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HEALTH & SAFETY LABORATORY

Survey findings from a national survey of MbOCA exposure

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EXECUTIVE SUMMARY

Objectives

The report analyses the data collected from urine, air, surface and glove samples taken from 18 companies using and 2 companies distributing the chemical 2,2'-Dichloro-4,4' methylene dianiline (MbOCA).

The statistical analysis aimed to summarise the data and to assess for consistency of results across comparable companies and comparable jobs and to investigate the relationships between MbOCA in urine, air, surface and glove samples and the relationship between MbOCA and isocyanate metabolites in urine samples.

Main Findings

The statistical analysis found that

- The concentrations of MbOCA in urine were generally below the biological monitoring Benchmark Guidance Value (BMGV).
- The data suggested that the companies using automated processes had similar results (in terms of MbOCA in urine) to companies using purely manual processes. However, the comparison was based upon few data.
- The concentrations of MbOCA in air were very small and well below the Workplace Exposure Limit (WEL).
- Wrapped drums and pallets at the two distributing companies were contaminated with MbOCA. One of the two distributing companies had greater levels of contamination than the other.
- Of the 71 samples tested for isocyanate metabolites, 22 distinct samples were above the isocyanate BMGV with 3 samples containing traces above the BMGV for two isocyanates. The largest concentration was over 15 times larger than the BMGV.
- The concentrations of MbOCA and isocyanate metabolites in urine appeared to be correlated.
- Samples taken from subjects who were selected as controls, i.e. without direct exposure to MbOCA or isocyanates, contained traces of both substances in urine, which may be an indication of poor control.
- A relationship between MbOCA on gloves in urine was found however the nature of the relationship needs further investigation.

Recommendations

The data suggest that current BMGV for MbOCA in urine of 15 μmol/mol creatinine should be reduced. The data from the current study suggest that a conservative estimate of the 90th percentile of urine data would be10 μmol/mol creatinine.

A further investigation of the relationship between the concentrations of MbOCA in urine and MbOCA on gloves samples would be of interest in order to fully determine the extent of the relationship.

1 INTRODUCTION

MbOCA (chemical name 2,2'-Dichloro-4,4' methylene dianiline or alternatively methylene bis (2-Chloroaniline)) is a substance that is commonly used in the polyurethane industry alongside isocyanates. MbOCA is a suspect human carcinogen. Isocyanates are a significant cause of occupational asthma and Chronic Obstructive Pulmonary Disease (COPD).

Both MbOCA and isocyanates are among a list of hazardous substances that have Biological Monitoring Guidance Values (BMGV). The BMGVs for both MbOCA and Isocyanates are not health based but practicable achievable levels for workplace exposure set at the 90th percentile of available biological monitoring results collected from a representative sample of workplaces with good occupational hygiene practices.

Current guidelines are:

Substance	Workplace Exposure Limit (WEL) (in air) (8h TWA)	BMGV (in urine)
MbOCA	0.005 mg m^{-3}	15 μmol/mol creatinine
Isocyanates	0.02 mg m^{-3}	1 μmol/mol creatinine

There are currently no exposure limits for surfaces or gloves, although if relationships between these and air and/or urine MbOCA levels were identified it might be possible to establish appropriate guidance values.

This report presents a statistical analysis of the results obtained from measurement of MbOCA in urine, air, glove and surface measurements and on measurements of isocyanate metabolites in urine. Samples were collected by HSL's occupational hygienists from 20 companies in the polyurethane industry, comprised of 18 users and 2 suppliers. Data were expected from 22 companies however 2 users supplied no samples.

1.1 AIMS

The specific aims of the statistical analysis were

- An exploratory analysis of the MbOCA data collected from urine, air, surface and glove samples.
- Assess for differences in concentrations between different jobs and different companies.
- Investigate the relationship between MbOCA in air and urine samples.
- Investigate the relationship between surface and glove concentrations.
- Investigate the relationship between MbOCA concentrations on inner and outer gloves.
- Calculate the 90th percentile of the MbOCA in urine concentrations and to evaluate the evidence for a revision of the BMGV.

- Investigate relationships between MbOCA concentrations in surface and glove samples and MbOCA in air and urine samples.

- To assess whether companies using automated processes had different concentrations of MbOCA than the companies using purely manual processes.

- Investigate the concentrations of MbOCA on drums held in storage at two companies in the sample who distributed MbOCA and to assess if these differed from concentrations on drums in storage at the manufacturing companies.

- To investigate the isocyanate concentrations in urine and the relationships between isocyanate concentrations and jobs and isocyanate concentrations and MbOCA concentrations in urine.

2 METHOLODOLOGY

2.1 ANALYSIS OF MBOCA AND ISOCYANATES

Urine samples were analysed for MbOCA (and its labile conjugates) and isocyanate metabolites using methodology described in detail in Cocker *et al.*(1996) and Williams *et al* (1999). Air, surface and glove samples were analysed for MbOCA; the filters from the air samples, the surface wipes and the glove samples were dissolved in a solvent (acetonitrile) and then analysed using either Liquid or Gas Chromatography.

2.1.1 Limits of Detection

The limits of detection (LOD) for urine analysis were 0.5 μmol/mol creatinine and 0.1 μmol/mol creatinine (assuming a typical creatinine level of 9 μmol/l) for MbOCA and isocyanate metabolites respectively. The LOD for MbOCA using Liquid Chromatography was

Air	-	1 μg m^{-3} for a 200-litre sample
Surfaces	-	5 μg/sample for 22ml desorption volume
Gloves	-	80 μg/sample for a 400 ml desorption volume

The LOD for some of the samples, analysed using the more sensitive Gas Chromatography method was approximately 10 fold lower than those quoted above. The LOD on surface and glove concentrations was influenced by the desorption volume so the differing quantities of solvent used to dissolve the sample resulted in differing limits of detection.

2.2 DATA CLEANING

Prior to statistical analysis some amendments were to be made to the data by analysts at HSL. All readings denoted as ND (Non Detected) or less than LOD in the urine, air, surfaces and gloves data were re-coded as Non Detected. Some of the air, surface and glove concentrations were corrected since the units of measurement were erroneous, after consultation with relevant experts from HSL. The measurements from air, surfaces and glove samples were all converted to milligrams prior to analysis.

2.3 DERIVATION OF VARIABLES

In order to thoroughly analyse the data from urine, air, surface and glove samples and to achieve the aims of the study, the descriptions about the samples, recorded by the on site occupational hygienists, were used to derive variables.

2.3.1 Urine

All workers were categorised as Directly Exposed or Controls. Directly exposed workers were working in the manufacturing environment whereas controls were working within the same building but in jobs (such as office based work) where they should not be exposed to MbOCA. Those workers thought to be directly exposed were further sub-classified into 7 groups based upon different types of possible exposure; Handling/Scooping, Weighing/Melting/Mixing, Casting, Moulding, Maintenance, Other (Non-specific) exposure and all parts of the process. These categories denote the main type of work undertaken by workers as recorded by the HSE inspectors on site although it is likely that many workers were involved in all parts of the process.

2.3.2 Air

The air samples were categorised into personal and static samples. The static samples were classified into those taken from Directly Exposed and control areas of the workplace. The controls samples were taken from areas such as offices and canteens. The exploratory analysis of the data showed that MbOCA was detected in air in few samples and a further sub-classification into workplace areas was not necessary.

2.3.3 Surfaces

Surface samples were classified into those taken from Directly Exposed and control surfaces. The control samples were taken from surfaces in areas such as canteens, offices and toilets. The directly exposed areas were sub-classified, based on the description of the sample, into Fume cupboard/Degassing, Storage, Weighing/Pouring, Mixing, Ovens, Hopper, Casting and Other (non-specific).

2.3.4 Gloves

Glove samples were classified, where possible, as inner or outer glove samples. When the description of the sample did not specify inner/outer explicitly the sample was taken to be an outer glove when the concentration of MbOCA on the sample was in excess of 1 mg. When the sample concentration was less than 1 mg no classification was made.

2.4 STATISTICAL METHODOLOGY

The data on each of the measurements had a mixed categorical/continuous form. Resultantly, a two-phased statistical approach was used to analyse the data. The first of these involved recoding all continuous data to the categorical value of greater than LOD and analysing the data using statistical methods for ordered categorical data. The second method concentrated on the continuous data only, those samples where a concentration was recorded and more sophisticated numerical analyses were used on this subset.

Fishers exact test was used in order to test for association between categorical variables; the test is the exact test for associations in contingency tables and is often approximated by the chi-squared test. For the continuous data correlations were calculated using Kendall's tau, a non-parametric test of correlation based on data that is ranked in order of magnitude. The Mann-Whitney U test, the non-parametric equivalent of a two-sample t-test, was used in order to test for a difference in median between two subsets and the Kruskall-Wallis test, the non-parametric equivalent of a one way Analysis of Variance (ANOVA), was used to test for a difference in medians when more than two subsets were being compared.

2.4.1 Data Sensitivity

Prior to statistical analysis the 20 companies where data were available were each allocated a letter A – U. Due to commercial sensitivity, when the results from different companies have been compared the companies have been referred to by letter rather than by name. A list mapping letters to companies is provided in a separate document for the use of the HSE authorising officer.

3 SURVEY RESULTS

The statistical analysis is presented in four sections each focusing on the locations where samples were made.

3.1 URINE SAMPLES

A total of 78 urine samples were taken from workers at 19 companies although no urine samples were taken from one of the companies using MbOCA (company S). All the samples were tested to determine the concentration of MbOCA in the urine and 71 samples (from 17 of the companies) were also tested to determine isocyanates concentrations. Approximately 75% (n=59) of the samples were taken from workers who could be classified as directly exposed (i.e. involved in at least one aspect of the manufacturing process) and the remainder (n=19) were controls who were not involved in any part of the manufacturing process, but who may have been exposed to MbOCA if best practice was not followed.

3.1.1 MbOCA in Urine

Table 1 reports the frequency of urine samples in which the sample was recorded as ND or greater than LOD (in excess of 0.5 μmol/mol creatinine). In addition the frequency of samples that were in excess of the present BMGV of 15 μmol/mol creatinine is reported. Note the percentages in the first two columns sum to 100, the cases where the readings were in excess of 15 μmol/mol creatinine are a subset of those greater than LOD.

Table 1: **Frequencies for MbOCA concentration in urine**

MbOCA concentrations in urine		
ND	> LOD	> BMGV
38	40	3
(49%)	(51%)	(4%)

As can be seen from Table 1 a little over half (51%) of the samples analysed had a level of MbOCA that was above the limit of detection. The rest of the samples had levels within the range of 0 – 0.5 μmol/mol (49%). Of all the samples only 4% (n = 3) were above the BMGV whereas by the definition of the BMGV 10% of samples might be expected to above this value if controls had not improved since the BMGV was set in 1996.

A numerical analysis of the 40 samples where the MbOCA concentrations were above the limit of detection was conducted with some summary statistics presented in Table 2. The analysis showed a large range of concentrations (1.33 to 24.99 μmol/mol creatinine) with a respective arithmetic mean and median of 6.597 and 4.27 μmol/mol creatinine. The readings were positively skewed with statistical tests indicating that the data could be approximated by a log normal distribution, that is the majority of readings were concentrated around the lower end of the range; the large differences between the arithmetic and geometric means and arithmetic and geometric standard deviations reflect this feature of the data. Two readings were well in excess of the current BMGV (24.4 and 24.99 μmol/mol creatinine respectively).

