DATA ON MANUFACTURE, IMPORT, EXPORT, USES AND RELEASES OF 4-4' DIAMINODIPHENYLMETHANE AS WELL AS INFORMATION ON POTENTIAL ALTERNATIVES TO ITS USE

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EXECUTIVE SUMMARY

This report presents data on the manufacture, use, releases and alternatives to 4-4' diaminodiphenylmethane (MDA) (EC No 202-974-4, CAS 101-77-9), collated by Entec. The report has been produced according to a format and structure provided by ECHA. Draft reports have been reviewed and commented on by ECHA and this final report has been accepted by ECHA.

Manufacture and use for MDI

As 98% of MDA is used as a precursor to methylene diphenyldiisocyanate (MDI), the production tonnage of MDA has been calculated, from the production tonnage of MDI, to be in the region of 1,400,000t in 2008.

Other uses

Other uses of MDA are:

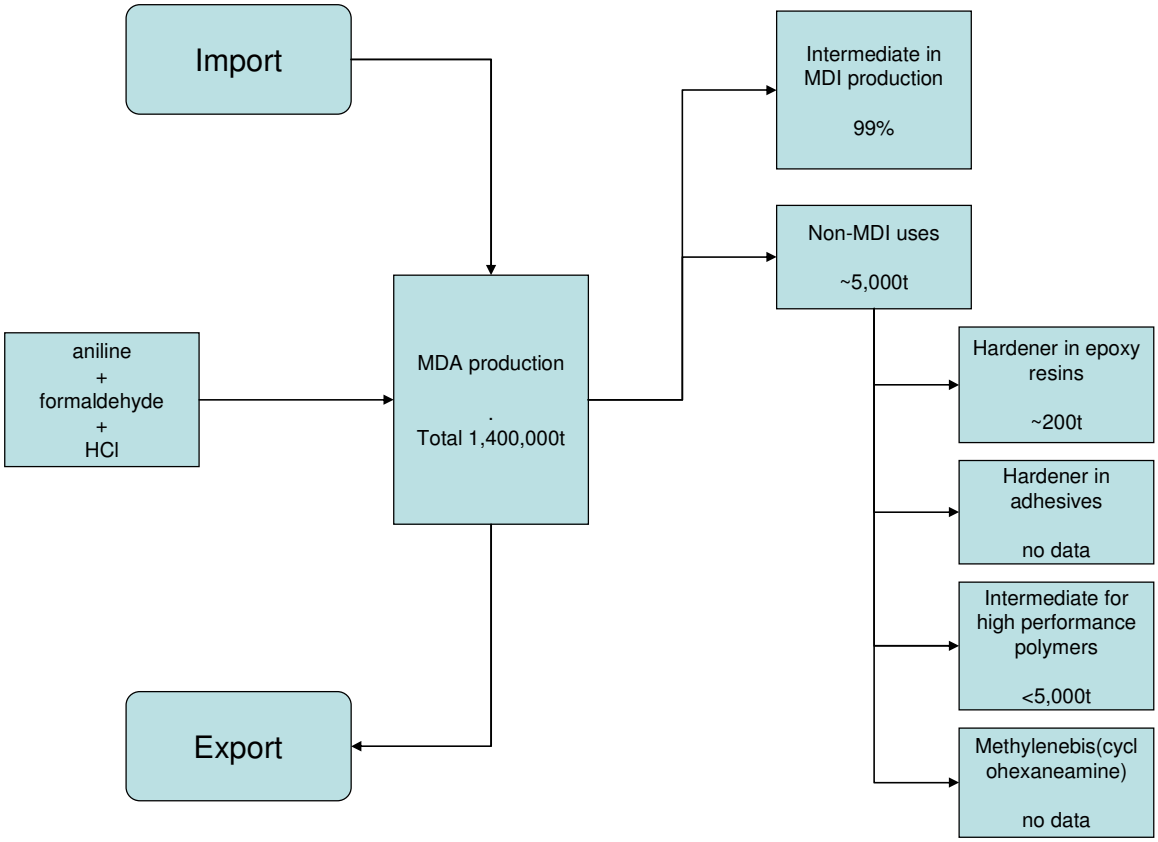
- as a hardener in epoxy resins and adhesives,
- in the production of high performance polymers and
- as a starting point for the synthesis of 4,4'-methylenebis(cyclohexaneamine) (PACM).

Tonnages involved in use of MDA as a hardener in epoxy resins are confidential (see Annex 3) and are unknown for adhesives. The overall EU consumption for use as a hardener in epoxy resins is estimated by one company to be around 200t, however further confidential information suggests that this figure may be regarded as a minimum. A number of applications for the use of MDA as a hardener in adhesives are understood to have been phased out.

A producer of high performance polymer using MDA as a raw material indicated using less than 5,000tpa at a single site.

No information on the tonnages involved in the manufacture of PACM has been made available, although PACM is believed to be produced in the EU.

A summary of uses and indicative volumes for each use based on information gathered for this study is presented below (Figure 3.1 in this report).



The table below summarises the uses of MDA and their relevance to authorisation based on use.

Table 0.1 MDA summary use volumes and relevance to authorisation.

Use	**Volume (tonnes per annum)**	**Intermediate use?**	**Except from authorisation?**
Exported out of the EU	No data	N/A	Y
Production of MDI	1,400,000	Y	Y
Hardener in epoxy resins	**~200**	**N**	**N**
Hardener in adhesives	No data	**N**	**N**
Intermediate for high performance polymers	<5,000	Y	Y
Production of methylenebis (cyclohexaneamine)	No data	Y	Y

Alternatives

MDA is mainly used in the synthesis of MDI, which is itself used in the manufacture of polyurethanes. Although polyurethanes can be made from several diisocyanates.

