, pp 267-72, 1988.
8. Wan KC, Dare BR, Street NR, 'Biomedical Surveillance of Workers Exposed to 4,4' Methylene-bis-(2-chloroaniline)(MBOCA) in Perth, Western Australia', *Journal of the Royal Society for the Promotion of Health*, vol 109(5), pp 159-165, 1989.
9. Sarodsy MF, deVere White RW, Soloway MS, Sheinfeld J, Hudson MA, Schellhammer PF, Jarowenko MV, Adams G and Blumenstein BA, 'Results of a Multicenter Trial using the BTA Test to Monitor for and Diagnose Recurrent Bladder Cancer', *The Journal of Urology*, vol 154, pp 379-384, 1995.
10. D'Hallewin M-A and Baert, L, 'Initial Evaluation of the Bladder Tumour Antigen Test in Superficial Bladder Cancer', *The Journal of Urology*, vol 155, pp 475-476, 1996.
11. Leyh H, Mazeman E, Hall RR, and Bennett AH, 'Results of a European Multicenter Trial Comparing the BARD BTA Test to Urine Cytology in Patients Suspected of having Bladder Cancer', *The Journal of Urology*, vol 155, pp 492A, 1996.

4,4'-METHYLENE BIS(2-CHLOROANILINE) [MOCA]

12. Woolhandler S, Pels RJ, Bor DH, Himmelstein DU and Lawrence RS, 'Dipstick Urinalysis Screening of Asymptomatic Adults for Urinary Tract Disorders, I. Haematuria and Proteinuria', *Journal of the American Medical Association*, vol 262(9), pp 1214-1219, 1989.
13. Modest G, 'Letters-Screening for Haematuria', *Journal of the American Medical Association*, vol 263(13), pp 1763-1764, 1990.
14. Jacobs R, 'A Review of the Effectiveness of Urinary Cytology as a Screening Technique for Occupational Bladder Cancer', *Journal of the Society of Occupational Medicine*, vol 37, pp 24-26, 1987.
15. Koss LG, Deitch D, Ramanathan R, Sherman AB, 'Diagnostic Value of Cytology of Voided Urine', *Acta Cytologica*, vol 29, pp :810-816, 1985.
16. Schulte PA, Ringen K, Hemstreet GP and Ward E, 'Occupational Cancer of Urinary Tract', Chapter 7, pp 85-107, in *Occupational Cancer and Carcinogenesis*, Brandt-Rauf PW (ed), vol 2(1), 1987, in the series Occupational Medicine: State of Arts Reviews , Hanley and Belfus Inc., Philadelphia.

FURTHER READING

American Conference of Governmental Industrial Hygienists (ACGIH), *Documentation of the Biological Exposure Indices*, 7th Ed, Cincinnati, 2011.

American Conference of Governmental Industrial Hygienists (ACGIH), *Documentation of the Threshold Limit Values for Chemical Substances*, 7th Ed, Cincinnati, 2011.

Cocker J, Boobis AR, Wilson HK and Gompertz D, 'Evidence that a β -N-Glucuronide of 4,4'-Methylenebis (2-chloroaniline) (MbOCA) is a Major Urinary Metabolite in Man: Implications for Biological Monitoring', *British Journal of Industrial Medicine*, vol 47, pp 154-161, 1990.

International Agency for Research on Cancer, *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Volume 57: Occupational Exposures of Hairdressers and Barbers and Personal Use of Hair Colourants, Some Hair Dyes, Cosmetic Colourants, Industrial Dye Stuffs and Aromatic Amines*, International Agency for Research on Cancer, Lyon, 1993.

Schulte PA, Ringen K and Hemstreet GP, 'Optimal Management of Asymptomatic Workers at High Risk of Bladder Cancer', *Journal of Occupational Medicine*, vol 28(1), pp 13-17, 1986.

