WORKING FOR A HEALTHY FUTURE

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Health, socio-economic and environmental aspects of possible amendments to the EU Directive on the protection of workers from the risks related to exposure to carcinogens and mutagens at work

4,4-Methylenedianiline (MDA)

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SUMMARY

4,4'-Methylenedianiline (MDA) has been classified by the International Agency for Research on Cancer (IARC) as possibly carcinogenic to humans based on sufficient animal toxicity (IARC category 2b). MDA is structurally similar to other chemicals that are known or suspected of causing bladder cancer and it is assumed it may have a similar mode of action. Under the classification and labelling legislation in Europe it is classified as a Cat 2 carcinogen and is therefore within the scope of the EU Carcinogens Directive. However, there is no occupational exposure limit (OEL) for MDA specified in the Directive. MDA is identified as a candidate "substance of very high concern" under the REACH regulations.

This report considers the likely health, socioeconomic and environmental impacts associated with possible changes to the Carcinogens Directive, in particular the possible introduction of an occupational exposure limit (OEL) of 0.8 mg/m^3 (0.1 ppm) or 0.08 mg/m^3 (0.01 ppm). MDA may be taken up into the body by inhalation and skin exposure and it is generally assigned a skin notation along with the numeric limit value.

MDA is an aromatic diamine used is used in the production of polyurethane foams and this accounts for 99% of the total quantity produced in the EU. In 2008, about 1.4 million tonnes of MDA was produced in the EU. MDA is also used as a hardener in epoxy resins and other adhesives, although these uses have been decreasing over time as alternative substances have been introduced.

It is estimated that there are between 70 and 140 people exposed to MDA in the EU chemical industry, primarily in the manufacture of polyurethane foam. The number of people potentially exposed in construction and other manufacturing is unknown, but could be between about 390,000 and 3.9 million people. MDA inhalation exposures are judged to be low. Exposure in 2010 was estimated to be at most 0.14 mg/m^3 during manufacture in the chemical industry and 0.07 mg/m^3 in other industrial sectors. There is more uncertainty about potential dermal exposure and there is very little quantitative information available to inform the assessment of exposure. However, it is likely that in the chemical industry dermal exposures are low and in other sectors exposure may be higher.

Information about the hazard from MDA is limited. It is carcinogenic in animal toxicity studies but there is no human epidemiological evidence that occupational exposure causes cancer. By analogy with other aromatic amines it is presumed that MDA may cause bladder cancer. However, we were unable to identify a suitable risk estimate. We have not undertaken a health impact assessment because of the uncertainties surrounding the hazard in humans and the exposures in construction and sectors other than chemical manufacturing.

We have not been able to assess the health benefits that might arise from setting an OEL, although we believe the impact of setting a limit at 0.8 or 0.08 mg/m^3 would be relatively small because of the low current estimated inhalation exposures. We judge that there would be no significant economic costs associated with complying with an airborne OEL. The cost of reducing dermal exposures, aggregated over the period 2010 to 2069, might range between about €1,400m and €29,000m. These high costs arise from the potentially large number of workplaces that might be affected (between about 60,000 to 600,000). There are also no social or macro-economic costs

associated with introducing an OEL or of introducing measures to reduce dermal exposure to MDA. There are no significant environmental impacts foreseen.

There are considerable uncertainties concerning estimates of skin exposure to MDA, although it seems this is probably the predominant route of exposure in most industry sectors. Given the potentially large number of people exposed in the EU it would be prudent to collect further MDA exposure data using biological and personal exposure monitoring.

1 PROBLEM DEFINITION

1.1 OUTLINE OF THE INVESTIGATION

4,4'-Methylenedianiline (MDA), which is structurally similar to MbOCA (2,2'-dichloro-4,4'-methylenedianiline) a known bladder carcinogen, is suspected of also causing bladder cancer. Exposure to MDA has been classified as Group 2b (possibly carcinogenic to humans) carcinogen by IARC[1]. It is also classified as a Cat 2 carcinogen in the EU under the classification and labelling legislation[2]. MDA is therefore currently regulated as a carcinogen in the EU. In addition, The European Chemicals Agency (ECHA) identified MDA as a "substance of very high concern" and it has been recommendation for inclusion in the list of priority substances in Annex XIV of the REACH Regulations, which would require authorisation of uses of this substance.

The key objectives of the present study are to identify the technical feasibility and the socioeconomic, health and environmental impacts of introducing a regulatory occupational exposure limits (OEL) for MDA of 0.8 mg/m^3 (0.1 ppm) or 0.08 mg/m^3 (0.01 ppm).

1.2 OELS/EXPOSURE CONTROL

Existing national occupational exposure levels (OELs) for MDA in EU member states, Switzerland and the US OSHA OEL are presented in Table 1.1. The OELs for 8hr-time weighted average (TWA) exposure levels differed by about a factor of ten (0.08 to 0.82 mg/m^3). Short Term Exposure Limit (STEL), i.e. 15 minutes, ranged from 0.2 in the Czech Republic to 1.6 in Denmark mg/m^3.

Many of these limits have an associated skin notation assigned and/or a biological monitoring limit value proposed, e.g. in the UK there is Biological Monitoring Guidance Value (BMGV) of 50 µmol total MDA/mol creatinine in urine (Post shift for inhalation and pre-shift next day for dermal exposure). There is evidence that skin contact with MDA is an important route of exposure, perhaps the predominant route for many work situations.

[1] Available at: http://monographs.iarc.fr/ENG/Classification/ClassificationsAlphaOrder.pdf
[2] Available at: http://ecb.jrc.ec.europa.eu/esis/

Table 1.1 Occupational Exposure Limits[3] for airborne MDA in some EU member states and the USA

Country	OEL - TWA (mg/m^3)	STEL (mg/m^3)
Austria	0.1	0.4
Belgium	0.82	
Bulgaria		
Czech Republic	0.1	0.2
Denmark	0.8	1.6
Germany	0.7[1] / 0.07[2,3]	
Hungary		0.81
Spain	0.82	
Netherlands	0.009	
Poland	0.08	0.4
Slovenia	0.1	
Slovakia	0.1	0.4
United Kingdom	0.08	
Switzerland		0.1
USA - OSHA	0.08	0.8

[1] Workplace exposure concentration corresponding to the proposed tolerable cancer risk.
[2] Workplace exposure concentration corresponding to the proposed preliminary acceptable cancer risk.
[3] When using a technique that represents the state of the art the target concentration will not be exceeded.

1.3 DESCRIPTION OF DIFFERENT USES

4,4'-methylenedianiline (MDA) is an aromatic diamine used as a precursor to 4,4'-methylenediphenyldiisocyanate (MDI), which is used in the production of polyurethane foams. MDA is synthesised by the reaction of formaldehyde and aniline in the presence of hydrochloric acid. It is sold in its pure state as flakes, granules or as a prill (EC, 2001).

The use of MDA in the chemical industry, as an intermediate in the production of MDI represents 99% of the total production volume (ENTEC, 2008). The remaining is used in pure state or in mixtures as a precursor in the manufacture of plastic fibbers, as a curing agent in the manufacture of epoxy resins, a hardener in adhesives, polyurethane co-reactants an antioxidant in rubber, high performance wire coatings, and lubricating oils, corrosion preventatives for iron under highly acidic conditions, and special polymers, an intermediate for dyes and in pigments and in defence applications[4].

In 2008, the annual tonnage of MDA produced in the EU was estimated in 1.4 million tonnes (ENTEC, 2008).