(usually either based on MDI or on toluene diisocyanate (TDI), but also aliphatic isocyanates), it is not clear if a switch in the isocyanate used would represent a suitable option for substitution (due to technical or environmental considerations).

For alternatives for the uses that could be subject to authorisation (i.e. when MDA is considered not to be an intermediate), it is understood that other aromatic amines or aliphatic amines can be used as alternatives as curing agents in some circumstances although information on alternatives for specific applications has not been found

Based on the literature review undertaken (see Annex 3), it has not been possible to gain a good overview of the current status of development of alternatives for the remaining non-MDI uses (particularly as hardener in epoxy resins and adhesives). Some promising alternatives have obviously been identified (as evidenced by a number of patents), though the actual market suitability of these alternatives is unknown.

1 Introduction

This report presents data on the manufacture, use, and alternatives to 4-4' diaminodiphenylmethane (MDA) (EC No 202-974-4, CAS 101-77-9), collated by Entec. This report is intended to provide ECHA with information on the substance for:

1. Priority setting of substances in the candidate list for inclusion in Annex XIV of the REACH Regulation.
2. Defining the conditions related to the entries on Annex XIV (cf. Article 58(1)).

The report has been produced according to a format and structure provided by ECHA. Draft reports have been reviewed and commented on by ECHA and this final report has been accepted by ECHA.

The starting point for this study was the Annex XV dossier submitted by the German authorities to identify MDA as a substance of very high concern (SVHC), as well as the risk assessment report for the substance (EC, 2001) and the draft risk reduction strategy (BAuA, 2000)[1] developed under the existing substances regulation[2].

The information presented here has been collected by using the sources mentioned above and consultation with relevant industry organisations and trade associations. The organisations contacted are as follows:

1) ISOPA (the European trade association for producers of diisocyanates and polyols)
2) BASF
3) Huntsman UK
4) PU2PU
5) Plastics Europe[3]
6) ALIPA (the European Aliphatic Isocyanates Producers Association)
7) Air Products
8) Victrex
9) FEICA (Association of European Adhesives and Sealants Manufacturers)
10) Sika
11) Huntsman Advanced Materials

In addition to consultation with industry the literature has been searched for relevant information on non-intermediate uses of MDA, in particular:

- on possible alternatives (and research programmes on alternatives and substitution);
- for its use as a hardener in epoxy resins and in adhesives; and

[1] Of these two documents, most information on uses is from the RAR (EC, 2001) as the risk reduction strategy (BAuA, 2000) was draft and did not reveal further new information on uses, releases and alternatives.

[2] Council Regulation (EEC) No 793/93 of 23 March 1993 on the evaluation and control of the risks of existing substances

[3] Plastics Europe contacted 10 companies interested in the epoxy resins market for the purposes of this study with specific information requests from Entec.

- possible exposure information relating to workers making and using epoxy resins and adhesives containing MDA.

For this purpose, specific on-line databases[4] were consulted as well as searches for information on the internet.

[4] Databases consulted were: Chemical Abstracts and CIN (Chemical Industry Notes) including APOLLIT (Applied Polymers Literature), CIN (Chemical Industry Notes) and RAPRA (rubber, plastics, adhesives and polymeric composites)

2 Information on manufacture, import and export and releases from manufacture

2.1 *Manufacturing sites and manufacturing processes*

2.1.1 Manufacturing data and sites

The risk assessment report (RAR) indicated that more than 98% of total production of MDA was used as an on-site intermediate for the production of 4,4´-methylene diphenyl diisocyanate (MDI)[5]. It was reported in the RAR (EC, 2001) that in 1990, MDI was further processed to polyurethanes by almost 1,000 users in Western Europe. As it is understood that MDA is usually not isolated, the tonnage of MDA indicated in the RAR was calculated on the basis of the market for MDI at that time. Considering 540,000t of MDI was produced in Western Europe in 1993, the RAR concluded that the equivalent production of MDA amounted to 432,000t for the same period.

In 1989, MDI production capacity in Western Europe was estimated at just over 500,000 tonnes per year (see Table 2.1). This corresponds to a production of 400,000 tonnes of MDA.

Table 2.1 MDI production facilities in Western Europe in 1989 and their capacity

Company	Plant	Capacity (kt)
BASF	Antwerp, Belgium	60
Bayer	Krefeld, Germany	126
Bayer	Leverkusen, Germany	20
Bayer	Tarragona, Spain	6
Bayer-Shell	Antwerp, Belgium	26
ICI	Fleetwood, UK	45
ICI	Rosenberg, Netherlands	30
Montedison	Brindisi, Italy	70
Dow	Isopor, Portugal	50
Dow	Delfzijl, Netherlands	70
Total		503

Source: Kirk Othmer (2000)

Some of the firms set out in Table 2.1 have changed hands since 1989, new facilities have been built and existing facilities expanded (some may also have closed). The European trade association for producers of diisocyanates and polyols (ISOPA) has indicated that there are currently five or six companies producing MDA and MDI in the EU, but the exact number and location of the production sites is

[5] Processing to MDI takes place on the same site as the production of MDA, but this is done by a number of manufacturers at different sites (see table 2.1), not all at one site.

unknown. Members of ISOPA include Bayer, Dow, Elastogran (BASF Group), Huntsman, Repsol and Shell. It can therefore be assumed that the MDA production facilities are mainly the same ones that were involved in the production of MDA historically[6].

Information gathered for this study suggests that there has been a significant increase in volumes of MDI (and hence MDA) manufactured in the EU. For example:

- In 2004, Bayer was forecasting growth in demand for MDI of around 6% per year from 2004 to 2008[7].

- BASF was reported to be expanding its production complex for MDI in Antwerp, Belgium (Verbund), to make it the largest of its type in the world by the second quarter of 2007 (from 450,000 to 560,000 tonnes)[8].