Ward E, Clapp D, Tolos W and Groth D, 'Efficacy of Urinary Monitoring for 4,4'-Methylenebis (2-Chloroaniline)', *Journal of Occupational Medicine*, vol 28(8), pp 637-642, 1986.

WorkCover NSW, *Work Involving the Use of MOCA (4,4'- Methylene Bis (2-Chloroaniline))*, WorkCover NSW Health and Safety Guide, July 2003. http://www.workcover.nsw.gov.au/formspublications/publications/Documents/work_involving_use_moca_4_4_methylene_bis_2_chloroaniline_1283.pdf

HEALTH MONITORING REPORT 4,4'-METHYLENE BIS(2-CHLOROANILINE) [MOCA]

This health monitoring report is a **confidential** health record and must not be disclosed to another person except in accordance with the Work Health and Safety Regulations or with the consent of the worker.

There are two sections. Complete both sections and all questions if applicable.

Section 1 is to be forwarded to the PCBU who has engaged your services. A copy of laboratory report(s) must be attached > > >

Section 2 may contain confidential information which may not be relevant to the health monitoring program being carried out. This section should be retained by the medical practitioner. Information which is required to be given to the PCBU should be summarised in part 7 of section 1.

SECTION 1 - THIS SECTION TO BE RETURNED TO THE PCBU			
1. PERSON CONDUCTING A BUSINESS OR UNDERTAKING			
Company / Organisation name:			
Site address:			
Suburb:			Postcode:
Site Tel:	Site Fax:	Contact Name:	
2. OTHER BUSINESSES OR UNDERTAKINGS ENGAGING THE WORKER			
Company / Organisation name:			
Site address:			
Suburb:			Postcode:
Site Tel:	Site Fax:	Contact Name:	
3. WORKER (✓) all relevant boxes			
Surname:		Given names:	
Date of birth: DD/MM/YYYY	Sex:	<input type="checkbox"/> Male	<input type="checkbox"/> Female
Address:			
Suburb:			Postcode:
Current Job:	Tel(H):	Mob:	
Date started employment : DD/MM/YYYY			
4. EMPLOYMENT IN MOCA RISK WORK (✓) all relevant boxes			
1. <input type="checkbox"/> New to MOCA work			
2. <input type="checkbox"/> New worker but not new to MOCA work			
3. <input type="checkbox"/> Current worker continuing in MOCA work			
4. Worked with MOCA since DD/MM/YYYY			
5. Satisfactory personal hygiene (for example nail biting, frequency of hand washing)			<input type="checkbox"/> Yes <input type="checkbox"/> No
6. Risk assessment completed			<input type="checkbox"/> Yes <input type="checkbox"/> No

HEALTH MONITORING REPORT 4,4'-METHYLENE BIS(2-CHLOROANILINE) [MOCA]

5. WORK ENVIRONMENT ASSESSMENT		(✓) all relevant boxes
Date of assessment: DD/MM/YYYY		
MOCA Industry		
<input type="checkbox"/> Polyurethane Production <input type="checkbox"/> Other (specify):	Controls: Wear gloves <input type="checkbox"/> Yes <input type="checkbox"/> No Respirator use <input type="checkbox"/> Yes <input type="checkbox"/> No Process enclosed <input type="checkbox"/> Yes <input type="checkbox"/> No Worker isolated from exposure <input type="checkbox"/> Yes <input type="checkbox"/> No Local exhaust ventilation <input type="checkbox"/> Yes <input type="checkbox"/> No Overalls / work clothing <input type="checkbox"/> Yes <input type="checkbox"/> No Laundering by employer <input type="checkbox"/> Yes <input type="checkbox"/> No Wash basins & showers (with hot & cold water) <input type="checkbox"/> Yes <input type="checkbox"/> No Smoking or eating in workshop <input type="checkbox"/> Yes <input type="checkbox"/> No	
	Personal hygiene: Clean Shaven <input type="checkbox"/> Yes <input type="checkbox"/> No Shower & change into clean clothes at end of shift <input type="checkbox"/> Yes <input type="checkbox"/> No	
6. BIOLOGICAL MONITORING RESULTS Include at least the previous two test results (if available)		
Date	Tests performed	Recommended Action and/or Comment
1. DD/MM/YYYY		
2. DD/MM/YYYY		
3. DD/MM/YYYY		
4. DD/MM/YYYY		
5. DD/MM/YYYY		
6. DD/MM/YYYY		
7. DD/MM/YYYY		