Table 2: **Summary statistics of MbOCA concentration in urine**

MbOCA concentrations in urine							
n	Max	Min	Median	Arithmetic mean	Arithmetic standard deviation	Geometric mean	Geometric Standard deviation
40	24.99	1.33	4.27	6.597	5.73	4.965	2.092

3.1.1.1 Analysis by Exposure

Table 3 reports the frequency of urine samples in which the sample was recorded as ND or greater than LOD and the frequency of samples that were in excess of the BMGV for the groups of workers classified as directly exposed to MbOCA and controls. For each of the two groups the percentages in the first two columns reported in Table 3 sum to 100, the cases where the MbOCA concentration was in excess of the BMGV are a subset of those greater than LOD.

Table 3: **Frequencies for MbOCA concentration in urine by exposure**

	MbOCA concentrations in urine		
Exposure	ND	> LOD	> BMGV
Control	15 (79%)	4 (21%)	- -
Directly exposed	23 (39%)	36 (61%)	3 (5%)

It can be seen from Table 3 that there were noticeable differences between the directly exposed workers and the controls with the former more likely to have a urine reading above the limit of detection. Only 21% of the controls had levels in their urine greater than the limit of detection whereas 61% of those directly exposed to MbOCA had a detectable concentration. Workers directly exposed were statistically more likely to have a measurable concentration of MbOCA in urine ($p=0.003$). In addition, as can be seen from Table 3, all of the urine samples exceeding the BMGV could be identified as originating from those working in directly exposed jobs. However, despite the obvious differences between the two groups it is surprising that 21% of the controls had a detectable concentration of MbOCA in their urine and may be an indication that best practice was not followed.

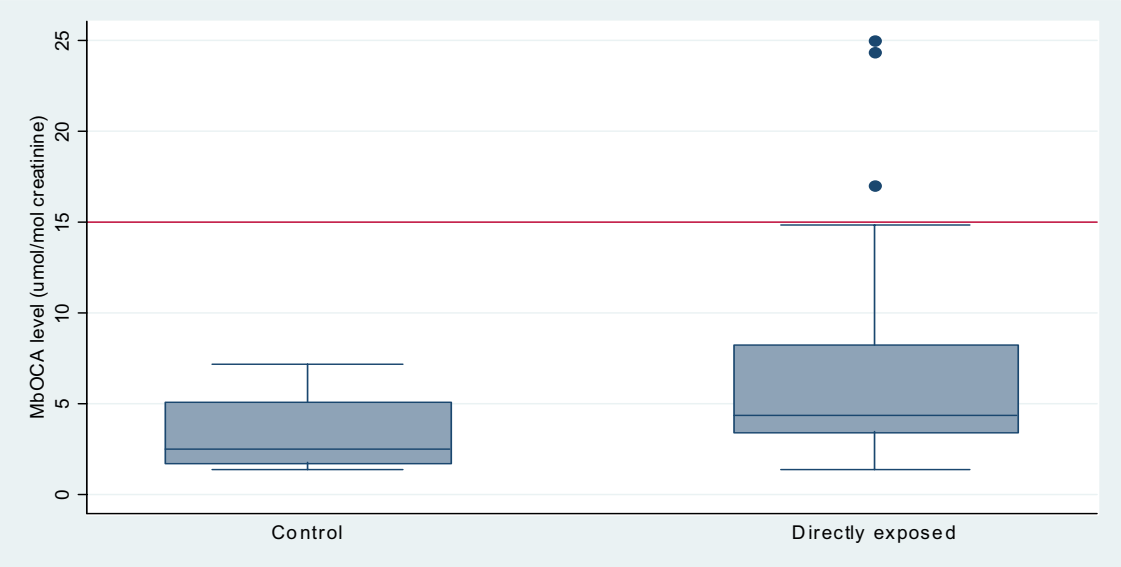
A numerical analysis of the subset of 40 samples where the MbOCA concentration was above the limit of detection was also performed, with some summary statistics presented in Table 4.

Table 4: **Summary statistics of MbOCA concentration in Urine by exposure**

MbOCA concentrations in urine								
Exposure	n	Max	Min	Median	Arithmetic mean	Arithmetic standard deviation	Geometric mean	Geometric Standard deviation
Control	4	7.17	1.33	2.535	3.3925	2.60	2.781	2.033
Directly exposed	36	24.99	1.35	4.33	6.95	5.896	5.291	2.058

Figure 1 shows Boxplots of MbOCA levels in urine for the controls and directly exposed workers. Also shown in Figure 1 is the BMGV for MbOCA. A detailed note on how to interpret a boxplot is included in appendices.

Figure 1: **MbOCA concentrations in urine by exposure**



Both the summary statistics presented in Table 4 and Figure 1 clearly show concentrations of MbOCA were higher in the directly exposed group. The median concentrations were 4.33 and 2.35µmol/mol creatinine for the directly exposed and control groups respectively and the arithmetic mean concentrations were 3.39 and 6.95 µmol/mol creatinine respectively. The range of MbOCA concentrations was much larger for the directly exposed workers than the controls, (1.35, 24.99) compared with (1.33, 7.17) µmol/mol creatinine. For both groups the distributions of MbOCA concentrations were positively skewed. The urine samples exceeding the BMGV are shown as the dots above the red line, which the statistical analysis indicated as outlying (unusually large) observations.

Workers directly exposed had significantly higher levels of MbOCA in their urine than controls ($p=0.039$). Although the controls had lower concentrations of MbOCA in urine, the magnitude of the concentrations was surprisingly large with a largest recorded concentration for a control of 7.17 µmol/mol creatinine, which was just below a half of the current BMGV.

3.1.1.2 Analysis by job

As previously described in section 2.3.1, the exposed workers were sub-classified using information about the worker into seven groups which were chosen to reflect the different stages of the manufacturing process and hence potential differences in exposure to MbOCA. These were: Handling; Weighing/Melting/Mixing; Casting; Moulding; Maintenance; Other non-specific exposure and all parts of the process. As discussed in 2.3.1 most workers would be involved in more than one stage of the process so these categories describe the main type of exposure at the time of the inspection.

Table 5 below reports the frequency of urine samples in which the sample was classified as ND or greater than LOD and the frequency in which the BMGV of 15 μmol/mol creatinine was exceeded for the seven classes of exposed workers. For each row in Table 5 the percentages in the first two columns sum to 100.

Table 5: **Frequencies for MbOCA concentrations in urine by job type**

	MbOCA concentrations in urine		
Job Classification	ND	> LOD	> BMGV
Handling & Scooping	5 (100%)	- -	- -
Weighing, Mixing & Melting	4 (50%)	4 (50%)	- -
Casting	- -	3 (100%)	1 (33%)
Moulding	1 (8%)	12 (92%)	1 (8%)
Maintenance	1 (33%)	2 (67%)	- -
Other exposure	6 (86%)	1 (14%)	- -
All parts of the process	6 (30%)	14 (70%)	1 -

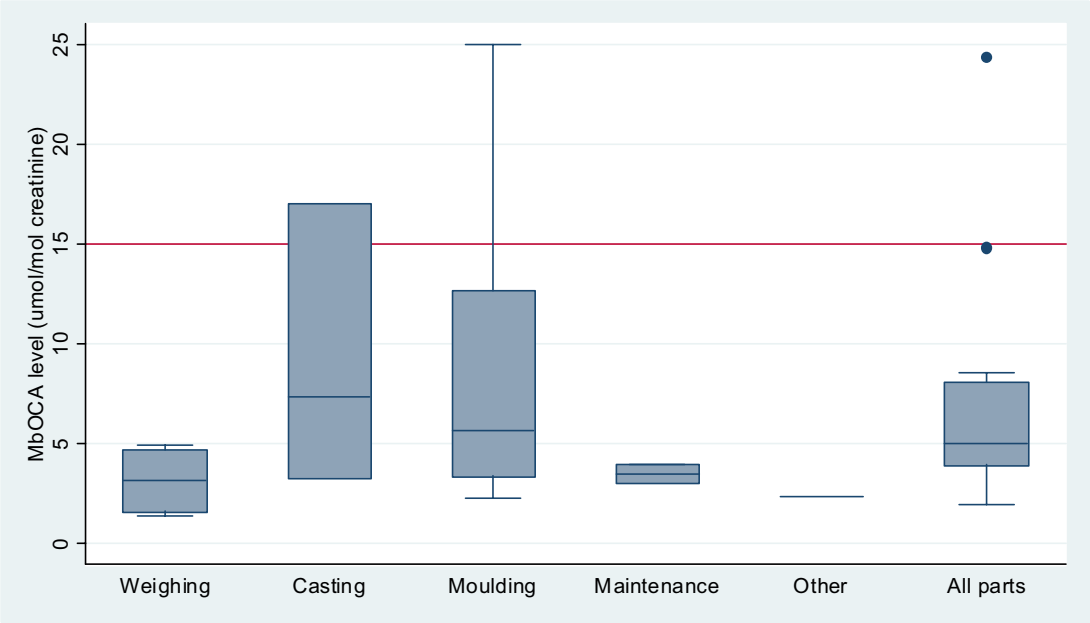
It can be seen from Table 5 there were differences between the job classifications in the proportions of workers where MbOCA was above the LOD, with it detectable in the samples from almost all those involved in Casting and Moulding whereas those involved in Handling or Other non-specific exposure often had a concentration below the LOD. A significant association between job classification and MbOCA levels in urine was found ($p = 0.002$).

A numerical analysis of the 36 samples where the MbOCA concentration was above the limit of detection was also performed. Table 6 shows some summary statistics[1] for the different job categories and Figure 2 shows Boxplots of MbOCA levels in urine for each of the job classifications and an indication of the BMGV for MbOCA in urine.

Table 6: **Summary statistics of MbOCA concentrations in urine by job**

	MbOCA concentrations in urine							
Job	n	Max	Min	Median	Arithmetic mean	Arithmetic standard deviation	Geometric mean	Geometric Standard deviation
Handling	-	-	-	-	-	-	-	-
Weighing	4	4.92	1.35	3.155	3.145	1.763	2.74	1.872
Casting	*3*	*17.01*	*3.3*	*7.35*	*9.22*	*7.04*	*7.44*	*2.27*
Moulding	*12*	*24.99*	*2.23*	*5.67*	*8.34*	*6.84*	*6.265*	*2.19*
Maintenance	2	3.92	3.07	3.495	3.495	0.60	3.469	1.18
Other	1	2.37	2.37	2.37	2.37	-	2.37	-
All parts	*14*	*24.2*	*1.91*	*4.965*	*7.185*	*5.88*	*5.787*	*1.896*

Figure 2: **MbOCA concentrations in urine by job classification**



[1] *Whilst summary statistics are given for all job categories for completeness, the arithmetic and geometric standard deviations should be viewed with caution given the small samples in some of the categories (n < 5).*

As can be seen from Figure 2, the results showed a contrast between the groups "All parts of the process", "Casting" and "Moulding" (highlighted in Table 6 as the categories in italics) and a second group "Maintenance", "Weighing/Melting & Mixing " and "Other exposed". The former of these groups had higher median and more variable concentrations. The second group showed low variability (although the sample sizes were small in all three groups and the measures of variability were sensitive) with all concentrations well the BMGV for MbOCA. "All parts of the process", "Casting" and "Moulding" all had one sample which was above the current BMGV. A formal statistical test of equality in the medians was performed but did not show significant differences between concentrations in the different jobs. The samples were very small however and resultantly the power of the test was low.