- MDI production by Bayer at Brunsbüttel is planned to be expanded to a total capacity of 400,000 tonnes/year, by making use of the existing capacity of 160,000 tonnes/year and the existing infrastructure, and by converting the present TDI plant to an MDI facility[9].

Information from industry (ISOPA) suggests that current production of MDA and MDI is around 3-4 times that suggested for 1993 in the RAR. If a value of 1,400,000 tonnes of MDA production is taken as a current value (around three times the value for 1993 in the RAR), this corresponds to an annual compound growth rate of around 8%[10]. This is consistent with growth rates reported in the literature and therefore has been used to estimate MDI production in this study[11].

Consultation with industry[12] indicated that growth in production of MDA and MDI relates largely to expansion of existing sites rather than to the creation of new plants or the integration of existing plants in the EU owing to EU enlargement. Industry (ISOPA) estimates that one site in Italy had closed down and one site exists in Hungary (not mentioned in Table 2.1 above). Therefore, production figures for the EU27 are likely to be broadly the same as for Western Europe.

This increase in production is consistent with – and would appear to be corroborated by – a significant increase in export of related products from the EU (based on Eurostat data[13]):

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[6] Note that Huntsman Polyurethanes operates a plant in Rosenburg (Netherlands), acquired from ICI in 1999 (http://www.chemicalonline.com/article.mvc/ICI-Divests-Urethanes-Titanium-Dioxide-Petroc-0001?VNETCOOKIE=NO).

[7] http://www.allbusiness.com/manufacturing/chemical-manufacturing-paint/339778-1.html.

[8] http://www.azom.com/News.asp?NewsID=7354.

[9] http://www.bayer.com/en/News-Detail.aspx?id=11306.

[10] Isopa reported an indicative growth rate of 5% per year. We consider this value as an indicative minimum considering growth rates reported in the literature.

[11] This figure has not been confirmed by industry.

[12] Personal communication with ISOPA, November 2008.

[13] http://epp.eurostat.ec.europa.eu/portal/page?_pageid=0,1136217,0_45571467&_dad=portal&_schema=PORTAL.

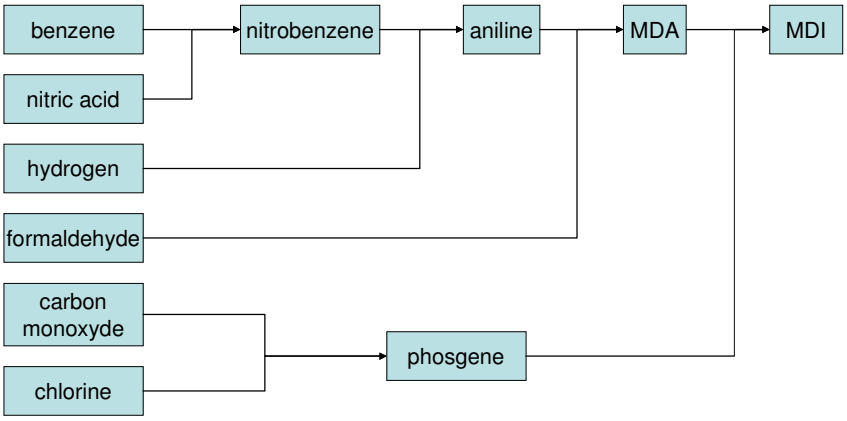
- Exports of isocyanates from the EU27 increased from 162,506t in 2000 to 267,131t in 2007 (equivalent to an annual growth rate of 7%);

- Exports of polyurethanes in primary forms from the EU27 increased from 235,800t in 2000 to 380,874t in 2007 (equivalent to an annual growth rate of 7%).

2.1.2 Manufacturing process

MDA is synthesised by reaction of formaldehyde and aniline in the presence of hydrochloric acid. This reaction is carried out either in a batch reactor or in a continuous process. After the reaction, a neutralisation step takes place using caustic soda. The reaction product is then purified by washing with water and aniline (EC, 2001). Figure 2.1 illustrates the different steps in the synthesis of MDA and MDI[14].

Figure 2.1 Steps in the manufacture of MDA and MDI (BASF, 2007)



2.2 *Import and export of the substance on its own or in preparations*

The EU RAR (EC, 2001) does not give data on EU import and export volumes. However Eurostat[15] provides data on total isocyanates imported and exported from the EU. Whilst this does not provide an indication of the trade in MDA (in any case, the majority of MDA is believed to be used almost exclusively on the same production sites for the synthesis of MDI), it is relevant in the context of total trade in the main substance in which MDA is used (i.e. MDI is believed to constitute the major part of isocyanate production). The data for trade in isocyanates in 2007 are as follows:

- 45,212t imported to the EU27;
- 267,131t exported from the EU27.

Industry (ISOPA) indicated that there was no import or export of MDA involved in the production of MDI.

[14] The polyurethane MDI handbook, BASF 2007
[15] http://epp.eurostat.ec.europa.eu/

A producer of high performance polymers indicated that part of the MDA used in this application is imported.

Consultation with an epoxy resins manufacturer indicated that they import finished curing systems containing MDA. The corresponding quantities are presented in the confidential annex (Annex 3).

Consultation with the plastics industry[16] indicated that at least one company acted as a distributor of MDA, importing and exporting MDA from/to outside the EU. However, no indication of the tonnages involved in these movements was made available.

2.3 *Import and export of articles containing the substance*

Given that MDA is converted into MDI and then reacted to form polyurethanes, such articles will not generally contain MDA in any significant quantities. However, to provide additional context, information on external EU trade in polyurethane in primary forms in 2007 is included, as below[17]:

- 53,084t imported to the EU27;
- 380,874t exported from the EU27.

It is possible that MDA is imported or exported in articles containing/made of epoxy resins or adhesives (see section 3). However, no further information has been gathered for this study on the possible content of MDA in articles containing/made of epoxy resins or adhesives.