HEALTH MONITORING REPORT 4,4'-METHYLENE BIS(2-CHLOROANILINE) [MOCA]

7. RECOMMENDATIONS (by Medical Practitioner)		(✓) all relevant boxes
1.	<input type="checkbox"/> Suitable for work with MOCA	
2.	<input type="checkbox"/> Counselling required	
3.	<input type="checkbox"/> Review workplace controls	
4.	<input type="checkbox"/> Repeat health assessment in _____ month(s) / _____ week(s)	
5.	<input type="checkbox"/> Removal from work with MOCA	On DD/MM/YYYY
6.	<input type="checkbox"/> Medical examination by Medical Practitioner	On DD/MM/YYYY
7.	<input type="checkbox"/> Fit to resume MOCA risk work	From DD/MM/YYYY
8.	<input type="checkbox"/> Referred to Medical Specialist (respiratory/dermatology/other): On DD/MM/YYYY	
Specialist's name:		
Additional comments or recommendations arising from health monitoring:		
Medical Practitioner (responsible for supervising health monitoring)		
Name:	Signature	Date: DD/MM/YYYY
Tel:	Fax:	Registration Number:
Medical Practice:		
Address:		
Suburb:	Postcode:	

HEALTH MONITORING REPORT 4,4'-METHYLENE BIS(2-CHLOROANILINE) [MOCA]

SECTION 2 - THIS SECTION TO BE RETAINED BY THE MEDICAL PRACTITIONER			
1. PERSON CONDUCTING A BUSINESS OR UNDERTAKING			
Company / Organisation name:			
Site address:			
Suburb:			Postcode:
Site Tel:	Site Fax:	Contact Name:	
2. OTHER BUSINESSES OR UNDERTAKINGS ENGAGING THE WORKER			
Company / Organisation name:			
Site address:			
Suburb:			Postcode:
Site Tel:	Site Fax:	Contact Name:	
3. WORKER (✓) all relevant boxes			
Surname:		Given names:	
Date of birth: DD/MM/YYYY	Sex:	<input type="checkbox"/> Male	<input type="checkbox"/> Female
		<input type="checkbox"/> Pregnant/Breast Feeding?	
Address:			
Suburb:			Postcode:
Current Job:	Tel(H):	Mob:	
Date started employment : DD/MM/YYYY			
4. GENERAL HEALTH ASSESSMENT (if applicable)			
Symptoms of:	Comments	Further testing?	
Skin disorders		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Headaches, dizziness		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Respiratory tract		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Eyes		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Cough		<input type="checkbox"/> Yes	<input type="checkbox"/> No
CNS		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Haematuria/proteinuria		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Hypoxia/cyanosis		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Others		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Height ____cm			
Weight ____kg			
Bp ____/____ mmHg		<input type="checkbox"/> Yes	<input type="checkbox"/> No

HEALTH MONITORING REPORT 4,4'-METHYLENE BIS(2-CHLOROANILINE) [MOCA]

5. OTHER MEDICAL HISTORY, FAMILY MEDICAL HISTORY, CURRENT MEDICATION, COMMENTS, TESTS OR RECOMMENDATIONS (use separate sheet if necessary)			
Medical Practitioner (responsible for supervising health monitoring)			
Name:		Signature	Date: DD/MM/YYYY
Tel:	Fax:	Registration Number:	
Medical Practice:			
Address:			
Suburb:		Postcode:	