Other uses of MDA are in estimated to account for 5,000 tonnes per year (ENTEC 2008):

- Manufacture of high performance polymers (less than 5,000 tonnes/ year)

[3] Available at: http://bgia-online.hvbg.de/LIMITVALUE/WebForm_gw.aspx
[4] Available at: http://www.osha.gov/doc/outreachtraining/htmlfiles/mda.html

- As a starting point for the synthesis of 4-4, methylenbis(cyclohexaneamine) (H_{12}MDA or PACM), which is use in the synthesis of polyurethanes (no data)
- Hardener in epoxy resins (200 tonnes/ year)
- Hardener in adhesives (no data)

The use of MDA as a hardener in adhesives has been reduced (ENTEC, 2008) as some alternative materials have been introduced.

The use of MDA has increased in the EU from 503,000 tonnes in 1989 to 1.4 million tonnes in 2008, which correspond to an annual growth rate of 8% (ENTEC, 2008). Therefore annual production in 2010 is estimated in 1.8 million tonnes.

The geographical distribution of its production in EU is unknown. The following countries have been mentioned in the different reports consulted during the preparation of this document: UK (Cocker *et al* 1994, ENTEC, 2008), the Netherlands (Brouwer *et al* 1998, ENTEC, 2008), Belgium, Germany, Spain, Finland, Denmark, Hungary and Portugal (ENTEC, 2008). Other production countries are those with an OEL for MDA: Austria, Poland, Slovenia and Slovakia.

In 1989 the capacity of MDI production (tonnes/ year) in the EU was as follows:

- Germany: 146
- The Netherlands: 100
- Belgium: 86
- Italy: 70
- Portugal: 50
- UK: 45
- Spain: 6

A report by the UK HSE in 2006 stated that there are no producers of MDA in the UK but that approximately 2,500 tonnes/year are imported (HSE, 2006).

The annual tonnage in 2006 in Finland and Denmark is shown in Table 1.2 for each NACE code.

Table 1.2 Tonnage on use of MDA in 2006 (EC 2001)

NACE industry and code	Denmark	Finland
24- Manufacture of chemicals and chemical products		5.5
25- Manufacture of rubber and plastic products		
28- Manufacture of fabricated metal products, except machinery and equipment	0.3	15
29- Manufacture of machinery and equipment		15
31- Manufacture of electrical machinery and apparatus		
36- Manufacture of other transport equipment		
45- Construction		5
Total	**0.3**	**40.5**

Inhalation and dermal exposure is possible during MDA and MDI manufacture, and during the handling of technical grade MDA and other mixtures (EC, 2001). When used as an additive, for example as a hardener or a curing agent, the formulation (pure MDA or MDA mixture) is usually mixed (e.g. with resins for epoxies or polyurethane) immediately before use. Therefore exposure can occur in a wide range of industrial sectors, since MDA have applications in many fields. The EU RAR reported that exposure is usually higher in this skill trade sector than during manufacturing of MDA and MDI, mostly because exposure controls and personal protective equipment are not as established as in the chemical manufacturing sector.

Lewandowski *et al* (2005) indicated that MDA is also released in the production of polyurethane foam, during the polymerization of MDI.

MDA released from newly manufactured polyurethane products is believed to be insignificant as MDA has a very low pressure Lewandowski *et al* (2005).

1.4 RISKS TO HUMAN HEALTH

1.4.1 Introduction

Bladder cancer is the fourth commonest malignant neoplasm amongst men in Europe and the twelfth in women, accounting for over 35,000 deaths in Europe each year (Ferlay *et al*, 2007). The main environmental cause is cigarette smoking – both active smoking and from environmental tobacco smoke. Genetic factors are also important determinants of risk with first-degree relatives of bladder cancer patients have between two and six times increased risk of bladder cancer. Environmental factors, in addition to tobacco smoke, that are suspected of playing an important role in the development of bladder cancer include the presence of arsenic and disinfection by-products in drinking water, fluid intake, dietary factors (coffee and alcohol intake, artificial sweeteners), drugs (analgesics, cyclophosphamide and chlornaphazine), hair dyes and a number of urologic conditions (Silverman *et al*, 2006). Most cases of bladder cancer occur in people over the age of 75 years (only 2–4% of men and 0.5–1% of women have their bladder cancer diagnosed before this – Grasso; 2008).

In most European countries bladder cancer is at least three times more frequent in men than in women, which has been seen as suggestive of an important occupational contribution to risk (Parkin *et al*, 1992). Female rates have generally changed little from around 3.3 in the early 1970s to 2.9 in 2004, whereas male rates have shown a consistent fall since 1992, from 12.2 to 8.4 per 100,000 in the year 2004.

The highest incidence rates of bladder cancer amongst men in Europe occur in northern Italy and Spain (more than 30 per 100,000) with lower rates in United Kingdom, Germany, and France (20-25 per 100,000) (Grasso, 2008).

About 70% of patients survive for five years after diagnosis, with slightly poorer survival in women than men and better survival amongst younger patients (Grasso, 2008). Survival rates vary across Europe; highest in Finland, Germany, Sweden, Italy, and Spain – lowest in Estonia, the Czech Republic, Slovakia, Poland, Scotland, and Denmark.

There are a number of occupational exposures or exposure circumstances that have been classified by IARC as causes of bladder cancer in humans (Group 1). The identified agents include: aromatic amine dyes, benzidine, 2-naphthylamine, coal tars and pitches, polyaromatic hydrocarbons and mineral oils, (untreated and mildly treated). Exposure circumstances identified by IARC as a risk for bladder cancer are: aluminium production, auramine manufacture, magenta manufacture, boot and shoe manufacture and repair, coal gasification, coke production, working in the rubber industry and being a painter.

1.4.2 Summary of the available epidemiological and toxicological literature

MDA can cause cancer in rats and mice by ingestion, inhalation, or dermal absorption of the substance. There is some evidence that MDA is genotoxic.

Acute effects in humans

Several episodes of acute human exposure to MDA have resulted in hepatotoxicity producing jaundice including an incident in Epping in 1965 resulting from ingestion of bread made with flour contaminated with MDA during transport (Kopelman *et al,* 1966a). Eighty-four people had abdominal pain and some degree of jaundice. All patients had elevated serum bilirubin levels over 5 mg/100ml. Liver biopsies from 8 people showed an unusual liver lesion; all but 2 patients had complete recovery within several weeks (Kopelman *et al,* 1966b).

Nausea, abdominal pain muscle pain and vomiting were reported in 6 people who drank alcohol contaminated with MDA (Tillman, 1997). Williams *et al* (1974) reported symptoms in 6 workers involved in mixing powder containing MDA for surface coating walls with epoxy resins. Symptoms of clinical hepatitis appeared 2 days to 2 weeks after beginning work and included elevated bilirubin levels. All workers recovered.

Chronic effects in epidemiological studies

A two year follow up of 14 individuals from the Epping contaminated bread incident showed that 10 still had symptoms of some severity 7 to 23 months after onset including food intolerance, gastrointestinal disturbances, fatigue and visual disturbance (Kopelman, 1968). A follow-up in 1992 found that 18 had died but that the observed over expected ratios were less than 1 for cancers and non-neoplastic causes of death (Hall *et al*, 1992). There was one case of biliary duct carcinoma. In a further follow-up from 1965 to 2002 37 had died. The SMR for all causes of deaths was 65 (95% CI 46-89). There were 8 deaths from malignant neoplasms (SMR=60, 95% CI 26-118). One was from cancer of the gall bladder; there were no deaths from liver or bladder cancers.