2.4 *Releases from manufacture*

2.4.1 Overview

No additional site-specific data on releases from manufacture have been made available for the purposes of this study. Therefore, the information presented in this study is based on the risk assessment report (RAR, EC 2001) and also updated calculations based on the significantly increased production of MDA and MDI.

Given that MDA production facilities are understood to be located in several Member States (including, but not necessarily limited, to Belgium, Germany, Spain, UK, Netherlands and Portugal), releases from manufacture are considered to be potentially geographically widespread across a number of point sources in the EU.

2.4.2 Aquatic environment

Releases from production and processing of MDA

The RAR (EC, 2001) provides information on releases from 11 sites producing and processing[18] MDA (production had stopped at three additional sites). This is

[16] Personal communication with Plastics Europe, November 2008

[17] There are various other polyurethane products imported to and exported from the EU which are not included in these figures.

[18] Processing refers in this case to production of MDI.

summarised in Table 2.2. As MDA is largely used as an on-site intermediate for the production of MDI, it is not possible to separate production and processing data.

Table 2.2 Emissions to water based on the MDA production and processing installations included in the RAR (EC, 2001)[19]

Site	Emission (kg/year)
A	60
B	75
C	14
E	360
F	76
H	110
I	38
G	51
J	144
K	1,870
M	29
Total	**2,827**

Note: Sites A-I discharged to rivers; sites G-M discharged to estuaries

Using the generic release estimate to waste water of 0.3% for production and processing to MDI (EC, 2001), worst case releases to waste water assuming a current production quantity of 1,400,000 tonnes per year would be 4,200 tonnes per year. Given the release estimates in the risk assessment, this value is considered to significantly over-estimate releases. A more realistic estimate could be to uplift the emission estimates from the RAR by a factor of three (as has been assumed for the production volumes); this would give a total emission of 8,481 kg/year. Even this value could be an overestimate, given that all of the installations should be covered by the IPPC Directive and emission limit values (or equivalent parameters or technical measures) would be expected to be set for releases of substances such as MDA[20]. Thus, whilst the overall trend is for increased production and use of MDA, it is possible that the trend in releases to the environment may have reduced over time.

As indicated in the RAR (EC, 2001), releases to water from polyurethane manufacture are considered to be negligible.

[19] It is noted that 11 sites are reported in Table 2.2 while only 10 are reported in Table 2.1. The data are from two different sources and this discrepancy has not been resolved.

[20] Annex III of Directive 2008/1/EC refers to the main substances to be taken into account if they are relevant for fixing emission limit values and includes 'substances and preparations which have been proved to possess carcinogenic or mutagenic properties or properties which may affect reproduction' in relation to both emissions to air and emissions to water.

2.4.3 Atmosphere

As indicated in the RAR (EC, 2001), no significant releases of MDA into the atmosphere are expected from MDA production and processing installations. Emissions from one company were estimated to be less than 1kg per year.

2.4.4 Terrestrial compartment

As indicated in the RAR (EC, 2001), no significant releases of MDA into soil are expected during production and processing of MDA (though trace amounts may be disposed of to landfill in polyurethane and epoxy resin wastes).

Similarly, deposition from air to soil was not considered to be a source of MDA releases to the terrestrial compartment because no significant releases into the atmosphere are expected.

Given that adsorption during waste water treatment was considered to be negligible, no significant releases into agricultural soils due to use of sludge as fertiliser were expected.

2.4.5 Releases to the working environment

For the workplace it is the exposure of workers that is of importance as this allows an understanding of the contact that humans may have with the substance, rather than what is simply released (the later will be most likely captured by estimation of environmental releases).

Releases from manufacture are considered in section 3.3.5 (Releases to the working environment) along with the releases from other uses.

3 Information on uses and releases from uses

3.1 *Identification of uses*

3.1.1 Production of MDI

As indicated in the Annex XV proposal submitted by Germany, more than 98% of the total production volume is processed to methylenediphenyl diisocyanate (MDI). According to industry (ISOPA), this occurs exclusively on the production sites in the EU. MDA is considered by industry to be an on-site isolated intermediate, used under strictly controlled conditions. MDI is further used for polyurethane production. The following information on polyurethane is reported here to give an illustration of at the main use of MDA and therefore set the context for MDA production and use.

According to ISOPA (2003) the main end use applications for polyurethane products include infrastructure and building products such as insulation panels, coatings and adhesives plus binders for forest products. ISOPA (2003) indicate that polyurethanes are key components for refrigerators and freezers, automobiles, furniture and shoes.

The main applications for polyurethane are as follows, including the relevant share of use in 1999 (ISOPA, 1999):

- adhesives/sealants (7%);
- appliances (7%)
- automotive applications (16%)
- binders (2%)
- building construction (22%)
- coatings (9%)
- elastomers (7%)
- footwear (8%); and
- furniture/bedding (23%)

The market for polyurethanes has grown significantly in recent years, resulting in increased demand for MDI and hence for MDA. Based on data reported in ISOPA (2003):

- There were 390 companies identified as chemical producers for polyurethanes (this will include, for example, producers of isocyanates such as MDI and TDI but also others such as polyols, the other main component of polyurethanes, and potentially others). These companies employed 13,900 workers.

- These firms manufactured 3.35 million tonnes of polyurethane chemicals.

There were around 1,500 polyurethane converters based on 2003 data so it can reasonably be expected that these firms will be spread widely across the EU (ISOPA, 2003).

3.1.2 Other uses of MDA

Apart from its use in the synthesis of MDI, the RAR (EC, 2001) identifies the following uses of MDA:

- Hardener in epoxy resins;
- Hardener in adhesives;
- Intermediate in the manufacture of high performance polymers;
- Processing to 4-4'methylenebis(cyclohexaneamine) (H12MDA).