3.1.1.3 Analysis by company

As previously described, the urine samples in this survey came from 17 companies who used MbOCA directly within their premises and 2 companies who distributed it. From the information regarding job classification previously described in section 3.1.1.2 it was possible to group five companies together where the directly exposed workers that were sampled carried out "all parts of the process". In addition it was possible to group another four companies where the directly exposed workers that were sampled were mainly carrying out the "Moulding" part of the process. Summary statistics of the readings greater than the LOD are given in Table 7 and the data are displayed in Figures 3 "All parts of the process" and 4 "Moulding". Also shown in Figures 3 and 4 is the BMGV for MbOCA.

Table 7: **Summary statistics of MbOCA concentrations in urine by company**

	MbOCA concentrations in urine							
Company	n	Max	Min	Median	Arithmetic mean	Arithmetic standard deviation	Geometric mean	Geometric Standard deviation
All Parts								
G	4	14.86	2.14	7.685	8.0925	5.223	6.58	2.25
H	2	5.64	1.91	3.775	3.775	2.638	3.281	2.15
I	3	5.7	4.25	4.29	4.75	0.826	4.70	1.18
J	-	-	-	-	-	-	-	-
U	2	24.4	3.65	14.025	14.025	14.67	9.44	3.832
Moulding								
M	4	11.59	2.23	2.995	4.95	4.44	3.90	2.09
N	6	14.8	2.33	4.44	6.03	4.51	5.027	1.87
P	1	24.99	24.99	24.99	24.99	-	24.99	-
Q	3	13.66	7.17	8.4	9.74	3.45	9.36	1.40

Figure 3: MbOCA concentrations in urine by selected companies

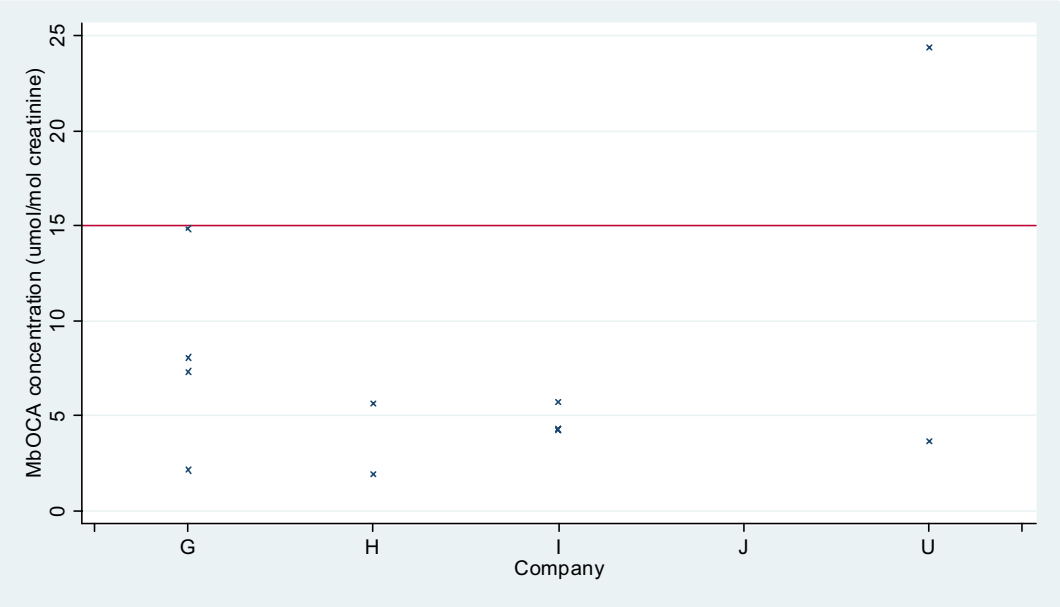
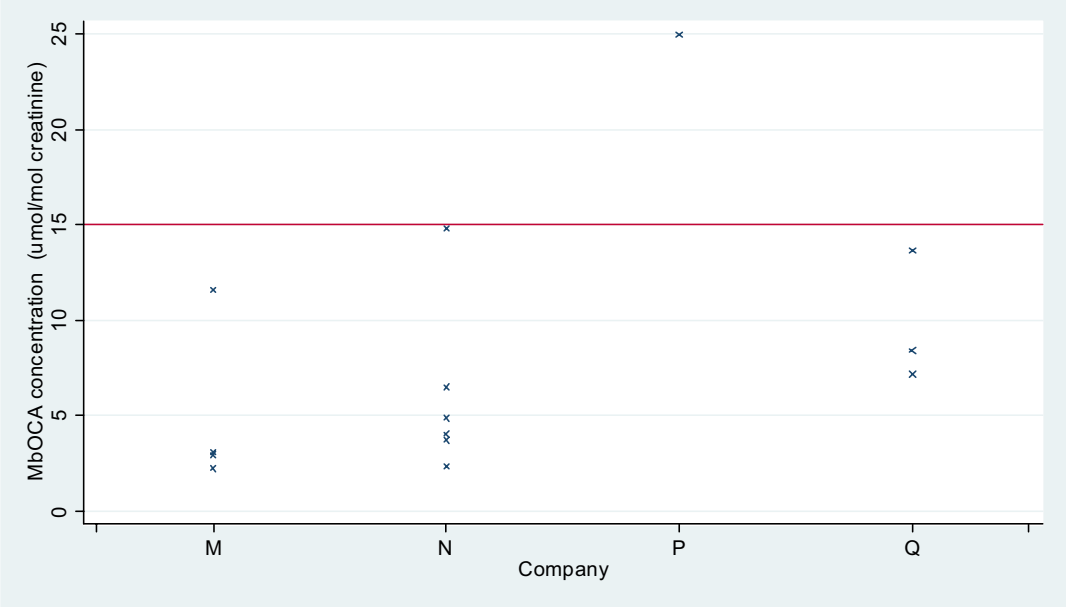


Figure 4: MbOCA concentrations in urine by selected companies



As can be seen from Figure 3 and the summary statistics in Table 7, there were differences in the variability of concentrations between companies with G and U having very large ranges. There was no evidence to suggest any of the companies had significantly larger concentrations of MbOCA in urine, which was confirmed by formal statistical tests. Figure 4 suggested that there might be differences between the different companies for the samples taken from Moulders, in particular the samples from company Q were all above the global median, however this was not confirmed by statistical tests. The power of the statistical tests was low due to the small sample sizes.

Company N was the only one of the five companies using automated processes where enough samples were taken to allow for a meaningful analysis. The comparison with other similar companies (similar in terms of the job tasks the workers were carrying out) showed there were no significant differences between the companies using automated and manual processes however sample sizes were small in all companies and the power of the statistical test was low.

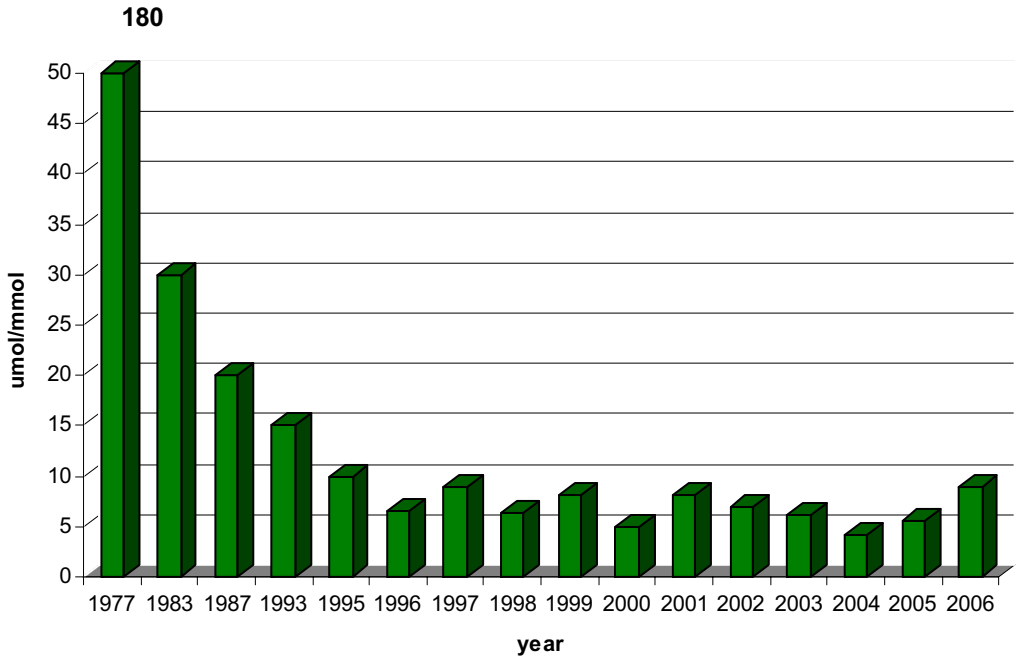
3.1.1.4 Biological Monitoring Guidance Values for MbOCA

The current BMGV for MbOCA is 15 μmol/mol creatinine. This is the good practice guideline that employers should aim for and is set around the 90th percentile of available validated data collected from representative workplaces with good occupational health practices. The BMGV was agreed by The Working Group on Action to Control Chemicals (WATCH) in 1996 based on data from 1993.

Of the 78 urine samples analysed for MbOCA concentrations, 3 were over the BMGV. By the very definition of the BMGV 10% of the samples (or 8 in this dataset) might exceed the BMGV even in workplaces with good controls so values above 15 μmol/mol creatinine do not necessarily imply that good practice is not followed. However, whilst only three concentrations were above the BMGV, two of these were far in excess of 15 μmol/mol creatinine.

One of the specific aims of the statistical analysis was to assess how the BMGV agreed by WATCH in 1996 compared to the 90th percentile of data from workplaces with good practice. The 90th percentile of the current study, based on all 78 samples, was 8.85 μmol/mol creatinine, which was far below the current BMGV. Moreover, the 90th percentile from this study was consistent with previous data collected by HSL over the last 10 years. Figure 5 shows the 90th percentile for MbOCA concentrations in urine from samples taken from 1975 up to and including the data in this survey.

Figure 5: 90th percentile for MbOCA in urine from 1975 to 2006



As can be seen from Figure 5 there has been a downward trend in the 90th percentile for some years and since 1995 the 90th percentile has been below 10 μmol/mol creatinine. The 90th percentile reported in this survey, which was the largest since 2001, is likely to be an overestimate of the 90th percentile since the data from all companies have been used rather than just those with good occupational health practices (an occupational hygienist would have to make judgements on which data to discard) although if data were discarded due to being inconsistent with the other data (the 24.4 and 24.99 μmol/mol creatinine concentrations in particular were identified as 'outliers'), the 90th percentiles of the current and previous data suggest the BMGV may be as low as 7.3 μmol/mol creatinine. The data from this and previous studies suggest that a reduction of the BMGV to10 μmol/mol creatinine would be conservative.

3.1.2 Isocyanate metabolites in urine

The urine samples were analysed for 2,4 Toluenediamine (2,4 TDA), 2,6 Toluenediamine (2,6 TDA), 2,4 Hexanediamine (HDA), Isopherone diamine (IPDAu) and Methylendianinine (MDA). The first two of these, 2,4 TDA and 2.6 TDA, are derived from 2,4 and 2,6 Toluene diisocyanate the individual isomers used in varying proportions in industry, however since these reflect exposure to the same isocyanate the sum of the metabolites is used as a measure of total exposure. The BMGV for isocyanates is 1.0 μmol/mol creatinine.

Samples from 17 companies were tested (none of the samples from companies J and O were assessed for any of the isocyanates), yielding a maximum of 71 samples for testing. A further two samples were not analysed for HDA and IPDA.