A proportionate mortality study (PMR) was carried out of 179 white male workers in the blade and pattern shops of a manufacture of helicopters and helicopter parts who had been employed for 10 years or longer and had been assigned for at least one month in the area where there was potential exposure to epoxy resins and curing agents, including MDA (NIOSH, 1982). The concentrations of MDA in the air for three samples were: <19µg/m^3 for a 20 litre sample, 0.23µg/m^3 and 0.46µg/m^3. Statistically significant excesses of cancer of the bladder (PMR=3.74, p≤0.05, n=3), cancer of the large intestine (PMR=2.26, p≤0.05, n=7) and lymphosarcoma/reticulosarcoma (PMR=3.45,

p≤0.05, n=3) were found. In a proportional cancer mortality ratio (PCMR) analysis on cancer of the bladder remained significant (PCMR=3.41, p≤0.05). Two more cases of bladder cancer were found in exposed living workers. It was noted that workers were exposed to a number of other chemicals.

A historical cancer incident cohort study was carried out on 595 power generation workers in Sweden exposed primarily by the dermal route to an epoxy resin containing 35% MDA (Selden *et al,* 1992). The standardised incidence ratios (SIR) were less than one for all cancer sites, including for bladder cancer.

A follow up was carried out to 1991 of 10 individuals who had worked at a plant in Ontario that manufactured and epoxy concrete hardening material containing MDA and had suffered acute episodes of jaundice between 1967 and 1976) (Liss and Guirguis, 1994). One case of bladder cancer was diagnosed in 1990 giving an SIR of 19.3 (95% CI 0.5-107). Smoking histories were unknown.

1.4.3 Choice of risk estimates to assess health impact

The evidence of carcinogenicity in humans is sparse and somewhat contradictory. However, the animal evidence, the suggestive human evidence and the fact that MDA is structurally related to benzidine and MbOCA, which are known or suspected human bladder carcinogens, has led to the suggestion that the carcinogenicity of MDA on the human urothelium cannot be ruled out. However, in our view the human evidence is insufficient to make a reliable assessment of the risk amongst the exposed working population in Europe.

In the EU Risk Assessment Report a T25 dose (the dose giving a 25% incidence of cancer in an appropriately designed animal experiment) was identified for both inhalation and dermal routes. They wrote that, “For workplace risk assessment a T25 of 12 mg/m^3 was calculated. It was assumed that the higher sensitivity of humans concerning liver toxicity applies to carcinogenic potency as well. There are no further data to clarify species differences concerning carcinogenicity. If there is no species difference at all the T25 might be up to one order of magnitude greater than calculated above (EC, 2001).” For dermal exposure a, “T25 of greater than 250 mg/person/day was calculated. Again, it was assumed that humans are more sensitive than rats and that there may be a genotoxic mechanism (EC, 2001).”

Non-malignant adverse health effects of importance are the hepatotoxic and dermatological effects (allergic contact dermatitis) resulting from exposure to MDA, although these have not been considered in detail in this document.

2 BASELINE SCENARIOS

2.1 STRUCTURE OF THE SECTOR

MDA is manufactured at several sites in Europe, primarily as a raw material for the production of MDI, and in a variety of other industries where the use is likely to be less well controlled than in the primary manufacturing sector.

2.2 PREVALENCE OF MDA EXPOSURE IN EU

The prevalence of exposure has not been estimated by CAREX. Information from the European industry was also not available.

Manufacture of chemicals and chemical products (NACE code 24)

MDA production has tripled since 1993 and the EU RAR indicates that growth in MDA production has occurred through expansion of existing sites rather than the creation of new factories.

However, the number of MDA manufacturing sites has decreased since 1989. The EU RAR mentions there were 15 companies in 1989 in the EU in the field of production and further processing of MDA in the chemical industry. The report by ENTEC (2008) indicates that production, as reported by the European trade association for producers of diisocyanates and polyols (ISOPA, 2003) has stopped at three of the sites. ECHA (2008) indicated that ISOPA pointed out that there are 5-6 companies producing MDA and MDI in the EU but the exact number and location of the production sites in unknown. So, we assumed that the manufacturing sites are still located in the same countries as those indicated by ENTEC (2008) in 1989 (UK, the Netherlands, Belgium, Italy, Germany, Spain, Finland, Denmark, Portugal), in addition to those countries where there is an OEL (Austria, Poland, Slovenia and Slovakia).

The manufacture of MDI (for which MDA is needed) is believed to occur on the same production sites as MDA is produced (ENTEC, 2008).

We estimated the prevalence of exposure based on information on the annual tonnage and prevalence of exposure of propylene oxide, as this compound is manufactured in a similar way to MDA. The EU RAR estimated that 35-70 workers are potential exposed during the manufacture of propylene oxide and that the annual tonnage in 2009 was 2.02 million (EC, 2002). The estimated annual production of MDA in 2010 is 1.8 million tonnes. Therefore, it seems reasonable to suppose that the number of workers exposed to MDA is similar to those involved in the production on propylene oxide. We have indicated earlier than the production of MDI occurs at the same facilities where MDA is produced. However, it is likely that different workers are involved in the production of both substances. Since, 99% of the total MDA is used for MDI production, we assumed a similar number of workers are exposed in the production of MDI. Therefore, we estimate that there are a total of 70-140 workers exposed to MDA in the UK, the Netherlands, Belgium, Italy, Germany, Spain, Finland, Denmark, Portugal, Austria, Poland, Slovenia and Slovakia. The distribution of these workers across these countries is unknown.

Across the EU the number of female workers in the manufacturing industry is 30% and the number of males is 70%[5]. Therefore it is estimated that 10-42 employees are female and 25-98 are male.

[5] Available at:
http://epp.eurostat.ec.europa.eu/portal/page/portal/european_business/data/database

Other industrial sectors (NACE code 25, 28, 29, 31, 35, 45)

The number of exposed employees in these industry sectors is unknown. It is likely that the prevalence of exposure in these industries is larger and more widespread across the EU than in the manufacturing industry, as there are a larger number of MDA users than manufacturers. Despite, only 5,000 tonnes/year being employed in these uses, dermal exposure may be high and exposure is not as well controlled as in the chemical/manufacturing industry (EC, 2001).

Exposure is likely to occur in all sub-sectors in the manufacture of rubber and plastic, since exposure occurs during polyurethane curing and rubber processing[6]. The US OSHA[6] indicates that there is a potential for exposure during filament winding, moulding/bolding of tools, wire coating, application of heat and chemical coatings (e.g. in pipes, concrete floors, etc.…), coatings of printed circuit boards. These activities are typical in all sub-sectors of the manufacture of metal products (NACE code 28), machinery (NACE code 29) and electrical machinery (NACE code 31). Therefore we considered there is a potential for exposure in all the sub-sectors. Exposure also occurs during the manufacture of aircraft, automobiles, bicycles and boats, so all sub-sectors in NACE code 35 were estimated to involve potential exposure. In the construction industry we considered that there is a potential for exposure during building installation (NACE code 45.3) and building completion (NACE code 45.4).

We assumed that in these industries all workers in the following International Standard Classification of Occupations (ISCO) occupational groups are potentially exposed:

i) 300 Technicians and associate professionals
ii) 720 Metal machinery and related trades workers
iii) 820 Machine operators and assemblers.

The assumption that everyone in these sectors in exposed is an overestimate since not everyone will be in contact with MDA and because of the nature of the uses contacts are unlikely to occur each day.

The proportion of workers in the above occupational groups in NACE group D (Manufacturing) and G (Construction) was obtained from the Labour Force Survey available on the EUROSTAT database.[7] These proportions were applied to the total number of workers employed for each NACE code in 2006, unless otherwise indicated (Table 2.1).

Data for Malta was not available in the Eurostat database. Estimates on number of employees for this country was estimated based on the number of exposed employees in countries with similar figures for the GDP contribution from industry and number of people working in industry. Information on these figures as well as on whether there was industrial activity in the country was obtained from the factworld section in the CIA website[8]

[6] Available at: http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=PREAMBLES&p_id=992
[7] Available at: http://epp.eurostat.ec.europa.eu/portal/page/portal/eurostat/home/
[8] Available at: https://www.cia.gov/library/publications/the-world-factbook/

We estimated there are up to 3.9 million workers exposed in these industrial sectors, although it could be as little as 390,000 exposed.