An objective of the present study was to confirm these uses and gather information on the quantity of MDA they represent. These uses are addressed in turn below.

Hardener in epoxy resins

Consultation with industry[21] confirmed that MDA is still used as a hardener in epoxy resins. The company Air Products indicated that they use MDA as a hardener in epoxy resins curing agents. Information from consultation with this firm on the uses of MDA in epoxy resins is set out below.

A curing agent is mixed with epoxy resin to form a cured coating system which reacts chemically, forming the final coating. Such coatings are used where high chemical resistance is required, such as coatings for tank linings and similar applications. Aromatic coatings are usually spray or roller applied by certified personnel using the appropriate level of personal protective equipment.

Air Products also indicated that another area of application is for the manufacture of pipes using the filament winding process[22].

The materials containing aromatic amines are used in combination with glass fibres in "composite" applications and, according to Air Products, are used in factories where the plant imposes strict exposure controls and monitors the air. This is specialist processing technology developed and practiced by their customers.

Another company (that requested not to be named in this report) using MDA as a hardener in curing agents, suggested that identification of other companies producing and using these formulations was difficult as no identified trade association is really relevant for this activity. Discussion with this company suggested the main actors in that sector had been contacted by Entec for this study. All relevant information received through these contacts is presented in this report.

This company reported that they do not knowingly sell curing agents containing MDA to the skilled trade area and that the products developed are intended to be applied in an industrial environment.

[21] Personal communication with Plastics Europe, November 2008, and Air Products, November 2008.
[22] Filament Winding is the process of winding resin-impregnated fibre or tape on a mandrel (shaft or spindle) surface in a precise geometric pattern. This is achieved by rotating the mandrel while a delivery head precisely positions fibres on the mandrel surface. By winding continuous strands of carbon fibre, fibreglass or other material in very precise patterns, structures can be built with properties stronger than steel at much lighter weights. (http://www.entec.com/filament%20winding.shtml)

For this report it has not been possible to present an overview of the number and the type of companies using epoxy resins containing MDA, in particular for users in the skilled trade area. This is because the companies contacted for this study did not wish to provide information on their customers.

It is understood that companies using MDA as hardener in epoxy resins cover the development of coatings and filament wound pipes, and do not relate to possible epoxy adhesives. Adhesives are considered in the next section.

Hardener in adhesives

Communication with FEICA[23] (Association of European Adhesives and Sealants Manufacturers) indicated that MDA is not likely to be used in adhesives or is being phased out from that use. Some FEICA member companies indicated having phased MDA out 8 to 15 years ago, although none revealed what alternative/s were used.

A company member of FEICA revealed using MDA-containing hardener to formulate a two-component adhesive sold for use in the automotive industry to produce 'sand forms' to cast engine parts[24]. Each form is thought to be used to produce up to 70,000 parts.

In this use, MDA is said to increase durability of the sand form. It has not been possible, in the scope of this project, to get more details on the use of MDA by this company and no information on the quantities used has been provided.

Intermediate in the manufacture of high performance polymers

Consultation with industry[25] indicates that MDA is used in the synthesis of polymers other than polyurethane.

A company contacted for this study is understood to use MDA in reactions to form (possibly after a number of steps) a monomer that is further polymerised. This polymer is different from polyurethane, marketed under the trade name PEEK (polyetheretherketone).

Processing to 4-4'methylenebis(cyclohexaneamine) (H_{12}MDA or PACM)

It is indicated in the literature (OECD, 2005) that MDA can be hydrogenated to 4,4'-methylenebis(cyclohexaneamine) (H_{12}MDA or PACM). PACM can subsequently be used for the manufacture of the corresponding aliphatic diisocyanate (H_{12}MDI).

[23] Personal communication with FEICA, December 2008. FEICA indicated having consulted all their members (companies and national associations) on all substances of very high concern, which yield, indicating no use or a phasing out of all SVHCs.The information indicated in this report have been gathered upon specific consultation on MDA.

[24] In sand casting molten metal is poured into a mould and allowed to solidify into an object; sand is used to define the cavity inside a mould. In addition, sand is used to make any cores (used to create openings and various shaped cavities in the casting) that are contained in the mould. The sand used in sand casting can be bonded using chemical binders (information from: http://www.metal-technologies.com/SandCasting.aspx). It is believed that MDA is used in these binders.

[25] Personal communication with Victrex, November 2008

H_{12}MDA is used in aliphatic polyurethane manufacture in a similar way to the use of MDA in the polyurethane industry. However, as the sector is quite small, industry would not reveal the production tonnage of H_{12}MDA[26].

H_{12}MDI is used for the manufacture of:

- Binders or hardeners for coating materials or adhesives (60 %);
- Prepolymers (20 %);
- Others, e.g. for the production of elastomers (20 %).

It is also understood that PACM can be used itself as a hardener in epoxy resins[27].

3.2 *Quantification of uses*

As indicated in the RAR (EC, 2001), more than 98% of MDA was used for on-sie manufacture of MDI (data for 1993). Given the significant increase in MDA/MDI production, it is considered likely that the percentage used in MDA production is at least 98% and may well be greater.

Data from the Nordic product registers provide information on a number of different uses for MDA in products over the period 2000 to 2006, as outlined in Table 3.1.

[26] Personal communication with Alipa, November 2008
[27] http://www.freepatentsonline.com/y2007/0244269.html.