As with the statistical analysis of MbOCA in urine a two-phased analysis was performed. Initially all samples were coded as ND or greater than LOD before a separate analysis of the numeric samples was performed. Table 8 reports the frequency of urine samples in which the sample was coded as ND or greater than LOD and the frequency of samples which were greater than the BMGV. Results are given for HDA, IPDA and MDA, whilst concentrations of 2,4 TDA and 2,6 TDA are reported in addition to their sum, 'total TDA'. In each case the sum of the percentages in the first two columns sum to 100 since those greater than BMGV are a subset of greater than LOD.

Table 8: **Frequencies for Isocyanates concentrations in urine**

	Diamine concentrations in Urine		
Diamine	ND	> LOD	> BMGV
2,4 TDA	57 (80%)	14 (20%)	6 (8%)
2,6 TDA	49 (69%)	22 (31%)	7 (10%)
Total TDA	*48 (68%)*	*23 (32%)*	*16 (23%)*
HDA	56 (79%)	13 (21%)	9 (13%)
IPDA	66 (96%)	3 (4%)	- -
MDA	65 (92%)	6 (8%)	- -

As can be seen in Table 8 a measurable concentration was recorded in a total of 58 samples although in many cases the two TDA isomers were detected in the same sample and after adjusting for this a total of 45 samples were above the LOD for the four distinct isocyanates. In

the cases where TDA was detected, 2,6 TDA was measurable in all but one of the samples. A total of 25 samples were above isocyanate BMGV of 1.0 µmol/mol for TDA (16 samples) or HDA (9 samples). Of the samples in which the total TDA was above the BMGV, four samples were above the BMGV for just 2,4 TDA, five above the BMGV for just 2,6 TDA and two samples were above the BMGV for both of the isomers. A further five samples were below the BMGV for both the 2,6 TDA and 2,4 TDA isomers but above the BMGV for total TDA.

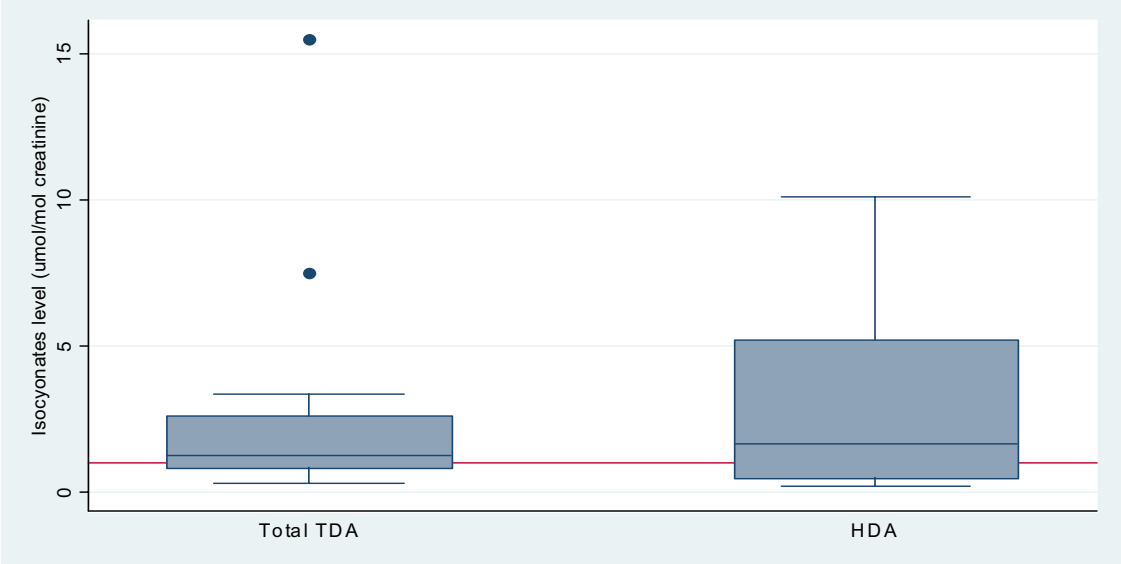
Summary statistics from the second phase analysis, looking at the numerical readings, are given in Table 9. Results are given for HDA, 2,4 TDA, 2,6 TDA and total TDA.

Table 9: **Summary statistics of diamine concentrations in urine**

Diamine concentrations in urine								
Diamine	N	Max	Min	Median	Arithmetic mean	Arithmetic standard deviation	Geometric mean	Geometric Standard deviation
2,4 TDA	14	5.55	0.32	0.7	1.37	1.40	0.96	2.28
2,6 TDA	22	13.23	0.45	0.77	1.64	2.69	1.037	2.19
Total TDA	23	15.5	0.32	1.26	2.40	3.23	1.54	2.40
HDA	13	10.11	0.22	1.67	3.41	3.38	1.81	3.69

Figure 6 shows Boxplots of total TDA and HDA readings. The BMGV is included as the red line.

Figure 6: **Diamine concentrations in urine**



The summary statistics in Table 9 reflect that the quantities of the two TDA isomers, when at a measurable concentration, had similar magnitudes with median concentrations for 2,4 TDA and 2,6 TDA of 0.7 and 0.77 µmol/mol creatinine respectively. The variability was also similar as seen by comparing the geometric standard deviations of 2.28 and 2.19 respectively, which are unaffected by the one very large concentration (13.23 µmol/mol creatinine) of 2,6 TDA. When

comparing HDA and total TDA the results were noticeably different with TDA exhibiting low variability (outliers excepted) whilst the HDA concentrations exhibited greater variability. For both of the isocyanates approximately 70% of samples where a measurable concentration was detected were above the BMGV.

3.1.2.1 Analysis by exposure

Table 10 below reports the frequency of urine samples in which the sample was coded as ND or greater than LOD and the frequency of concentrations in excess of the BMGV for both controls and workers who were directly exposed to MbOCA. For both controls and directly exposed workers the percentages classified as ND or greater than LOD sum to 100.

Table 10: **Frequencies for Isocyanates concentrations in urine by exposure**

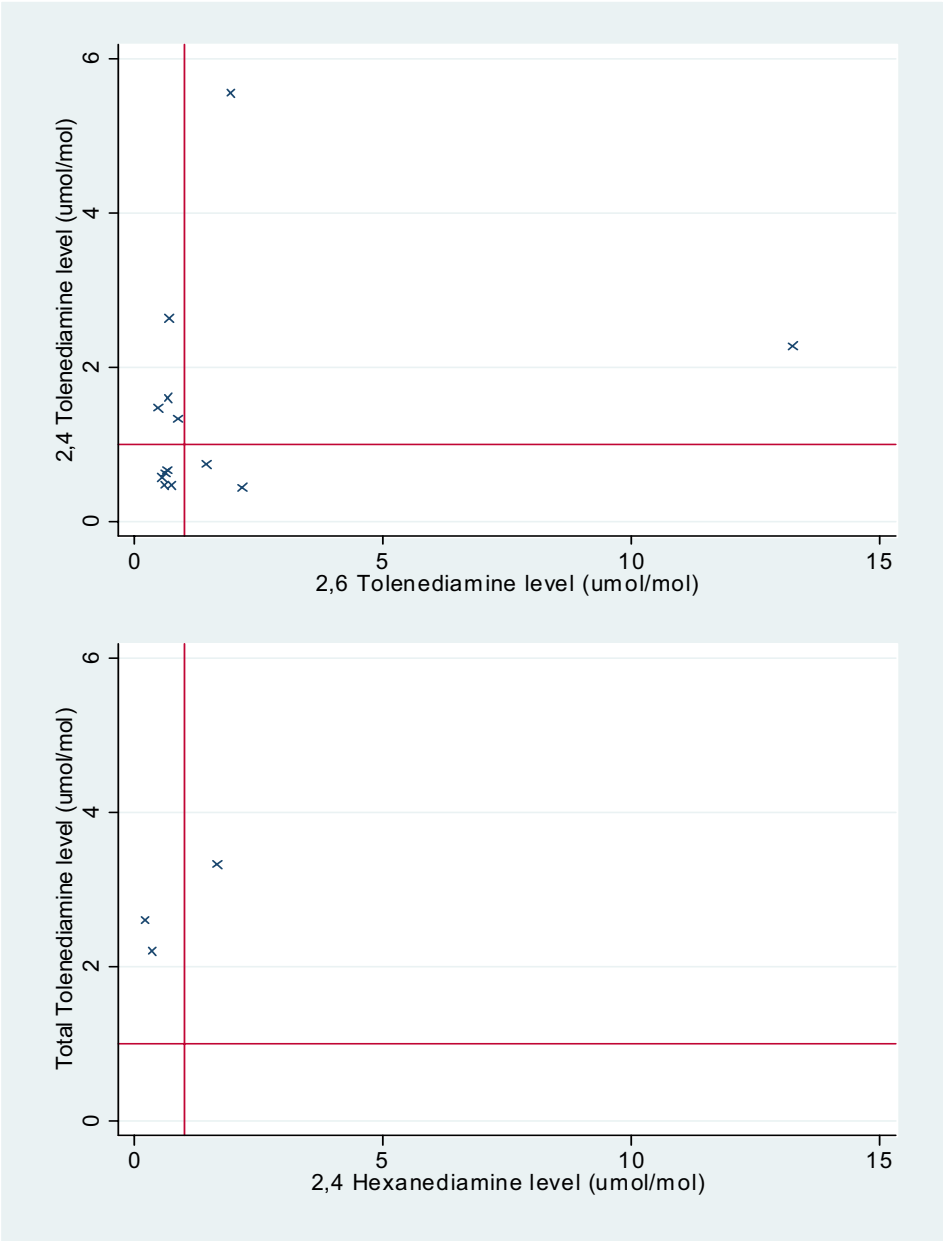
	Diamine concentrations in urine					
	Control			Directly exposed		
Diamine	ND	> LOD	> BMGV	ND	> LOD	> BMGV
2,4 TDA	16	1	-	41	13	6
	(94%)	(6%)	-	(76%)	(24%)	(11%)
2,6 TDA	17	-	-	32	22	7
	(100%)	-		(59%)	(41%)	(13%)
Total TDA	*16*	*1*	-	*32*	*22*	*16*
	(94%)	(6%)	-	(59%)	(41%)	*(30%)*
HDA	15	1	1	41	12	8
	(94%)	(6%)	(6%)	(77%)	(23%)	(15%)
IPDA	16	-	-	50	3	-
	(100%)	-	-	(94%)	(6%)	-
MDA	14	3	-	51	3	-
	(82%)	(18%)	-	(94%)	(6%)	-

It can be seen from Table 10 that samples where a measurement was obtained, they were almost exclusively from the workers who were directly exposed to MbOCA and 24 of the 25 concentrations that were above the BMGV were in the directly exposed group. MDA was noticeably different from the general pattern with both workers who were directly exposed to MbOCA and controls showing similar results.

3.1.2.2 Correlations between Diamine concentrations

The urine samples where both 2,4 TDA and 2,6 TDA were above the LOD and samples where total TDA (meaning that one or both of the isomers were above the LOD) and HDA were above the LOD were examined further to assess for correlations. Figure 7 shows plots of the TDA isomers and total TDA against HDA. Also shown in Figure 7 is the BMGV for isocyanates.

Figure 7: **Correlations between 2,4 TDA, 2,6 TDA and HDA concentrations in urine**



As can been seen from Figure 7 and the earlier discussion, a measurable concentration of both TDA isomers was often found in the same sample with a measurable concentration of 2,4 TDA present in only one sample when 2,6 TDA was not at a measurable concentration. However, the magnitudes of the two isomers appeared to be independent, as verified by statistical tests ($p=0.392$). Measurable concentrations of total TDA were rarely found in combination with HDA (only 3 cases) and statistical tests showed there was no evidence ($p = 1.00$) to support a correlation between the magnitudes of total TDA and HDA.