The estimated number of male and female employees in each industry group in each EU member state is shown in Appendix 8.1. The estimates were obtained by applying the average male to female employee ratio for the industry group for each country to the total number of employees. Male to female employee ratios were calculated with data from the Labour Force Survey. Managers, salespeople and office clerks were excluded from these calculations as they were assumed to be unexposed.

Table 2.1 Exposure prevalences by NACE code and country

	NACE Code							
Country	**25**	**28**	**29**	**31**	**35**	**45.3**	**45.4**	**Grand Total**
Austria	6,894	17,584	19,991	6,834	2,778	5,638	3,827	**63,547**
Belgium	6,841	17,201	11,064	4,617	2,390	3,257	3,116	**48,486**
Bulgaria	8,502	14,900	25,063	7,834	4,033	1,681	1,087	63,100
Cyprus[1]	243	780	209	83	30	250	123	1,717
Czech Republic	35,316	69,588	68,009	48,131	9,062	5,464	3,860	239,430
Denmark	6,324	14,474	19,115	7,303	2,403	3,134	3,709	56,461
Estonia	2,059	5,161	2,220	2,496	1,135	405	97	13,574
Finland	4,940	14,876	18,839	5,649	3,452	3,236	1,166	52,159
France	67,028	124,514	88,677	43,694	43,033	44,985	48,105	460,036
Germany	97,047	202,166	270,715	133,025	35,725	20,858	15,091	774,628
Greece	3,099	10,631	6,020	2,120	3,690	863	775	27,200
Hungary	16,636	30,205	27,809	27,993	3,276	3,431	1,889	111,240
Ireland	2,777	3,629	3,207	2,098	1,051	663	169	13,595
Italy	57,412	202,110	162,050	52,753	30,972	21,096	15,036	541,429
Latvia	1,109	2,340	1,742	862	1,307	1,315	1,155	9,829
Lithuania	1,787	3,457	2,049	1,233	1,351	1,679	965	12,521
Luxembourg[2]	2,797	1,930	1,085	213	13	305	211	6,553
Malta[3]	NA[5]	NA	NA	NA	15	122	60	197
Netherlands	7,697	23,188	21,092	4,069	5,925	5,945	4,206	72,121
Poland	44,969	83,026	61,969	32,054	21,249	11,151	5,904	260,323
Portugal[4]	7,195	24,579	13,269	6,863	2,957	4,585	3,102	62,550
Romania	17,870	39,008	39,226	31,867	22,910	46,292	9,773	206,946
Slovakia	8,015	13,252	17,421	17,699	2,812	697	215	60,111
Slovenia	6,060	15,189	12,104	6,759	1,185	908	1,009	43,215
Spain	40,218	125,872	64,861	29,361	19,431	21,712	19,108	320,563
Sweden	11,083	32,958	45,425	9,549	8,614	7,978	3,968	119,575
United Kingdom	53,710	85,825	71,758	32,251	37,982	12,435	7,515	301,475
Total	517,628	1,178,445	1,074,989	517,410	268,781	229,665	155,140	3,942,581

[1] Data for NACE code 45.3 is from 2005
[2] Data for NACE code 31 is from 2002
[3] Data based on data from Cyprus
[4] Data for NACE code 35 is from 2005
[5] NA = Not Available

Classification of Industries by Exposure Level

A list of the type of manufacturing industries that use pure MDA or MDA mixtures in the EU was obtained from the ENTEC report (2008) and OSHA information on MDA[9]. This list with the corresponding NACE codes and an evaluation of the degree of inhalation and dermal exposure is shown in Table 2.2.

MDA exposure has been classified as low, medium or high using the exposure information provided in the European Risk Assessment Report (RAR) (EC, 2001). The German Federal Institute for Occupational Safety and Health who prepared the risk assessment report indicated that according to the criteria used under Directive 793/93 inhalation exposure was of negligible concern in most scenarios but dermal exposure was of concern in all scenarios (ECHA, 2008).

Note that dermal exposure was assessed under the assumption that PPE (gloves) were not worn.

Table 2.2 Classification of industries by exposure levels

Industry	NACE (rev 1.1)	Exposure Level (inhalation)	Exposure Level (dermal)
Manufacture of chemicals and chemical products	24	low	low
Manufacture of rubber and plastic products	25	low	medium
Manufacture of fabricated metal products, except machinery and equipment	28	low	medium
Manufacture of machinery and equipment	29	low	medium
Manufacture of electrical machinery and apparatus	31	low	medium
Manufacture of other transport equipment	35	low	medium
Construction	45	low	medium

2.3 LEVEL OF EXPOSURE TO MDA

2.3.1 Estimation of exposure levels

Inhalation exposure

MDA has a low vapour pressure (<<1 Pa) and so inhalation of MDA vapour is not relevant. Exposure to MDA as an airborne dust is the main focus for this assessment.

[9] Available at: http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=PREAMBLES&p_id=992

The EU RAR (EC, 2001) provides information on inhalation exposure collected in 13 companies in the chemical industry during the 1990s. The Geometric Mean (GM) exposure level is provided for each job activity at each of the companies, where data was available. The total number of measurements was almost 650. Inhalable MDA concentration (GM) ranged from below the limit of detection (0.001 mg/m^3) to 0.43 mg/m^3 (note, that the report contains repeat measurements at this plant made a few years later where the GM MDA level was 0.002 mg/m^3). This reduction was attributed to modifications made to the technical ventilation systems). The next highest GM exposure level, which was 0.08 mg/m^3, was for a manufacturing plant in 1992. In 18 instances the GM was below the limit of detection (LOD). Only limited information on the type of samples (personal, static), duration of the measurements or the 95th or the measured data was provided.

For risk assessment purposes the EC estimated an inhalation exposure of 0.52 mg/m^3 for manufacturing in the chemical industry and of 0.6 mg/m^3 or less for manufacturing in industrial areas, although it was acknowledge that for the latter the workplace was not at the state of the art and that these data represented the maximum likely level of exposure. For other exposure scenarios (not involving MDA manufacture) the inhalation exposure levels reported by EC (2001) were estimated using the EASE model or by expert judgment. These were classified as "very low" up to 0.3 mg/m^3 (handling formulations up to 10% MDA in powder). Data reported by Chemie (1997), obtained during processing of epoxy and polyurethane resins and coatings for solder-masks, also showed low exposure. The tasks where measurements took place involved preparing and mixing the components, spraying, pouring, pressing and painting of the mixture. The TWA exposure levels were below the LOD (<0.001 mg/m^3).

Some studies have reported MDA exposure levels for users of MDI-containing products, although concentrations were generally in the range 0.002 – 0.2 mg/m^3. Rosenberg *et al* (2002) found MDA in urine samples from workers welding district heating pipes insulated with MDI-based polyurethane. Creely *et al* (2006) examined air concentrations of all isocyanates (consisting of TDA, 2,6-TDA, HAD, and MDA) in 22 manufacturing sites in the UK that used isocyanates to produce moulded polyurethane products, insulation material and those involved in industrial painting. From 120 samples only 20 showed MDA concentrations above the LOD (0.0001 mg/m^3). Concentrations ranged from 0.0005 (1/2 of the LOD) to 0.0029 mg/m^3.