Table 3.1 Data from the Nordic Product Registers on use of MDA in 2000 to 2006 (tonnes)

Member State	NACE code	2000	2001	2002	2003	2004	2005	2006
DK	24 - Manufacture of chemicals and chemical products	1.8	2.1	2.1	1.6			
	28 - Manufacture of fabricated metal products, except machinery and equipment	3.1	5.1	5.1	4.4	0.3	0.5	0.3
	31 - Manufacture of electrical machinery and apparatus			1.6				
	35 - Manufacture of other transport equipment n.e.c.	2.1	4.3	4.3	1.7	0.1	0.1	
	45 - Construction	3	7.4	7.4	7.6	0.1	0.1	
DK Total		10	18.9	20.5	15.3	0.5	0.7	0.3
FIN	24 - Manufacture of chemicals and chemical products			8.9	12.7		4	5.5
	25 - Manufacture of rubber and plastic products			0.9	0.1			
	28 - Manufacture of fabricated metal products, except machinery and equipment				20.5	16	16	15
	29 - Manufacture of machinery and equipment				20.5	16	16	15
	31 - Manufacture of electrical machinery and apparatus							
	35 - Manufacture of other transport equipment n.e.c.					5.6	5.5	
	36 - Manufacture of furniture; manufacturing n.e.c.							
	45 - Construction				5.6	5.6	5	5
FIN Total				9.8	59.4	43.2	46.5	40.5
N	24 - Manufacture of chemicals and chemical products	4.3	2.6	5	3.8	4.4	5.2	2
	35 - Manufacture of other transport equipment n.e.c.	1	1	0.1				
	45 - Construction	5.3	3.3	8.1	7	6	6.2	2.1
N Total		10.6	6.9	13.2	10.8	10.4	11.4	4.1
S	25 - Manufacture of rubber and plastic products		1	1				
	28 - Manufacture of fabricated metal products, except machinery and equipment	1	1	1	1			
	45 - Construction	1		1		1		
S Total		2	2	3	1	1		
Grand Total		22.6	27.8	46.5	86.5	55.1	58.6	44.9

The total tonnages in Table 3.1 do not show a clear trend (increase or a decrease) in the consumption of MDA between 2000 and 2006. However, it appears that consumption remains fairly constant over this period (at least within an order of magnitude). Therefore it is assumed (in the absence of more up-to-date information) that the overall European consumption of MDA in non-MDI uses follows the same trend and that the figure of 4,000t presented in the RAR (EC, 2001) for non-MDI uses in 1993 is still valid in 2008, or is at least within an order of magnitude of this figure.

Based on the above assumptions (which are obviously subject to uncertainty), this means that the share of non-MDI uses as a proportion of the total consumption of MDA is likely to have been reduced but the overall quantity used in formulations is assumed to have remained stable.

3.2.1 Production of MDI

As presented in section 2.1, the total EU production of MDA has been estimated on the basis of its consumption for the production of MDI.

It is therefore estimated that approximately 1,400,000t of MDA are used each year to make MDI. However, this figure has not been confirmed, and no information on the distribution of this quantity over the identified MDI production sites (*cf* Table 2.1) has been made available.

3.2.2 Non-MDI uses

Hardener in epoxy resins

The company Air Products indicated that they use oligomeric MDA, containing both 4,4'-MDA and higher molecular weight species. This is imported in finished curing agents (quantities imported are reported in the confidential annex, Annex 3). They also estimate that the overall quantity of oligomeric MDA used in epoxy curing agents in the EU is around 200 tpa.

Information from a distributor, provided by Plastics Europe, indicated that one company supplies 150t of MDA per year to be used exclusively in the filament wound pipe application.

Hardener in adhesives

The RAR (EC, 2001) did not include any specific estimate of use of MDA in adhesives.

For the purpose of this study, FEICA has been contacted, who in turn contacted their members. Only one company indicated using MDA as a hardener in adhesives (for sand forms, see section 3.1.2) while other members generally indicated a phase out of the substance in the last 8 to 15 years. A decrease in the quantities used in adhesives over that period is therefore expected. However, no information on quantities of MDA used in that sector has been obtained, either from FEICA or from individual companies.

As only one company confirmed using MDA, it is thought that, whilst there may be other (unidentified) uses in the adhesive sector it is likely that the number of companies involved for this use would be relatively limited.

Intermediate in the manufacture of high performance polymers

The UK based company Victrex indicated using less than 5,000tpa of MDA[28] to produce polymers. Their use of MDA is at one site (Rotherham, UK) and all is consumed in the process, which involves reaction of MDA with acid to form a salt and subsequent diazotisation.

Production of H12MDA (PACM)

On consultation for this study the company Air Products indicated that they produce PACM outside the EU. Information from Plastics Europe suggests PACM may be produced in the EU and possibly used in large quantities. However, no further details were made available.

3.3 *Summary of uses of MDA*

Figure 3.1 illustrates the manufacture and uses of MDA, indicating volumes used where data were available.

[28] Part of the MDA used is bought in the EU and part is imported.