3.1.2.3 Analysis by Job

Further analysis was performed on the directly exposed workers, sub-classified into the 7 different job categories defined in section 2.3.1.

The following tables report the frequency of urine samples in which the sample was NA or greater than LOD and the frequency of samples which were in excess of the BMGV for total TDA (Table 11), and HDA (Table 12) by job classification. In each table the percentages in the first two columns sum to 100.

Table 11: **Frequencies for total TDA concentrations in urine by job type**

	Total TDA concentrations in urine		
Job Classification	ND	> LOD	> BMGV
Handling & Scooping	5 (100%)	- -	- -
Weighing, Mixing & Melting	8 (100%)	- -	- -
Casting	1 (50%)	1 (50%)	1 (50%)
Moulding	6 (50%)	6 (50%)	6 (50%)
Maintenance	1 (100%)	- -	- -
Other exposure	3 (43%)	4 (57%)	4 (57%)
All parts of the process	7 (39%)	11 (61%)	5 (28%)

Table 12: **Frequencies for HDA concentrations in urine by job type**

	Total TDA concentrations in urine		
Job Classification	ND	> LOD	> BMGV
Handling & Scooping	5	-	-
	(100%)	-	-
Weighing, Mixing & Melting	2	6	4
	(25%)	(75%)	(50%)
Casting	2	-	-
	(100%)	-	-
Moulding	9	3	2
	(75%)	(25%)	(17%)
Maintenance	1	-	-
	(100%)	-	-
Other exposure	4	3	2
	(57%)	(43%)	(29%)
All parts of the process	18	-	-
	(100%)	-	-

Tables 11 and 12 show some common features, in particular that Moulders were exposed to both isocyanates, whilst those involved in Handling/Scooping MbOCA had no isocyanate concentrations above the LOD. Those working mainly in Weighing, Mixing & Melting only had measurable quantities of HDA in urine whilst those working in all parts of the process only had measurable quantities of TDA.

3.1.2.4 Analysis by company

An analysis of the results by company helped to explain the differences found in the different diamine concentrations by job type since the isocyanate concentrations in urine were strongly associated with the companies.

The important findings are summarised below.

- Large readings for TDA, with the 2,4 TDA isomer above BMGV, were found for all 3 samples taken from company R, from workers involved in work classified as 'other exposed'.

- Two readings taken from Moulders working at company Q and the single directly exposed sample taken from company P were above the guidance value for TDA, this time the 2,6 TDA isomer. The latter sample also had a high MbOCA concentration of 24.99.

- Two of the three moulders working at company M had readings above guidance values for HDA whilst all four samples from the workers involved mainly in Weighing/Mixing and Melting at company F had urine concentrations above the BMGV.

- The single worker in the control group with a urine isocyanate concentration above the BMGV worked at company E. All four of the workers who were directly exposed to MbOCA had concentrations below the BMGV for all of the isocyanates.

3.1.3 Correlations between MbOCA and diamines

The results from the urine analysis were subjected to a two-phased analysis to assess for correlations between MbOCA and the presence of isocyanates. The first phase involved coding MbOCA as ND or greater than LOD and a second variable, presence of Isocyanates, was derived as NA if neither TDA nor HDA were detected and greater than LOD if at least one of these was detected. Results from this simple analysis are shown in Table 13.

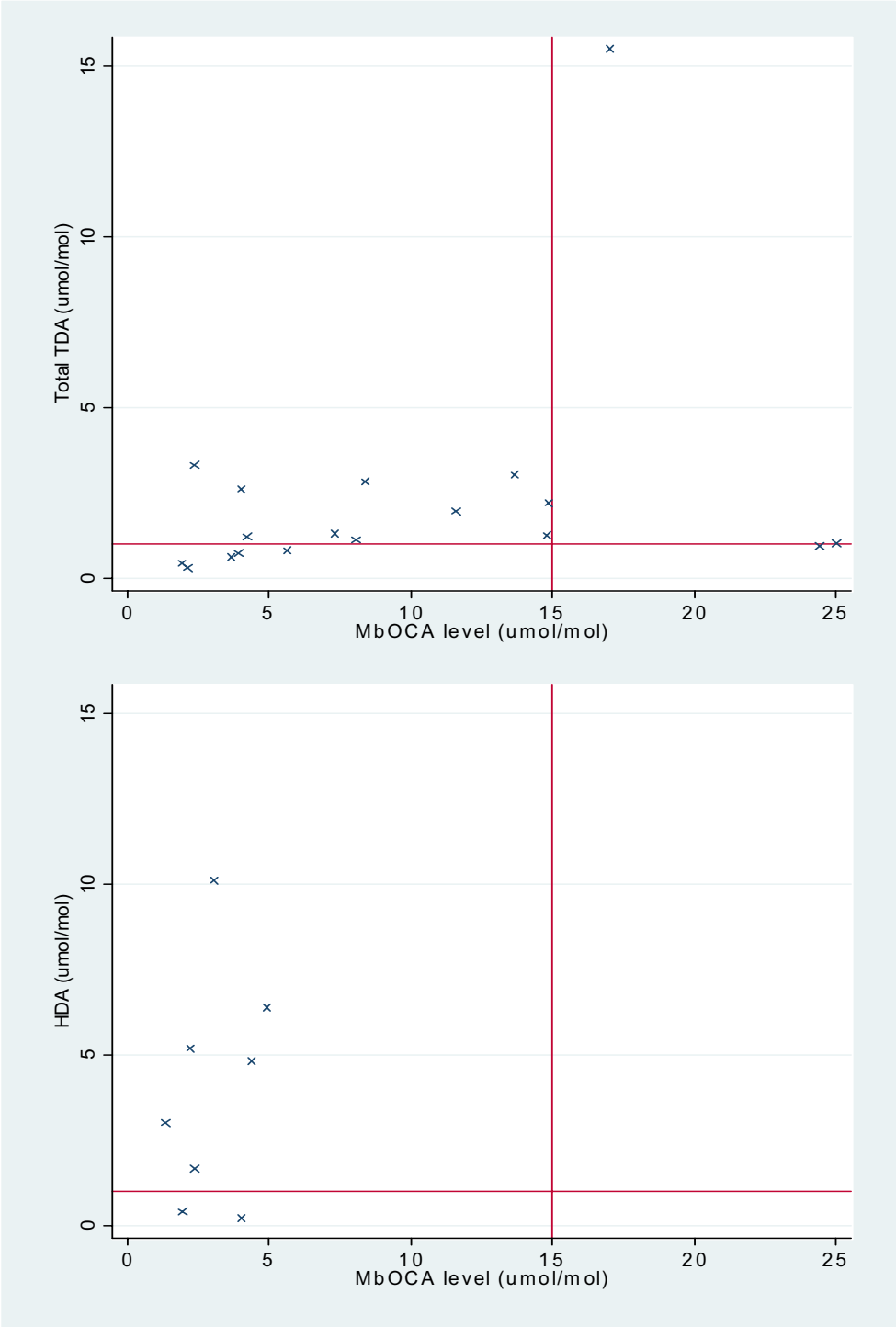
Table 13: **Frequencies for measurable quantities of MbOCA and diamines**

		Measurable quantity of MbOCA		Total
		No	Yes	
Measurable quantity of diamine	No	24	13	37
	Yes	10	24	34
	Total	34	37	71

As can be seen from Table 13 there was a strong association between a measurable quantity of MbOCA and at least one of the diamines ($p = 0.004$).

The second phase of analysis involved a more detailed examination of the cases where measurable concentrations of MbOCA and TDA or HDA were detected. Figure 8 shows scatter plots of total TDA and HDA against MbOCA. The BMGV limits for both MbOCA and the isocyanates are shown as the red vertical (MbOCA) and horizontal (isocyanates) lines.

Figure 8: **Correlations between MbOCA and diamine concentrations in urine**



From Figure 8 there appeared to be evidence of positive correlations between the MbOCA concentration and diamine concentrations in urine, particularly between MbOCA and total TDA ($p = 0.069$). Statistical tests ($p=0.53$) showed the relationship between MbOCA and HDA concentrations was weak however the number of matched pairs was small.

The 71 samples that were tested for both diamines and MbOCA were used to derive two further variables. Each sample was coded as either less than BMGV or greater than BGMV for MbOCA and the second variable, diamine above BMGV, was derived by categorising each of the samples as having at least one diamine concentration above the BMGV or all diamine concentrations below the BMGV. Table 14 below shows a cross tabulation of the two variables. In workplaces with good occupational health practices the two variables would not be expected to be related, and conversely, a relationship between the two variables could be an indicator of poor occupational health practices in some of the workplaces.

Table 14: **BMGV values of diamine and MbOCA**

		MbOCA level above BMGV		Total
		No	Yes	
Diamine level above BMGV	No	46	1	47
	Yes	22	2	24
	Total	68	3	71

As can be seen from Table 14, there did not appear to be a link between whether diamine concentrations were above the BMGV and MbOCA concentrations above the BMGV, however this clearly depended on the magnitude of the BMGV. In section 3.1.1.4 the analysis showed the BMGV could be reduced and when it was lowered to 10 μmol/mol creatinine and the above analysis repeated, the results showed that those workers above the revised BMGV for MbOCA would be more likely to be above the BMGV for at least one of the diamines.

3.1.4 Summary

- There was evidence to suggest that the current BMGV for MbOCA could be reduced since the 90th percentile for all companies (including some that may not have good occupational hygiene practices) has been consistently below 10 μmol/mol creatinine for the last ten years.

- Directly exposed workers had higher MbOCA concentrations in urine, particularly those working in Casting, Moulding and All parts of the process. The observation that many workers were above the BMGV for isocyanates is a new and important finding.

- Correlations between the different isocyanates diamine concentrations were weak.

- Correlations between MbOCA and diamine concentrations were positive and provided some evidence of a relationship, particularly between TDA and MbOCA.

3.2 AIR SAMPLES

A total of 210 air samples from 20 companies were collected, with samples taken at both Static and Person level. Person level samples were taken from the working area of one of the employees. Both the static and person level air samples were then analysed for MbOCA. The WEL for MbOCA in a person level air sample, calculated as an 8-hour average exposure, is currently set at 0.005 mg m^{-3}.

A total of 80 Personal air samples were collected. In some cases multiple samples were taken (at different times of the day) from the same working area. A total of 130 static samples were taken from the companies at a variety of locations. The static samples were almost exclusively taken at locations that could be classified as directly exposed whereas all personal samples were taken from directly exposed workers. In general the samples were taken over a period of approximately 100 minutes although some samples were taken over a much shorter period.