Assuming the maximum inhalation exposure levels in the 1990s were 0.6 mg/m^3 for manufacture of MDA or preparations containing MDA and below 0.3 mg/m^3 in other uses (EC, 2001), and that levels have decreased by 7% per year (Creely *et al* 2007), exposure estimates in 2010 are estimated to be at most 0.14 mg/m^3 during manufacture (NACE code 24), and 0.07 mg/m^3 in other industrial sectors.

Dermal exposure

Dermal exposure is considered to present a risk. The EU RAR report (EC, 2001) predicted dermal exposure levels using the EASE model, assuming an exposed area of 840 cm^2 (both hands). The predicted exposure concentrations are shown in Table 2.3.

Table 2.3 Relevant dermal exposure estimates for MDA made using the EASE model (EC, 2001)

	Form of exposure	Duration	mg/day
Chemical industry			
Manufacture and further processing	Flakes (dust)	Shift length	42-420
	Liquid (60% vapour approximately)	Shift length	25-252
Production of preparations:			
10%MDA	Powder (dust)	2hrs/day	4-42
60%MDA	Flakes (dust)	2hrs/day	25-252
5%MDA	Flakes (dust)	2hrs/day	2-21
Industrial area			
Manufacture of formulations	Powder (dust)	2hrs/day	42-420
	Liquid	2hrs/day	25-252
Production of preparations			
Preparations 10%MDA	Powder (dust)	2hrs/day	4-42
Curing of formulations: 60%MDA			
5%MDA	Flakes (dust)	2hrs/day	25-252
	Flakes (dust)	2hrs/day	2-21
Mixing curing formulations (max 60%MDA) with resins for epoxies	Flakes (dust)	0.5 hrs/day	50-504
Handling of formulations (4.5-30%)	Liquid	0.5 hrs/day	50-504
		Shift length	25-252
Mixing curing formulations (max 5%MDA) with resins for polyurethanes	Flakes (dust)	0.5 hrs/day	4.2-42
Handling of formulations containing MDA and polyurethane (2-3 %)	Liquid, pastes	Shift length	2.5-25
Handling formulation containing (0.1-10 % and amid resins)	Powder	0.5 hrs/day	8.4-84
	Paste	Shift length	8.4-84
Skilled trade			
Mixing of formulations containing MDA (9-60% with epoxy resins	Flakes (dust)		504-2,520
Handling of formulations containing MDA and epoxy resins (4-30%)			250-1,260

Exposures predicted by the EASE model are relatively high. However, the EASE model has been reported to overestimate measured exposures. Hughson and Cherrie (2005) reported that EASE predictions of exposure to Zn were 50 times greater than measured exposures, based on a comparison of the single-point GM exposures with the midpoint. In addition, the EASE estimates take no account of the protective effects of wearing protective clothing or gloves in reducing exposure.

Brouwer *et al* (1998) used hand washing (removal) techniques, glove (interception) samplers and biological monitoring to assess exposure in a plant producing glass fibre reinforced resin pipes in the Netherlands (mixing formulations containing 12% of MDA). They reported the GM exposure using the glove monitor between 81 and 1,762 µg MDA and from 84 to 1,783 µg MDA for hand wash samples. The highest individual hand exposure result was 4 mg MDA. The level of MDA in 24-hour urine samples ranged from 0.008 to 0.249 mg MDA. The authors found that the cumulative hand wash data and the MDA urinary excretion results over a week were highly correlation (r^2=0.94), which suggests that dermal exposure was the predominant route of exposure. Brouwer *et al* estimated that 8% of the dermal MDA exposure was absorbed.

In the absence of more extensive information it is not possible to estimate typical dermal exposure levels. The data from Brouwer *et al* (1998) are much lower than the exposure assessments made using EASE (Table 2.3) and this suggests that these data overestimate actual exposure by a considerable margin.

Cocker *et al* (1994) describe a cross-sectional biological monitoring survey of UK industry manufacturing or using MDA. They surveyed workers in 45 factories representative of nine work activities: manufacturing and formulation, paint making, formulation and packing, pattern and tool making, composite materials, potting and encapsulation, casting and moulding, miscellaneous and unknown. 91% of post shift and 88% pre-shift urine samples contained less than 50nmol/mmol. About 42% of the urine samples had no detectable MDA.

Summary exposure

The predominant route of exposure for MDA is most likely to be from skin contact rather than inhalation. Currently 4 million workers are estimated to be potentially exposed to MDA. A maximum of 140 employees in the manufacture sector (NACE code 25) who are likely exposed to very low concentrations and up to about 3.9 million people are exposed to higher concentrations.

2.3.2 Temporal change in exposure

It is likely that inhalation exposure to MDA has always been low; the highest measured exposures from the 1990s are around 0.5 mg/m^3. We have assumed that levels have decreased by 7% per year based on a general review of changes in exposure level over time (Creely *et al* 2007). There is very limited data on dermal exposure, although it seems probable that dermal exposures were higher in the past. However, it is not possible to quantify how much worse past exposures were in comparison to current exposure levels.

2.4 HEALTH IMPACT FROM CURRENT EXPOSURES

There is insufficient human data to enable the health impact assessment to be carried out. It is likely that there are a relatively large number of people who are potentially exposed to MDA on a regular basis, although we have insufficient information to make a reliable assessment of the number who may have exposure above a background level. It seems probable that inhalation exposures are relatively low but there is uncertainty about the level of dermal exposure that workers may experience.

2.5 POSSIBLE COSTS ASSOCIATED WITH NOT MODIFYING THE DIRECTTIVE

2.5.1 Health impacts – possible costs under the baseline scenario

There is insufficient information to make an assessment of the health costs.

3 POLICY OPTIONS

3.1 DESCRIPTION OF MEASURES

Methods that are effective in controlling worker exposure to MDA, depending on the feasibility of implementation, are those typical industrial hygiene control measures:

i) Process enclosure;
ii) Local exhaust ventilation (LEV);
iii) General dilution ventilation;
iv) Personal protective equipment (PPE), particularly respiratory protection and personal protective clothing including gloves.

Monitoring programs and/or continuous detectors to detect emissions are also used.

3.2 LEVEL OF PROTECTION ACHIEVED (OELS)

OELs in the EU are quite variable ranging from 0.08 in the UK to 0.82 mg/m^3 in Denmark for 8-hr TWA exposure. We have estimated that exposure during manufacture of MDA is less than 0.14 mg/m^3 and 0.07 mg/m^3 for use of products containing MDA, both as a conservative estimates. Therefore, is likely that all exposure current inhalation exposure levels would be below an OEL set at 0.8 mg/m^3 and that exposure in situations where preparations containing MDA are used the levels are likely below an OEL set at 0.08 mg/m^3. There may be low to moderate dermal exposure in all industry sectors.

Exposure Control Systems

Current exposure control methods in the manufacturing industry include the use of closed system with exhaust ventilation for the mixing MDA with other products and use of PPE (EC, 2001, BAuA, 2000). The EU RAR (EC, 2001) indicates that all employees are provided with suits, safety shoes, protective glasses and protective gloves. The use of PVC and chloroprene are recommended. However, there is a lack of information on the suitability of those materials (EC, 2001).

The German Federal Institute for Occupational Safety and Health (BAuA, 2000) highlighted that there is a need for process technologies to be developed further in the manufacturing industry. In addition, leak tightness and MDA permeability tests should also be carried out to ensured effectiveness of the gloves. A manufacturing facility in Germany indicated that pumps for MDA are leak-proof and as a rule MDA is transported through pipes directly to the further processing (EC, 2001).

There is less information on the exposure controls in the skill trade sector. The report by BAuA (2000) indicates that exposure controls are less effectively used than in the manufacturing sector. The main reasons are attributed to the lack of financial means (as most traders are small companies) and a lack of knowledge on the risk of exposure. The only protection strategy that has been successful has been to substitution of MDA with a safer chemical.