Figure 3.1 Mass balance for the manufacture and use of MDA

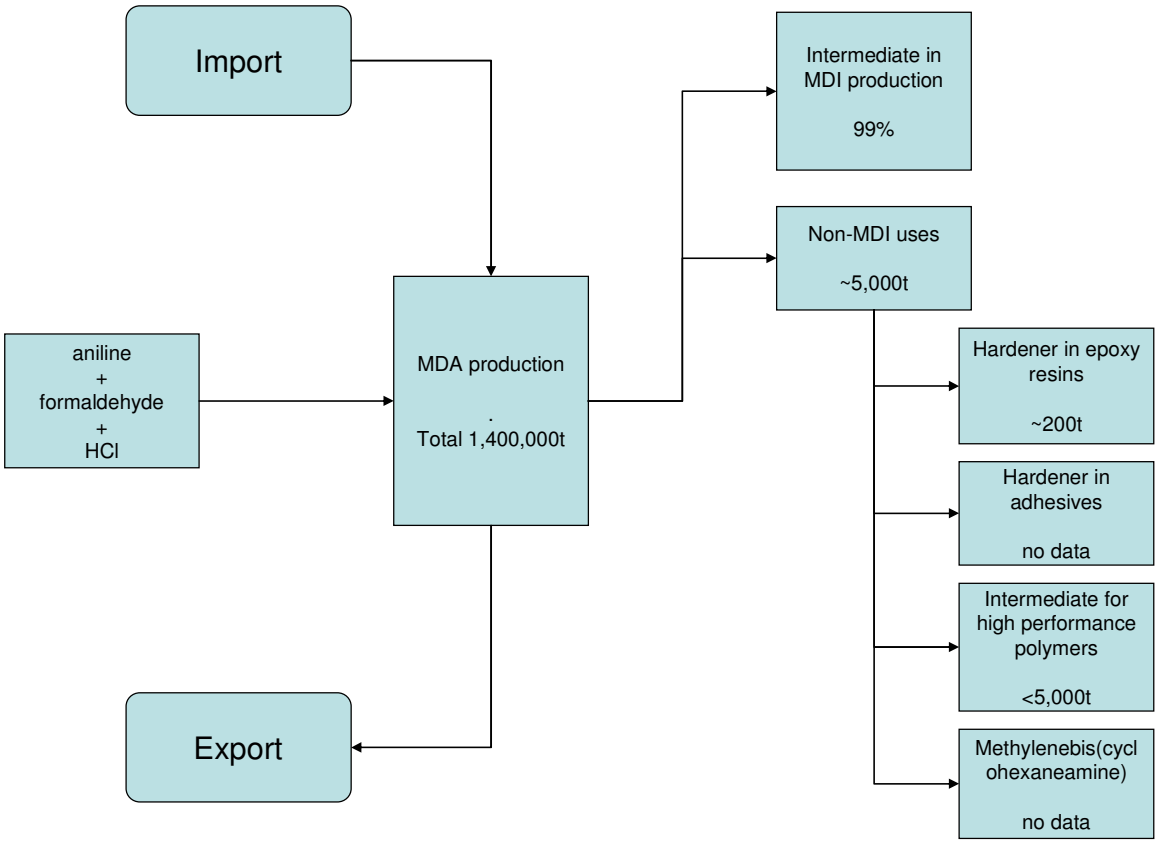


Table 3.2 summarises the uses of MDA and their relevance to authorisation based on the type of use.

Table 3.2 MDA summary use volumes and relevance to authorisation.

Use	Volume (tonnes per annum)	Intermediate use?	Except from authorisation?
Exported out of the EU	No data	N/A	Y
Production of MDI	1,400,000	Y	Y
Hardener in epoxy resins	**~200**	**N**	**N**
Hardener in adhesives	No data	**N**	**N**
Intermediate for high performance polymers	<5,000	Y	Y
Production of methylenebis (cyclohexaneamine)	No data	Y	Y

As such, the main uses potentially relevant for authorisation are use as a hardener in epoxy resins and use as a hardener in adhesives.

3.4 *Quantification of releases from uses*

3.4.1 Overview

No site-specific information on releases of MDA from its various uses was made available for this study. Therefore, the information presented here is mainly based on data from the RAR (EC, 2001).

There is a large number of polyurethane manufacturing facilities across the EU; ISOPA (2003) estimate around 1,500 polyurethane converters. Whilst this figure is not only expected to include polyurethane production facilities, it is expected that the number of sites using MDI will be geographically widespread across the EU.

Environmental releases of MDA into the environment from other uses are considered in the RAR to not be significant.

3.4.2 Aquatic environment

Releases from the use of MDI in polyurethane manufacture

The production of polyurethanes from MDI essentially does not involve water as equipment is not cleaned or washed down with water. The RAR (EC, 2001) speculated that there may be some hydrolysis of MDI to MDA. The environmental releases from this process are considered to be negligible (EC, 2001).

In terms of releases from use of MDI in polyurethane manufacturing, the RAR (EC, 2001) concluded that MDA releases can reasonably be considered as negligible. This

is based on conclusions drawn regarding the potential for formation of MDA by hydrolysis of MDI. The RAR quotes previous estimates of 5g/t of polyurethane produced; however, this was not considered to be applicable to current production units.

Releases from use as epoxy hardener, hardener in adhesives and intermediates for polymers

Again these are dry processes and in some cases for technical reasons must not involve exposure to water. The environmental releases from this process are considered to be negligible (EC, 2001).

Releases from polyurethanes and epoxy resins

The environmental releases from this process are considered to be negligible (EC, 2001).

3.4.3 Atmosphere

Emissions to atmosphere from use in the polymer industry were considered to be negligible in the RAR (EC, 2001). No further information has been obtained for this study to either confirm or dispute this conclusion.

3.4.4 Terrestrial compartment

Emissions to atmosphere from use in the polymer industry (non-intermediate use) were considered to be negligible in the RAR (EC, 2001). No further information for this study has been obtained to either confirm or dispute this conclusion.

Releases from other uses

The RAR (EC, 2001) states that only trace amounts of MDA may be deposited from use in the polyurethane and epoxy resin wastes in controlled landfills. No significant deposition to soils from via the atmosphere is expected. There is little absorption of the substance to sewage sludge and therefore deposition to agricultural land from sewage sludge spreading is also not expected.

3.4.5 Releases to the working environment

The results of the exposure assessment from the risk assessment report are reproduced in Table 3.2.

The German competent authority (BAuA) (who conducted the risk assessment (EC, 2001)), note in their Annex XV dossier (ECHA, 2008) that, with respect to inhalative exposure, most scenarios in these sectors showed only negligible concern according to the criteria used under Directive 793/93. For those scenarios that indicated a need for additional measures, the framework of worker protection was regarded sufficient for adequate control of inhalative exposure. With regard to dermal exposure, all scenarios resulted in concern according to the criteria used under Directive 793/93.