Table 15 below reports the frequency of person level and static level air samples in which the sample was recorded as ND or > LOD

Table 15: **Frequencies for MbOCA concentration in air by sample type**

		MbOCA concentration in air sample	
		ND	> LOD
Exposure	Personal Samples	67 (84%)	13 (16%)
	Static Samples	116 (89%)	14 (11%)

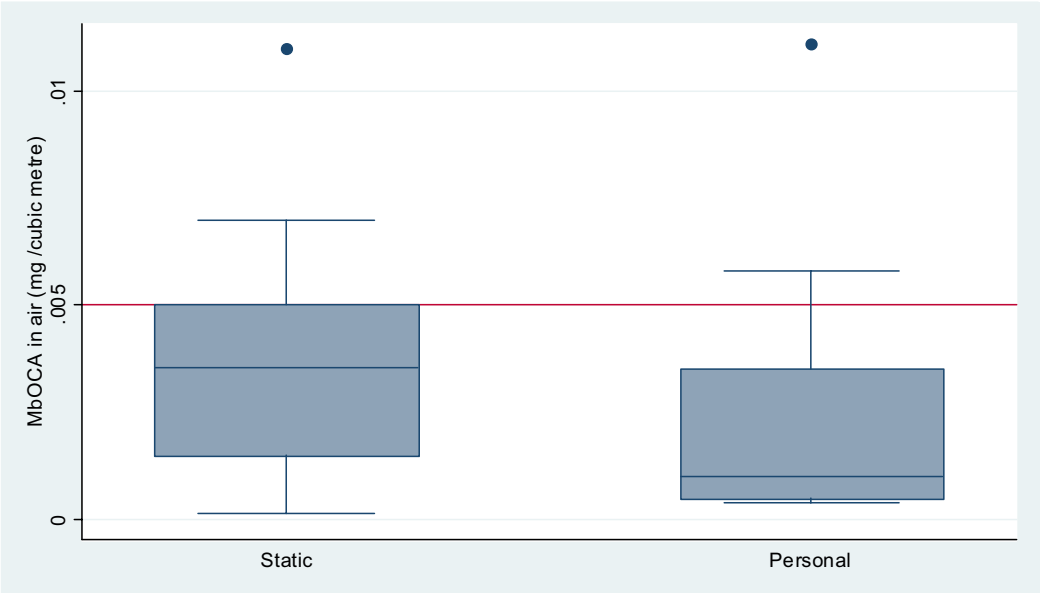
For both personal and static samples the concentrations of MbOCA were very low and found in only 10% of cases. Neither the Figures in Table 15 nor statistical tests suggested any differences between the static and personal samples.

Some summary statistics of the numeric readings are given in Table 16 and Boxplots of the readings are shown in Figure 9. The WEL of 0.005 mg m^{-3} is also shown.

Table 16: **Summary statistics of MbOCA concentration in air by sample type**

	MbOCA concentration in air sample							
Exposure	n	Max	Min	Median	Arithmetic mean	Arithmetic standard deviation	Geometric mean	Geometric standard deviation
Personal Level	13	0.011	0.0004	0.001	0.002366	0.00309	0.00246	3.404
Static	14	0.0111	0.00015	0.00355	0.00366	0.00286	0.00131	2.9082

Figure 9: MbOCA concentration in air by sample type



As can be seen from Figure 9 the concentrations (where the test was able to determine the quantity of MbOCA in the air sample) were small, with respective medians of 0.0036 and 0.001 for static and personal samples respectively. There was some evidence to suggest that the static samples had higher concentrations than the person level samples (p = 0.0848) however the power of the test was low due to the small number of numeric readings in both groups. Two of the concentrations from personal samples were above 0.005 mg m^{-3}, which, given that 75 samples were collected, would be consistent with good practice. However, the largest concentration observed of 0.011mg m^{-3} was taken over a 20-minute period and may not be representative of a working shift although it is representative of short-term exposure.

3.2.1 Correlation Between Air and Urine Samples

Where possible the air and urine samples were matched (n=75) in order to test for correlations between the samples. Air and urine samples could not be matched in all cases.

The results from the first phase analysis are shown in Table 17. Each of the urine and air samples was classified as ND or greater than LOD. The row percentages in Table 17 sum to 100.

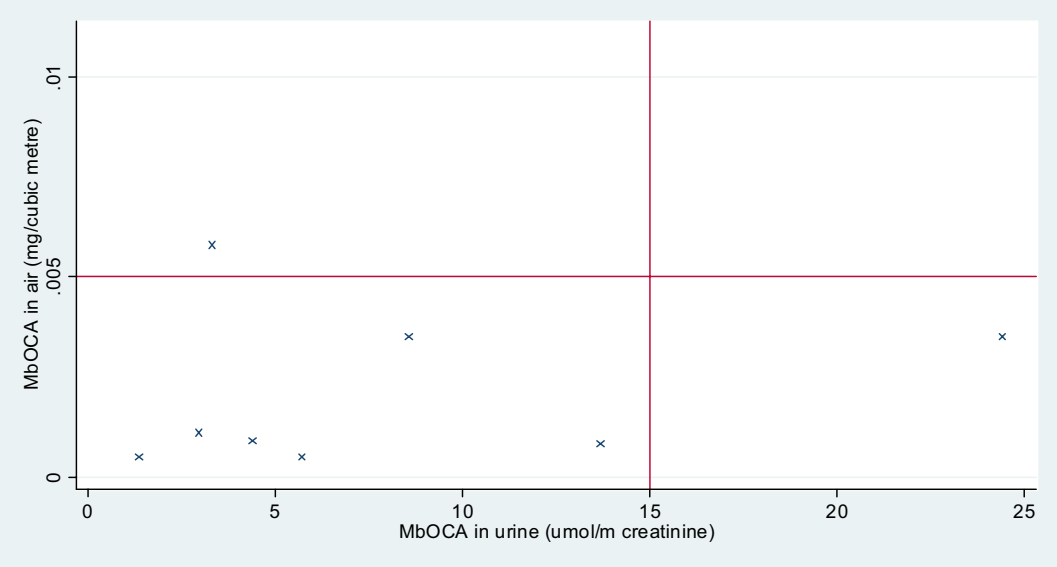
Table 17: Comparison of air and urine results

		MbOCA concentration in air	
		ND	> LOD
MbOCA concentration in urine	ND	28 (87%)	4 (13%)
	>LOD	35 (82%)	8 (18%)

It can be seen from Table 17 that there did not appear to be an association between the MbOCA concentrations in urine and personal air samples using this simple analysis. Formal statistical analyses were performed also and showed there was no evidence to suggest an association between MbOCA concentrations in urine and personal air samples (p= 0.54).

A graphical representation of the eight cases where numerical readings were obtained for both air and urine samples is show in Figure 10.

Figure 10: **Correlations between MbOCA and Isocyanate levels in urine**



From the small amount of data where numeric readings were obtained for both samples there was no evidence of a relationship. Moreover, there were no cases where an individual was above the BMGV for urine and the WEL for air.

3.3 SURFACE WIPE SAMPLES

A total of 334 surface wipe samples were taken from the 20 companies. Samples were mainly concentrated on surface areas that might be classified as directly exposed to MbOCA, with 259 taken from directly exposed areas and 75 taken from control surfaces (surfaces which should not contain traces of MbOCA if good practice was followed) such as canteen or office surfaces. In general the surface wipe was taken from an area of 100 square cm.

Table 18 reports the frequencies that the control and directly exposed surface samples were classified as ND and > LOD.

Table 18: **Frequencies for MbOCA level on surface wipes by exposure**

		MbOCA concentration on surface wipe	
		ND	> LOD
Exposure	Control	67 (89%)	8 (11%)
	Directly Exposed	103 (40%)	156 (60%)

The differences between the directly exposed and control areas of the workplace were large with the majority of control areas having no MbOCA present on the surface wipe whilst the majority of samples taken from exposed areas had a measurable concentration. However, the eight control samples (which came from a variety of control locations) had measurable concentrations of MbOCA and could be viewed as indication that best practice was not followed at all premises.

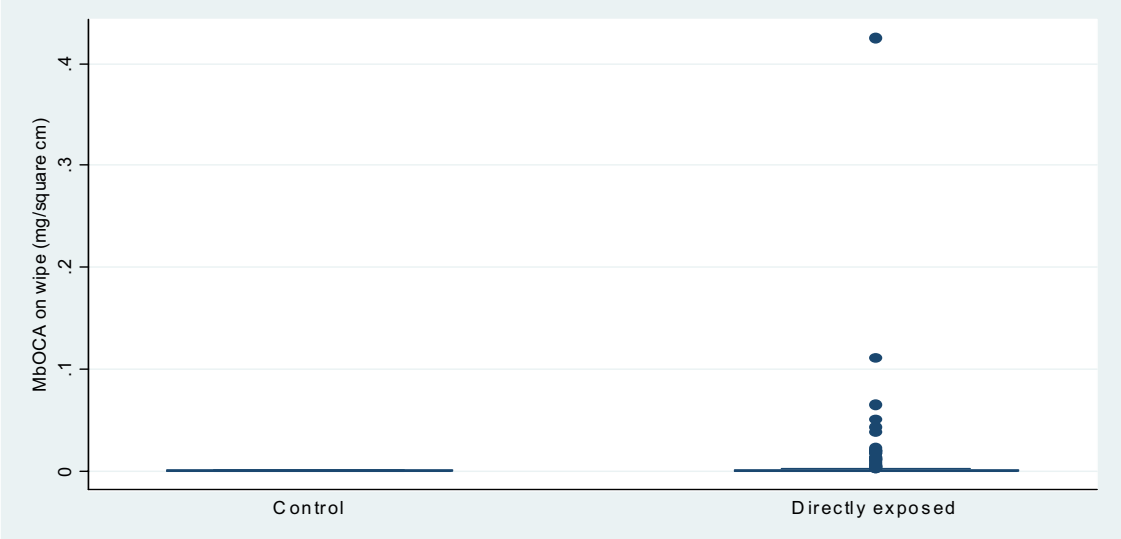
Summary statistics of the numeric readings are given in Table 19 by exposure.

Table 19: **Summary statistics of MbOCA concentration on surface by exposure**

	MbOCA concentrations on surface							
Exposure	n	Max	Min	Median	Arithmetic mean	Arithmetic standard deviation	Geometric mean	Geometric standard deviation
Control	8	0.0074	0.00002	0.0001	0.00026	0.000298	0.00012	4.1494
Directly exposed	156	0.425	0.00001	0.0002	0.00658	0.03597	0.000307	10.7757

Figure 11 shows Boxplots of the data where a numeric reading was obtained by exposure.

Figure 11: **MbOCA on surface wipe by exposure**



The quantity of MbOCA on surface wipes was broadly similar in the directly exposed and control areas with respective medians of 0.0002 and 0.0001 mg/cm^2 and respective interquartile ranges of 0.001086 mg/cm^2 and 0.000463. The directly exposed group had a median and interquartile range approximately twice as large as the control group, although in both cases these summaries of the data were of the same order of magnitude. However, Figure 11 highlights the differences in the large concentrations with a relatively small number of very high surface wipe concentrations solely in the directly exposed areas; the affect of these can be seen by comparing the arithmetic and geometric means for directly exposed areas which differ by an order of magnitude. Despite the obvious skew, the data from directly exposed areas[2] were not log-normally distributed (both the skewness and kurtosis of the data were too pronounced)

[2] *Due to the small number of control samples (n = 8) a corresponding test was not performed for this group.*

3.3.1 MbOCA concentration on surface wipes by location

As described in section 2.3.3 the areas which surface wipes were taken from were classified into 8 areas, with the areas chosen to reflect the stages of the manufacturing process. Results from the first stage analysis are presented in Table 20. All row percentages in Table 20 sum to 100.

Table 20: **Frequencies for MbOCA level on surface wipes by location**

	MbOCA levels in on surface wipe	
Location	ND	> LOD
Fume cupboard/degassing	10 (27%)	27 (73%)
Storage	34 (50%)	34 (50%)
Weighing/pouring	4 (16%)	21 (84%)
Mixing	6 (40%)	9 (60%)
Oven	14 (40%)	21 (60%)
Hopper	4 (50%)	4 (50%)
Casting	4 (40%)	6 (40%)
0ther non-specific	27 (44%)	34 (56%)

Table 20 shows that MbOCA was found in the majority of samples for almost all locations. The Weighing/pouring locations had a particularly high proportion of samples where a measurable quantity of MbOCA was present on surfaces.