The ENTEC report (2008) indicates that the use of alternative compounds to MDA have been explored and amines or aliphatic amines could be use as curing agents but the authors highlighted that no specific information was found in the review.

Toluene diisocyanate (TDI) has been suggested as a possible substitute for the use of MDA in the synthesis of MDI which is itself used in the manufacture of polyurethanes. (ENTEC, 2008). Alternative compounds have been developed for the use of MDA as hardener in adhesives. For the other non-MDI manufacturing uses a literature review carried out by ENTEC was inconclusive.

4 ANALYSIS OF IMPACTS

4.1 HEALTH IMPACTS FROM CHANGES TO THE EU DIRECTIVE

4.1.1 Health information

There are no health impacts estimated for the possible interventions.

4.1.2 Monetised health benefits

As it is not possible to estimate the possible reduction in cancer registrations and life years lost from reduced dermal exposure, it is therefore not possible to produce monetised health benefits.

4.2 ECONOMIC IMPACTS

As set out in Table 2.2 it is estimated that the risks of inhalation exposure to be low across all sectors affected as exposures are already well controlled. Therefore it is reasonable to assume that there is not estimated to be any significant economic costs associated with an airborne OEL.

This section therefore focuses on the possible economic costs associated with full compliance with reducing dermal exposure. Since a specific EU wide biological monitoring value has not been proposed (due to a lack of data) economic costs are based on the general costs associated with improved training, enclosure, housekeeping, personal protective equipment (PPE), which in any case would be considered to be 'best practice', but as set out in section 3.2 are not necessarily standard practice.

4.2.1 Operating costs and conduct of business

Compliance costs

In Section 2.2 the numbers of workers potentially exposed to MDA were estimated to be:

- 70-140 in the EU from the production of MDA; and
- 3.9 million workers from the use of MDA in a variety of uses (a large use being the manufacture of rubber and plastic (e.g. polyurethane curing and rubber processing) as well as other uses (e.g. filament winding, moulding/bolding of tools, wire coating, application of heat and chemical coatings (e.g. in pipes, concrete floors) and coatings of printed circuit boards.

It is recognised that the estimate of 3.9m is an overestimate which is based on the sum of certain job occupations. However, it is very difficult to get a better estimate due to a lack of data. The 3.9m is therefore used as a high estimate and 10% (390,000 workers) is used as a low estimate. It is hoped that the true level of exposure is somewhere within this range.

Based on the number of workers potentially exposed and using a Eurostat data on the number of enterprises, it is estimated that between 61,659 to 616,585 enterprises could be affected. This is set out below (Table 4.1).

Table 4.1 Estimates of the number of enterprises affected

No: of employees bands	Average number of workers per class size (rounded)	Average composition of enterprises for all affected NACE sectors that use MDA*	Number of workers potentially exposed		Estimated number of enterprises affected by band size	
			Low	High	Low	High
Between 1 & 9	5	74%	287,066	2,870,658	57,413	574,132
Between 10 & 19	15	11%	42,913	429,127	2,861	28,608
Between 20 & 49	25	8%	30,392	303,921	1,216	12,157
Between 50 and 250	150	6%	23,352	233,522	156	1,557
Greater than 250	500	2%	6,277	62,771	13	126
Total	-	-	390,000	3,900,000	61,658**	616,579**

Notes:
* - The average composition of enterprises within each category is based on Eurostat data for NACE code sectors: 24,25,28,29,31,35,45. It is not known whether more exposures occurs in one NACE sector over another and therefore no weightings have been used to determine the average number of workers per enterprise.
** - Numbers exclude the number of enterprises manufacturing MDA who are potentially exposed. This is estimated to between 1 (low) and 6 (high).

There are expected to be relatively low costs for enterprises to implement improved training, enclosure, housekeeping, PPE, which in any case would be considered to be 'best practice'. It is assumed that these costs range between €1,000-2,000 per year per enterprise (including costs of equipment and the cost of time spent on e.g. cleaning and administration).

As illustrated in the Table 4.2, the total compliance cost over the assessment period is estimated to be between €62 to €1.2 billion per year which is estimated to be €1.4-29 billion in total over the period 2010-70 (in 2010 prices and discounted using a 4% discount rate).

Table 4.2 Estimated cost of compliance (2010 prices)

Number of enterprises affected		Annual cost per enterprise (2010)		Total annual cost in millions (2010)		Total cost 2010-2070 in millions*	
Low	High	Low	High	Low	High	Low	High
61,659	616,585	€ 1,000	€ 2,000	€ 62	€ 1,233	€ 1,451	€ 29,015

*- Costs over time have been discounted using a 4% discount rate

The high costs reflect the large number of people potentially exposed (up to 3.9m) although the high cost estimate is expected to be a significant overestimate.

Conduct of employers

The introduction of a possible EU-wide biological monitoring value may require certain enterprises to reorganise their workplace to ensure that exposure to MDA is minimised. Additional training and supervision of personnel handling the substance may be required to ensure that employees minimise their exposure by adhering to good practice in order to reduce exposure (e.g. good personal hygiene, wearing protective clothing, improved cleaning procedures and safety instructions). In particular, this relates to improved practices to reduce dermal exposure.

Potential for closure of companies

The cost of compliance per enterprise (€1-2k) is not thought to be prohibitive for any enterprise size and therefore there is not expected to be any potential risk of closures.

Potential impacts for specific types of companies

The exposure assessment (see section 2) suggests poor use and maintenance of PPE, poor housekeeping, poor training and inadequate health surveillance in certain companies when using MDA. Companies that do not currently implement 'best practice' procedures will be affected more by the implementation of an EU-wide biological monitoring value than those who already have adhere to such procedures. There is no information available on the types of companies that would be specifically affected most (e.g. smaller rather than larger companies, those in specific regions or those undertaking specific activities).

Administrative costs to employers and public authorities

Seven European Member States have an existing regulatory long-term OEL in place. However, these OELs are based on concentrations in air and, given the importance of dermal exposure, an EU-wide limit set as a biological monitoring value would be more appropriate.

This would require Member States to measure workers' urine concentration of MDA rather than airborne levels of MDA in the workplace. There may therefore be additional administrative costs as reporting structures may need to be altered and advice provided to companies to provide them with necessary information. Alternatively, the European Commission may decide to provide advice which could result in some cost-savings for national authorities.

Enterprises that already have urine sampling, monitoring and reporting systems in place will not be subject to any additional administrative costs. However, certain enterprises may not already be conducting biological monitoring under the baseline. The process of collecting samples may be fairly simple (sample bottle supplied by the laboratory, basic instructions given to workers and samples then returned to a laboratory). It is estimated that the cost of analysis per sample would be approximately €50/ worker and that monitoring of workers would take place once every five years[10].

[10] Estimate based on expert judgement from IOM (2010).

Third countries

Since it is not expected that the introduction of an EU-wide biological monitoring value will have a noticeable impact on companies, there is not expected to be any significant impact upon third countries such as through redistribution of investment, jobs or sales.

4.2.2 Impact on innovation and research

As set out in section 3.2 the German Federal Institute for Occupational Safety and Health (BAuA, 2000) highlighted that there is a need for process technologies to be developed further in the manufacturing industry. In addition, leak tightness and MDA permeability tests should also be carried out to ensured effectiveness of the gloves. A manufacturing facility in Germany indicated that pumps for MDA are leak-proof and as a rule MDA is transported through pipes directly to the further processing (EC, 2001).

Therefore it is possible that introducing an EU wide biological monitoring value for MDA that this will stimulate further R&D in protective equipment and improvements in the safe use of MDA to minimise risks of dermal exposure.