Further analysis of the numeric readings is given below with summary statistics presented in Table 21 and Box plots shown in Figure 12.

Table 21: **Summary statistics of MbOCA concentration on surface by location**

	MbOCA concentrations on surface							
Exposure	n	Max	Min	Median	Arithmetic mean	Arithmetic standard deviation	Geometric mean	Geometric standard deviation
Fume cupboard	27	0.0514	0.00001	0.0004	0.00295	0.00985	0.00038	8
Storage	34	0.0665	$9*10^{-6}$	0.0003	0.0042	0.0124	0.00027	12.07
Weighing /pouring	21	0.1116	$4*10^{-6}$	0.0005	0.0114	0.026	0.000266	18.26
Mixing	9	0.0145	$1.3*10^{-5}$	0.0001	0.0033	0.0061	0.000191	12.88
Oven	21	0.425	$7.4*10^{-6}$	0.0001	0.0207	0.0926	0.000191	11.78
Hopper	4	0.0209	0.0033	0.011	0.0116	0.0072	0.0096	2.1631
Casting	6	0.0003	$1.7*10^{-5}$	0.0001	0.00011	0.0001	0.000079	2.8
Other	34	0.0205	$7*10^{-6}$	0.0002	0.0015	0.004	0.000234	7.168

Figure 12: **MbOCA on surface wipe by location**

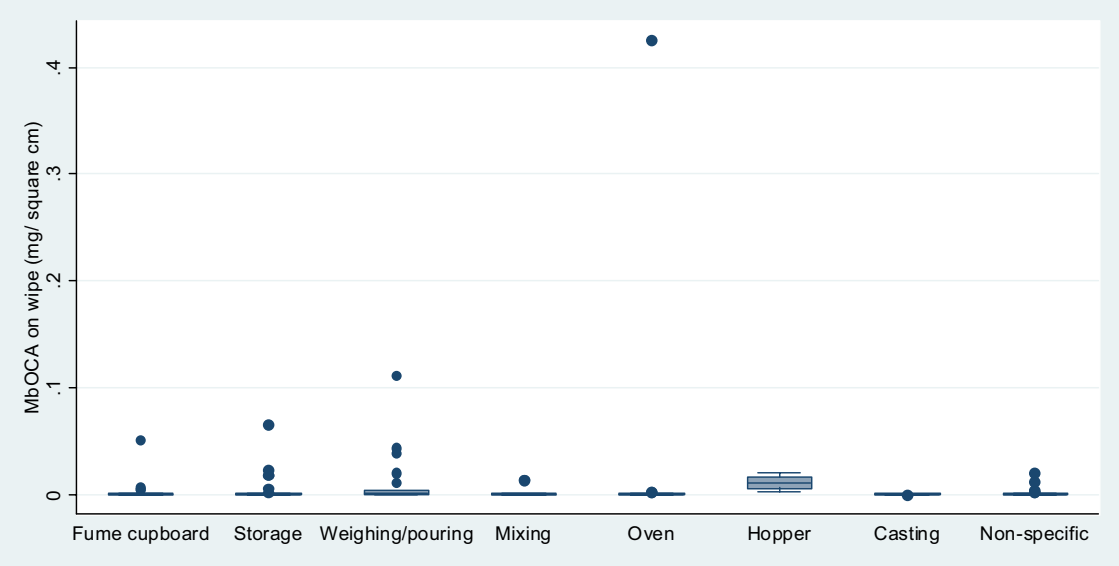


Figure 12 and the summary statistics presented in Table 21 show that the general level of surface concentrations was at a similar level for the different sample locations, with medians and geometric means very similar for different locations; Hopper was the one exception with an much larger median (an order of magnitude larger than at the other locations) and geometric mean. Many of the sample locations had concentrations that could be considered to be 'outlying' or unusual however the descriptions accompanying the samples showed that the very

large concentrations usually came from areas where MbOCA contamination would be expected such as weighing scales.

3.3.2 Storage Drums

One of the specific aims of the statistical analysis was to investigate the quantities of MbOCA found on wrapped drums in storage at the two distributors, companies R and T. The numbers of samples taken from the companies were not sufficient to allow for a thorough statistical analysis however the results from a simple exploration of the data are presented here. Of the 17 surface samples taken from the storage area at company T, two had small traces of MbOCA, 0.0002 and 0.0008 mg/cm^2 respectively. Of the 11 samples taken from the storage area at company R, four contained traces of MbOCA with respective concentrations of 0.0184, 0.0233, 0.0058 and 0.0011 mg/cm^2 from samples on wrapped pallets and wrapped storage drums. Collectively these samples from company R accounted for all but one of the large observations (see Figure 12) taken in storage facilities in all companies, the largest of all being a sample taken from the side of a drum at company C.

3.3.3 Correlations

It was not possible to correlate surface concentrations with air or urine results due to the way the samples were taken. Surface concentrations were taken from specific work areas and these could not be related to specific workers using the data collected.

3.4 GLOVE SAMPLES

There were a total of 147 glove samples, all of which could be classified as being potentially contaminated by MbOCA. More glove samples were taken from the companies however due to unspecified reasons a small number of samples were not tested.

3.4.1 Analysis by glove type

Gloves could be classified as an inner glove worn next to the skin and an outer glove, worn over the top of the inner glove and with a potential direct exposure to MbOCA. A two-phase analysis of all the glove data was not possible since not all gloves were explicitly classified as inner or outer by the on-site inspectors and the description accompanying the sample was insufficient for this judgement to be retrospectively made. Only 88 of the 147 glove samples could be classified as inner or outer.

Table 22 below shows the frequencies of glove samples where the measurements were either ND or greater than the level of detection by the glove type.

Table 22: **Frequencies for MbOCA concentration on gloves**

		MbOCA concentration on gloves	
		ND	> LOD
Glove Type	Inner	16 (52%)	15 (48%)
	Outer	6 (11%)	51 (89%)

Approximately 90% of the outer gloves contained a measurable concentration of MbOCA whereas approximately 50%of the inner glove samples contained a measurable concentration. The difference between glove types was highly significant ($p < 0.001$)[3].

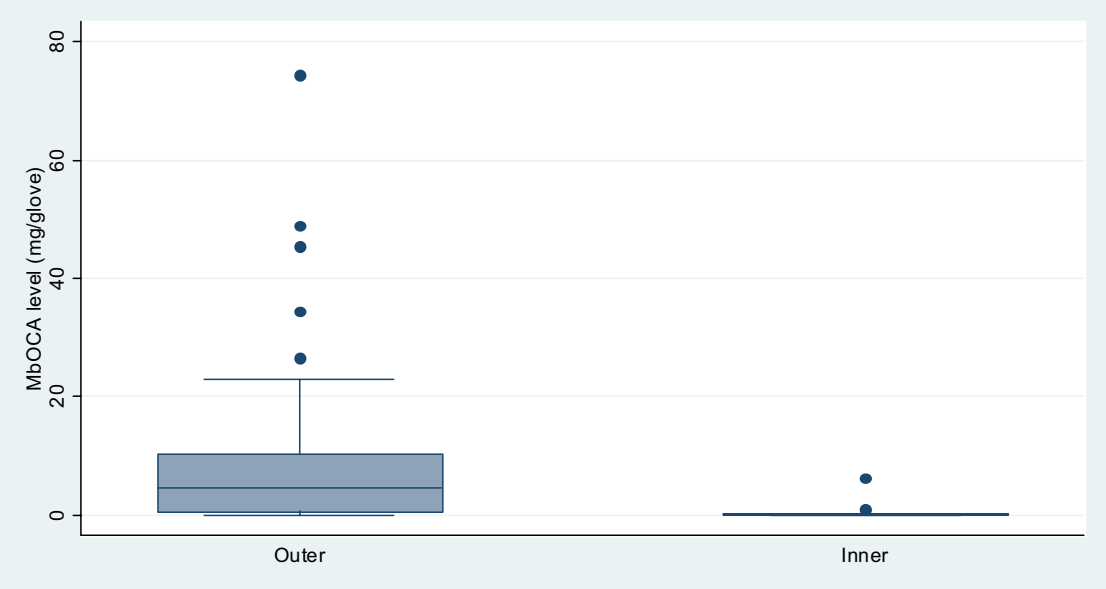
Table 23 shows summary statistics for the measurements from the two glove types.

Table 23: Summary statistics of MbOCA concentration on gloves

	MbOCA concentrations on gloves							
Exposure	n	Max	Min	Median	Arithmetic mean	Arithmetic standard deviation	Geometric mean	Geometric standard deviation
Inner	15	6.3	0.01	0.09	0.5619	1.604	0.107	4.854
Outer	51	74.44	0.016	4.534	9.2766	14.45	2.555	7.885

Figure 13 shows box plots of the concentrations measured in mg/glove found on the inner and outer gloves.

Figure 13: MbOCA concentration by glove type



The differences between the inner and outer glove concentrations are clearly visible from both the summary statistics in Table 23 and the plot in Figure 13 and statistically significant ($p < 0.001$). The respective medians were 0.09 mg/glove for inner compared with 4.534 mg/glove for outer, with respective ranges of (0.01, 6.3) and (0.016 to 78), which reflect that the concentrations on outer gloves were in general much larger than inner gloves; in general the concentrations on outer gloves were several orders of magnitude larger than the concentrations on inner gloves.

[3] *Given that 40% of samples were not classified as inner or outer the percentages in Table 22 should be viewed with caution*

3.4.2 Correlation between inner and outer glove samples

One of the specific aims of the statistical analysis was to investigate the correlation between inner and outer glove concentrations. At three of the site inspections inner and outer (and in one instance middle) glove samples were taken from the same individual whereas the data collected from other premises were not detailed enough to allow samples to be matched. It was only possible to match inner and outer glove samples for nine individuals and even in these cases the hand the gloves were worn on could not be matched for the inner and outer glove samples and hence a meaningful comparison between inner and outer glove concentrations was not possible. However, in one case where it was possible to match inner and outer gloves the very large inner glove concentration of 6.3 mg correlated with large outer glove concentrations of 12.8 and 22.9 mg.