4.2.3 Macroeconomic impact

Whilst there is expected to be a significant investment (€1-29bn) in protective equipment, training and general best practice in reducing risks of dermal exposure from the use of MDA (and products containing MDA) if a an EU wide biological monitoring value is introduced, this is expected to have a negligible macroeconomic impact since costs will be spread all over the EU (e.g. construction activities is applicable to all Member States) and insignificant compared to for example the total value of goods and services in the manufacturing sector of €5trillion in 2006.

4.3 SOCIAL IMPACTS

4.3.1 Employment and labour markets

There are not expected to be any noticeable changes to the numbers of workers required as a result of introducing an EU-wide biological monitoring value. However, job patterns may be altered as it is recognised that in order to meet best practice, behavioural change amongst employees and updating health and safety training will be required.

4.3.2 Changes in end products

There are not expected to be any noticeable changes to the end products since control measures do not change the characteristics of the product and since there is not expected to be any closure of companies, there should not be any change in supply of products relative to the baseline scenario.

4.4 ENVIRONMENTAL IMPACTS

As set out in the EU RAR (EC, 2001) there are not expected to be any significant releases to air, water and aquatic environment. Since the proposed control measures

should not affect end-uses or production quantity, there is not expected to be any significant change in environmental impacts relative to the baseline scenario.

5 COMPARISON OF OPTIONS

The main identified impacts of control measures to reduce dermal exposure. Since a specific EU wide biological monitoring value has not been proposed (due to a lack of data) impacts are based on the general costs and benefits associated with improved training, enclosure, housekeeping, personal protective equipment (PPE), which in any case would be considered to be 'best practice', but as set out in section 3.2 are not necessarily standard practice.

Table 5.1 Comparison of health impacts by scenario

Baseline Scenario		**Introduce 'best practice' control measures**	
Health Costs	**Health Benefits**	**Health Costs**	**Health Benefits**
The predominant route of exposure for MDA is most likely to be from skin contact rather than inhalation. Currently 4 million workers are estimated to be potentially exposed to MDA. Due to insufficient exposure data it has not been possible undertaken a health assessment.	There is expected to be health benefits without further intervention as it is assumed that levels will continue to decrease by 7% per year based on a general review of historical changes in exposure level.	There is expected to be any decline in health costs from the introduction of best practice measures to reduce dermal exposure	Due to insufficient exposure data it has not been possible undertaken assess the benefits of introducing best practice measures to reduce dermal exposure.

Note: Costs and benefits under the intervention options are relative to the baseline scenario (i.e. are not absolute impacts but differences)

Table 5.2 Comparison of economic impacts by scenario (Present Value – 2010 €m prices)

Baseline Scenario		Introduce 'best practice' control measures	
Economic Costs	**Economic Benefits**	**Economic Costs**	**Economic Benefits**
There is expected to be a 7% decline in exposure per year with some firms incurring costs on control dermal exposure (improved training, enclosure, housekeeping and use of PPE) which in any case would be considered to be 'best practice'. It is assumed that these costs range between €1,000-2,000 per year per enterprise (including costs of equipment and the cost of time spent on e.g. cleaning and administration).	-	It is estimated that between 61,659 to 616,585 enterprises could be affected. This is highly uncertain given a lack of exposure data. The total compliance cost over the assessment period for firms introducing measures earlier than maybe planned, is estimated to be around €62 to €1.2 billion per year which is estimated to be €1.4-29 billion in total over the period 2010-70. Some of these costs will have been incurred under the baseline but perhaps much later than with the introduction of 'best practice' control measures.	Having more consistent EU-wide controls should remove any EU competitive distortions between EU Member States with different limits.

Note: Costs and benefits under the intervention options are relative to the baseline scenario (i.e. are not absolute impacts but differences)

Table 5.3 Comparison of social impacts by scenario

Baseline Scenario		Introduce 'best practice' control measures	
Social Costs	**Social Benefits**	**Social Costs**	**Social Benefits**
There are not expected to be any noticeable social impacts under the baseline scenario at an EU level. At an installation level, some personnel may change their working practices (e.g. wearing PPE) to reduce risks of dermal exposure regardless of further intervention over the period 2010-2070.		There are not expected to be any noticeable changes to the numbers of workers required as a result of introducing an EU-wide biological monitoring value. However, job patterns may be altered as it is recognised that in order to meet best practice, behavioural change amongst employees and updating health and safety training will be required.	

Note: Costs and benefits under the intervention options are relative to the baseline scenario (i.e. are not absolute impacts but differences)

Table 5.4 Comparison of macro-economic impacts by scenario

Baseline Scenario		Introduce 'best practice' control measures	
Marco-economic Costs	**Marco-economic Benefits**	**Marco-economic Costs**	**Marco-economic Benefits**
There are not expected to be any noticeable macroeconomic impacts under the baseline scenario.		Since compliance with an OEL would not involve changing the current manufacturing or agricultural process there is unlikely to be any significant change to macro-economic impacts.	

Note: Costs and benefits under the intervention options are relative to the baseline scenario (i.e. are not absolute impacts but differences)

Table 5.5 Comparison of environmental impacts by scenario

Baseline Scenario		Introduce 'best practice' control measures	
Environmental Costs	**Environmental Benefits**	**Environmental Costs**	**Environmental Benefits**
As set out in the EU RAR (EC, 2001) there are not expected to be any significant releases to air, water and aquatic environment.		Since the proposed control measures should not affect end-uses or production quantity, there is not expected to be any significant change in environmental impacts relative to the baseline scenario.	

Note: Costs and benefits under the intervention options are relative to the baseline scenario (i.e. are not absolute impacts but differences)

6 CONCLUSIONS

MDA is suspected of causing bladder cancer, although there is no human epidemiological evidence to support this conclusion. We have considered the likely health, socioeconomic and environmental impacts associated with the possible introduction of an OEL of 0.8 mg/m^3 (0.1 ppm) or 0.08 mg/m^3 (0.01 ppm). MDA may be taken up into the body by inhalation and skin exposure.

About 99% of the total EU MDA production of 1.4 million tonnes is used to make polyurethane foam. MDA is also used as a hardener in epoxy resins and other adhesives, although these uses have been decreasing over time as alternative substances have been introduced.

It was estimated that there are between 70 and140 people exposed to MDA in the EU chemical industry and their inhalation and dermal exposure is low. The number of people potentially exposed in construction and other manufacturing is unknown, but could be between about 390,000 and 3.9 million people. The inhalation exposures for

these workers were also judged to be low, although dermal exposure were probably higher than in the chemical industry. Exposures in 2010 are estimated to be at most 0.14 mg/m^3 during manufacture in the chemical industry and 0.07 mg/m^3 in other industrial sectors.

We have considered it is not possible to undertake a health impact assessment because of uncertainties surrounding the risk and the exposures in construction and sectors other than chemical manufacturing. We were also unable to predicted potential health benefits from setting an OEL, although we believe the impact would be relatively small because of the low current estimated inhalation exposures. There are no significant economic costs associated with complying with an airborne OEL. The cost of reducing dermal exposures, aggregated over the period 2010 to 2070, might range between about €1,400m and €29,000m. The large cost is mainly due to the large number of workplaces that might be required to take steps to control exposure.

There are also no social or macro-economic costs associated with introducing an OEL or of introducing measures to reduce dermal exposure to MDA. There are no significant environmental impacts foreseen.

There are considerable uncertainties about the skin exposure to MDA, although it seems this is probably the predominate route of exposure in most industry sectors. Given the potentially large number of people exposed it would be prudent to collect further MDA exposure data in the EU using biological and personal exposure monitoring.