3.4.3 Correlation between glove samples and urine samples

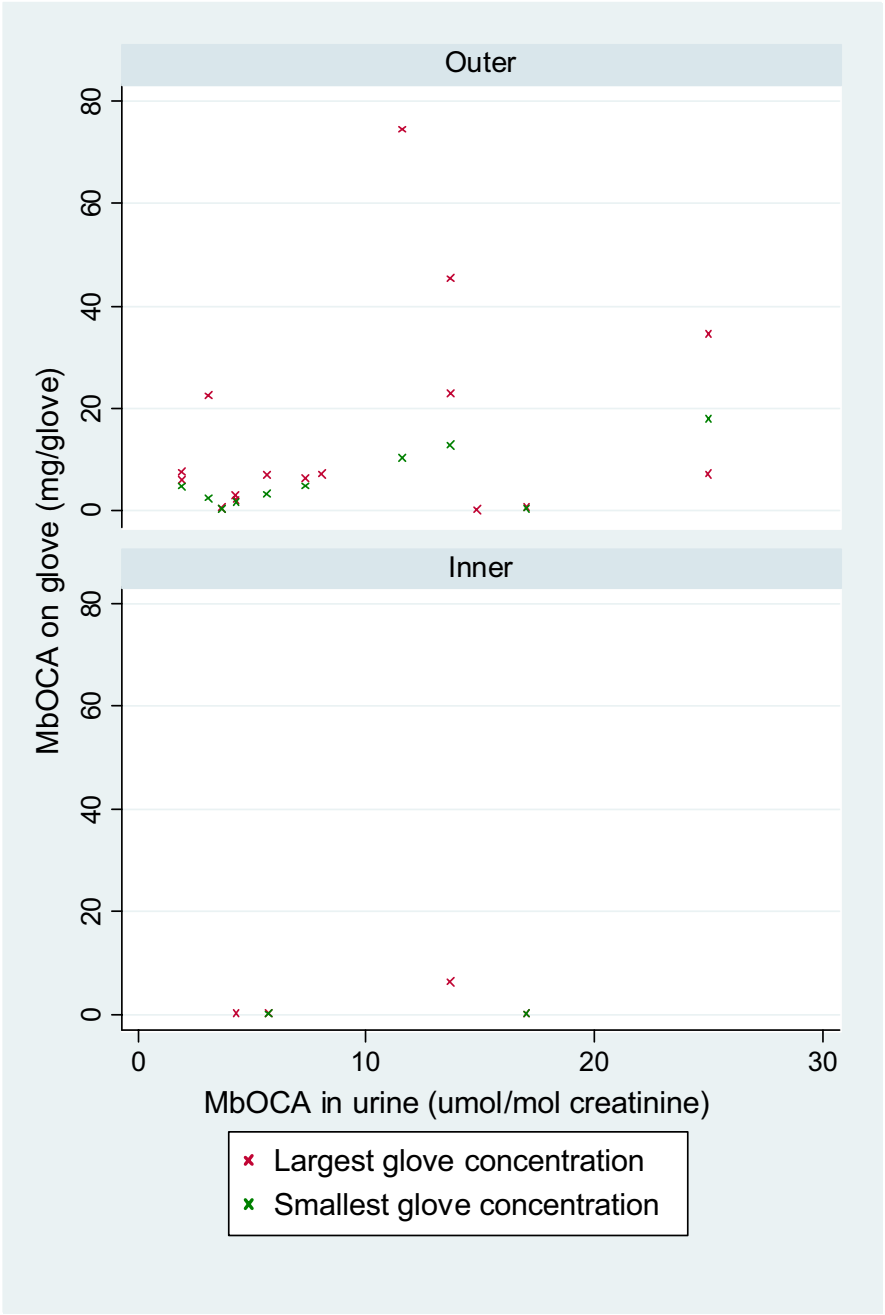
The descriptions that accompanied glove samples did make it possible to match glove samples to urine samples. Figure 13 shows the cases where numeric values were obtained in both glove and urine tests for both outer and inner glove samples. It was possible to match more than one glove sample to a urine reading (left, right hands) for some cases; when this was possible the largest of the readings is identified by the red cross and the smallest glove concentration is identified by the green cross.

Figure 14 shows that it was possible to match urine and outer gloves concentrations much more frequently than for inner gloves. The data on inner gloves were too sparse to establish a relationship however the data indicated that there may be a relationship between the level of contamination of MbOCA on gloves and the concentration of MbOCA in urine, with urine concentrations increasing with increases in the level of contamination of the gloves. In particular the two samples with very high concentrations of MbOCA in urine both had a large contamination on glove samples.[4]

A relationship between the level of contamination on outer gloves and MbOCA in urine would be more complex than Figure 14 suggests. Each point in Figure 14 corresponds to a case where both the level of contaminant on a glove and the concentration of MbOCA in urine were above limits of detection, the cases where one or both of these measurements were below the LOD are not seen. The variability in the data would suggest that factors such as the length of time the gloves were worn (single use gloves for quickly performed tasks versus continuous use), the material of the glove, the job being performed and whether the gloves were reused may be important. The data from the present study did not contain sufficient detail to investigate the relationship further. In order to establish for what combination of factors the relationship between glove contamination and urine concentrations was at its strongest additional research would be required.

[4] *Note a correlation coefficient is not provided since there was not a one to one mapping of urine readings to glove concentrations. A correlation could be calculated by using a summary of the two glove concentrations (i.e. maximum or mean) and relating this to the urine, however the correlation would depend on the summary used.*

Figure 14: **MbOCA concentration by glove type and MbOCA in urine**



4 DISCUSSION

This report has presented a thorough statistical analysis of urine, air, surface and glove samples collected from 20 premises (18 users and two distributors). In addition to the statistical summaries of the data, the analysis aimed to investigate the specific points laid out in the introduction and these are addressed below (although not in the order presented in the introduction).

- Assess for differences in results between different jobs and different companies.

Only the data on urine samples contained sufficiently detailed information in order to assess for differences between jobs and companies. The data showed that those working mainly in casting and moulding and those working in all parts of the manufacturing process had the highest levels of MbOCA in urine. Further statistical analysis concentrated on companies where samples were taken from individuals working in moulding and in all parts of the process and no differences between the companies was found although the power of statistical tests was weak due to the small numbers of samples taken from the companies.

- To assess whether companies using automated processes had different concentrations of MbOCA in the samples than the companies using purely manual processes.

Although five companies used automated processes there were only enough samples from company N (all from moulders) to compare with similar samples from other companies. The data suggested that the workers from company N had similar concentrations of MbOCA in urine to companies using purely manual processes.

- Calculate the 90^{th} percentile of the MbOCA in urine concentrations and to evaluate the evidence for a revision of the BMGV.

The 90^{th} percentile for MbOCA in urine, using all available data, was calculated as 8.85 μmol/mol creatinine. Based upon the results from this study and other data held at HSL the current BMGV could be reduced. The data suggest that a BMGV of 10 μmol/mol creatinine would be conservative with a figure as low as 8 μmol/mol creatinine consistent with the data held at HSL.

- To investigate the isocyanate diamine concentrations in urine and the relationships between isocyanate diamine concentrations and jobs and isocyanate diamine concentrations and MbOCA concentrations in urine.

The urine samples were tested to determine the concentrations of 4 different diamines that can be derived from urinary metabolites of isocyanates. A total of 25 urine samples contained a quantity of diamine that was above the BMGV for isocyanates with 16 samples containing a concentration above the BMGV for TDA and nine samples above the BMGV for HDA. The urine sample from one individual had concentrations of both TDA and HDA above the BMGV. Although most cases of isocyanate-derived diamines above the BMGV were due to exposure to TDI, the concentration of HDA, when detected, tended to be at a higher level. Moulders and those classified as other non-specific exposure were identified as groups with the highest concentrations of both diamines in urine.

- Investigate the relationship between MbOCA in air and urine samples.

The data indicated no relationships between airborne levels of MbOCA and the concentration of MbOCA in urine and there were no cases where a worker had a urine concentration above the BMGV and an air sample, collected from their working environment, above the WEL.

- Investigate the relationship between surface and glove concentrations.

The data on gloves and surface samples were insufficient to test for a relationship. However, the data indicated that, in general, the levels of contamination on gloves were several orders of magnitude larger than the levels of contamination of surfaces.

- Investigate the relationship between MbOCA concentrations on inner and outer gloves.

The descriptions accompanying the samples did not, in general, allow the inner and outer glove samples to be matched (this was possible in only nine cases). Additionally inner glove samples were not taken from many companies. For one individual where samples could be matched both inner and outer samples had very high concentrations of MbOCA with 6.3 mg/glove measured on one inner glove and concentrations of 12.8 and 22.9 mg on outer gloves.

- Investigate relationships between MbOCA concentrations on surface and glove samples and MbOCA in air and urine samples.

The data were only detailed enough to allow an assessment of the relationship between glove samples and urine samples. The data suggested that there was a tendency for those with high of contamination of outer gloves (worn over inner gloves) to have higher concentrations of MbOCA in urine samples although other factors such as the length of time wearing the glove may be important and are not fully understood. However, whilst there may be a relationship between the level of contaminant on gloves and the concentration of MbOCA in urine the data from the study were not able to establish the nature of the relationship. Further detailed research would be required in order to identify whether absorption into the body occurs through the hands or as a result of poor PPE or hygiene.

- Investigate the concentrations of MbOCA on drums held in storage at two companies in the sample who distributed MbOCA and to assess if these differed from concentrations on drums in storage at the manufacturing companies.

The data were insufficient to use formal statistical methods however the data suggested that there were differences between the two distributors, companies R and T. Of the samples taken from the storage area of company R, over 30% of samples contained large concentrations of MbOCA whereas the few samples from company T that did contain traces of MbOCA were at a much lower level. The samples taken from storage areas of the companies using MbOCA were generally lower than those from distributors although the largest concentration of all came from company C.

5 REFERENCES

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6 GLOSSARY

MbOCA 4,4'Methylene-bis-(2-Chloroaniline)

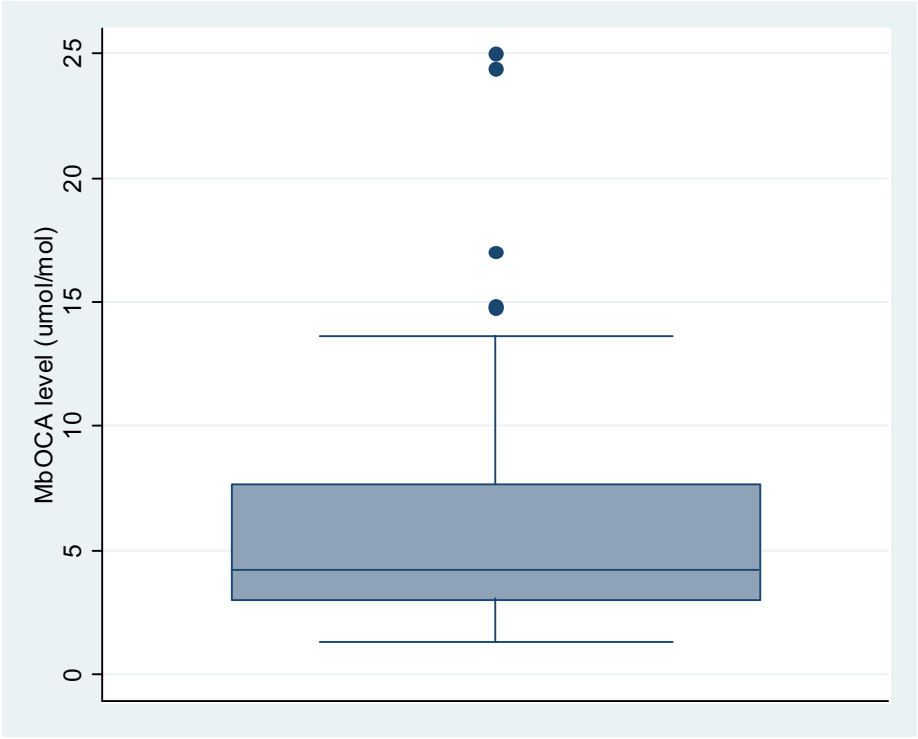
7 APPENDICES

7.1 INTERPRETATION OF A BOX-PLOT

A boxplot is an effective visual display of key summaries of a continuous variable and is particularly useful for displaying skewed data containing outlying (or unusual) observations, and for comparing two or more variables. The boxplots in this report are comprised of 4 elements.

- Median
- Quartiles – the 25th and 75th percentiles of the data
- Bounds of variability
- Outliers

The figure below using the MbOCA in urine readings is used to highlight these elements.



The 25th and 75th percentiles mark the bounds of the shaded area or 'box', the difference between these values being the interquartile range, which is a more reliable summary of dispersion than standard deviation for skewed data. The central line within the box is the median, an estimate of location that is more reliable than the mean for skewed data. The vertical lines or 'whiskers' that emerge from the box (above and below) indicate the maximum and minimum values unless outliers are present, in which case they extend to 1.5 times the interquartile range. The points that are beyond the 'whiskers' are outliers or unusual observations, seen in the above plot as the blue dots.