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8 APPENDIX

8.1 ESTIMATED NUMBER OF EMPLOYEES IN EACH INDUSTRY GROUP – MEMBER STATE BREAKDOWN – MALES AND FEMALES

Table 8.1.1 Number of workers exposed to MDA by Member State and NACE code – males and females

	NACE Code											
	25			28			29			31		
Country	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
Austria	6,894	5,584	1,310	17,584	14,243	3,341	19,991	16,193	3,798	6,834	5,536	1,299
Belgium	6,841	5,541	1,300	17,201	13,933	3,268	11,064	8,962	2,102	4,617	3,740	877
Bulgaria	8,502	4,421	4,081	14,900	7,748	7,152	25,063	13,033	12,030	7,834	4,074	3,760
Cyprus[1]	243	182	61	780	585	195	209	157	52	83	62	21
Czech Republic	35,316	22,956	12,361	69,588	45,232	24,356	68,009	44,206	23,803	48,131	31,285	16,846
Denmark	6,324	4,616	1,707	14,474	10,566	3,908	19,115	13,954	5,161	7,303	5,332	1,972
Estonia	2,059	1,132	927	5,161	2,839	2,322	2,220	1,221	999	2,496	1,373	1,123
Finland	4,940	3,656	1,285	14,876	11,009	3,868	18,839	13,941	4,898	5,649	4,180	1,469
France	67,028	51,612	15,416	124,514	95,876	28,638	88,677	68,281	20,396	43,694	33,644	10,050
Germany	97,047	75,697	21,350	202,166	157,689	44,476	270,715	211,158	59,557	133,025	103,760	29,266
Greece	3,099	2,355	744	10,631	8,080	2,552	6,020	4,575	1,445	2,120	1,611	509
Hungary	16,636	10,481	6,155	30,205	19,029	11,176	27,809	17,520	10,289	27,993	17,636	10,357
Ireland	2,777	2,083	694	3,629	2,722	907	3,207	2,405	802	2,098	1,573	524
Italy	57,412	43,059	14,353	202,110	151,582	50,527	162,050	121,537	40,512	52,753	39,565	13,188
Latvia	1,109	643	466	2,340	1,357	983	1,742	1,010	731	862	500	362
Lithuania	1,787	929	858	3,457	1,798	1,659	2,049	1,066	984	1,233	641	592
Luxembourg[2]	2,797	2,433	364	1,930	1,679	251	1,085	944	141	213	185	28
Malta[3]	Not Available			Not Available			Not Available			Not Available		
Netherlands	7,697	6,388	1,308	23,188	19,246	3,942	21,092	17,506	3,586	4,069	3,377	692
Poland	44,969	30,129	14,840	83,026	55,628	27,399	61,969	41,519	20,450	32,054	21,476	10,578
Portugal[4]	7,195	4,245	2,950	24,579	14,501	10,077	13,269	7,829	5,440	6,863	4,049	2,814
Romania	17,870	9,650	8,220	39,008	21,064	17,944	39,226	21,182	18,044	31,867	17,208	14,659
Slovakia	8,015	5,130	2,885	13,252	8,481	4,771	17,421	11,150	6,272	17,699	11,327	6,372

	NACE Code											
	25			28			29			31		
Country	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
Slovenia	6,060	4,000	2,060	15,189	10,025	5,164	12,104	7,988	4,115	6,759	4,461	2,298
Spain	40,218	31,370	8,848	125,872	98,180	27,692	64,861	50,591	14,269	29,361	22,901	6,459
Sweden	11,083	8,644	2,438	32,958	25,707	7,251	45,425	35,431	9,993	9,549	7,448	2,101
United Kingdom	53,710	43,505	10,205	85,825	69,519	16,307	71,758	58,124	13,634	32,251	26,123	6,128
Total	517,628	380,442	137,186	1,178,445	868,319	310,126	1,074,989	791,483	283,506	517,410	373,068	144,342

	NACE Code											
	35			45.3			45.4			Grand Total		
Country	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
Austria	2,778	2,250	528	5,638	4,567	1,071	3,827	3,100	727	**63,547**	**51,473**	**12,074**
Belgium	2,390	1,936	454	3,257	2,639	619	3,116	2,524	592	**48,486**	**39,274**	**9,212**
Bulgaria	4,033	2,097	1,936	1,681	874	807	1,087	565	522	**63,100**	**32,812**	**30,288**
Cyprus[1]	30	22	7	250	187	62	123	92	31	**1,717**	**1,288**	**429**
Czech Republic	9,062	5,890	3,172	5,464	3,552	1,913	3,860	2,509	1,351	**239,430**	**155,630**	**83,801**
Denmark	2,403	1,754	649	3,134	2,288	846	3,709	2,707	1,001	**56,461**	**41,217**	**15,245**
Estonia	1,135	624	511	405	223	182	97	53	44	**13,574**	**7,466**	**6,108**
Finland	3,452	2,554	897	3,236	2,395	841	1,166	863	303	**52,159**	**38,597**	**13,561**
France	43,033	33,136	9,898	44,985	34,639	10,347	48,105	37,040	11,064	**460,036**	**354,228**	**105,808**
Germany	35,725	27,866	7,860	20,858	16,269	4,589	15,091	11,771	3,320	**774,628**	**604,210**	**170,418**
Greece	3,690	2,805	886	863	656	207	775	589	186	**27,200**	**20,672**	**6,528**
Hungary	3,276	2,064	1,212	3,431	2,162	1,269	1,889	1,190	699	**111,240**	**70,081**	**41,159**
Ireland	1,051	788	263	663	498	166	169	127	42	**13,595**	**10,196**	**3,399**
Italy	30,972	23,229	7,743	21,096	15,822	5,274	15,036	11,277	3,759	**541,429**	**406,072**	**135,357**
Latvia	1,307	758	549	1,315	763	552	1,155	670	485	**9,829**	**5,701**	**4,128**
Lithuania	1,351	702	648	1,679	873	806	965	502	463	**12,521**	**6,511**	**6,010**
Luxembourg[2]	13	11	2	305	265	40	211	184	27	**6,553**	**5,701**	**852**
Malta[3]	15	11	4	122	87	35	60	43	17	**197**	**140**	**57**
Netherlands	5,925	4,918	1,007	5,945	4,934	1,011	4,206	3,491	715	**72,121**	**59,861**	**12,261**

	NACE Code											
	35			45.3			45.4			Grand Total		
Country	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
Poland	21,249	14,237	7,012	11,151	7,471	3,680	5,904	3,956	1,948	**260,323**	**174,416**	**85,906**
Portugal[4]	2,957	1,744	1,212	4,585	2,705	1,880	3,102	1,830	1,272	**62,550**	**36,905**	**25,646**
Romania	22,910	12,371	10,538	46,292	24,998	21,294	9,773	5,278	4,496	**206,946**	**111,751**	**95,195**
Slovakia	2,812	1,800	1,012	697	446	251	215	138	77	**60,111**	**38,471**	**21,640**
Slovenia	1,185	782	403	908	599	309	1,009	666	343	**43,215**	**28,522**	**14,693**
Spain	19,431	15,156	4,275	21,712	16,936	4,777	19,108	14,904	4,204	**320,563**	**250,039**	**70,524**
Sweden	8,614	6,719	1,895	7,978	6,223	1,755	3,968	3,095	873	**119,575**	**93,268**	**26,306**
United Kingdom	37,982	30,766	7,217	12,435	10,072	2,363	7,515	6,087	1,428	**301,475**	**244,195**	**57,280**
Total	268,781	196,991	71,790	229,665	162,841	66,824	155,140	115,178	39,961	**3,942,581**	**2,888,696**	**1,053,886**

[1] Data for NACE code 45.3 is from 2005
[2] Data for NACE code 31 is from 2002
[3] Data based on data from Cyprus
[4] Data for NACE code 35 is from 2005

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