Exposures were assessed under the assumption that personal protective equipment (PPE) - i.e. gloves, were not used because at that time there was no evidence about the availability of efficient gloves. However, they note that industry later launched studies and could provide information that effective gloves are available. It is generally accepted that gloves will eliminate 90% of dermal exposure of the hands. According to the Annex XV dossier: "*residual dermal exposure can be tolerated except for scenarios in skilled trade.*" Worker exposure to MDA reported in the German CA Annex XV dossier is reproduced for information in Table 3.2.

Table 3.2 Worker exposure to MDA (from German CA Annex XV dossier)

Exposure scenario	Form of exposure	Duration and frequency[2]	Inhalative exposure shift average [mg/m³]	Dermal exposure shift average [mg/p/d][1]
Chemical industry				
manufacturing and further processing as a chemical intermediate	flakes, granules (dust)	shift length, daily	0.52 (workplace measurements)	42 - 420
	liquid (vapour) (approx. 60 %)	shift length, daily	very low (exp. judg.)	25 - 252
production of preparations				
imid preparations max. 10 % MDA	powder (dust)	batch processing 2 hours/daily	0.05 - 0.125 (EASE)	4 - 42
curing formulations max. 60 % MDA	flakes; granules (dust)	batch processing 2 hours/daily	lower than above (exp. judg.)	25 - 252
max. 5 % MDA		batch processing 2 hours/daily	lower than above (exp. judg.)	2 - 21
Industrial area				
manufacturing of formulations using powdery MDA	powder (dust)	batch processing 2 hours/daily	0.6 (workplace measurements)	42 - 420
formulating putties using liquid MDA (approx. 60 %)	liquid MDA	batch processing 2 hours/daily	very low (exp. judg.)	25 - 252
production of preparations				
imid preparations max. 10 % MDA	powder (dust)	batch processing 2 hours/daily	0.1 - 1.25 (EASE)	4 - 42
curing formulations max. 60 % MDA	flakes; granules (dust)	batch processing 2 hours/daily	0 - 0.75 (EASE)	25 - 252
max. 5 % MDA			0 - 0.08 (EASE)	2 - 21
mixing curing formulations (max. 60 % MDA) with resin for epoxies	flakes, granules (dust)	short-term (0.5 h), daily	0 - 0.2 (EASE, without LEV)	50 - 504
	liquids	short-term (0.5 h), daily	very low (exp. judg.)	50 - 504
handling of formulations containing MDA and epoxide resins (4.5 - 30 %)		shift length, daily	very low (exp. judg.)	25 - 252
mixing curing formulations (max. 5 % MDA) with resin for polyurethanes	flakes, granules (dust)	short-term (0.5 h), daily	0 - 0.02 (EASE, without LEV)	4.2 - 42
handling of formulations containing MDA and polyurethane (2 - 3 %)	liquid, pastes	shift length, daily	very low (exp. judg.)	2.5 - 25
handling formulations containing MDA (0.1 - 10 %) and imid resins	powder	short-term (0.5 h), daily	0.03 - 0.3 (EASE)	8.4 - 84
	paste	shift length, daily	very low (exp. judg.)	8.4 - 84

Exposure scenario	Form of exposure	Duration and frequency[2]	Inhalative exposure shift average [mg/m^3]	Dermal exposure shift average [mg/p/d][1]
Skilled trade				
mixing of formulations containing MDA (9 - 60 %) with epoxide resins	flakes, granules (dust)	short-term (0.5 h), not daily	0 - 0.2 (EASE, without LEV)	504 - 2 520
handling of formulations containing MDA and epoxide resins (4 - 30 %)		duration and frequency not known assumed: not daily	very low (exp. judg.)	252 - 1 260

1 Estimation according to the EASE model (without PPE)
2 Information about frequency and duration of exposure not available

Intermediate in the manufacture of high performance polymers

Consultation for this study with the UK based company Victrex reported atmospheric MDA dust monitoring (2003/4) demonstrating MDA concentrations at their plant in Rotherham (UK) were below the limit of detection.

In addition, urinary monitoring of MDA plant workers has been undertaken by the UK Health and Safety Laboratory (HSL) for at least seven years. Results have been evaluated against the UK HSE Biological Monitoring Benchmark Guidance value (50µmol/mol creatinine). The overall exposures have been reduced with improvement in controls and by engineering measures. Occasional raised MDA levels have been recorded, usually as a result of unscheduled non-routine activities. Over 1,850 urine samples have been tested over 67 monitoring periods. A total of 99% of the monitoring results were below the UK Benchmark Guidance value (50µmol/mol creatinine). Four results exceeded 100µmol/mol creatinine.

Hardener in epoxy resins

According to Air Products (consulted for this study), aromatic coatings are usually spray or roller applied by certified personnel, who use the appropriate level of personal protective equipment. During this process a coating system containing MDA is formed from the reaction of two primary substances. If there are emissions, it is not emission of MDA, but emission of this reacting system which turns within hours or days into the cured epoxy-resin polymer. This polymeric material is very stable, typically non-reactive with the environment and exhibits non-hazardous properties[29].

Though this company did not make mention of any releases, releases of MDA during application of the coating by spray cannot be excluded.

A search of the literature for this study identified a paper reporting exposure in a factory that made glass fibre reinforced resin pipes (Brouwer *et al*, 1998)[30]. The study in that paper was aimed at evaluating two different techniques for assessing dermal exposure to MDA in a field study; the results were used to test the applicability of a recently proposed quantitative dermal occupational exposure limit (DOEL) for MDA in a workplace scenario. However, geometric means of daily exposure ranged from

[29]Personal communication with Air Products, December 2008
[30] This paper was not been reported in the RAR (EC, 2001)

81-1,783 micrograms MDA. The highest actual daily dermal exposure found seemed to be about 4 mg (about 25% of the external DOEL).

Hardener in adhesives

This aspect does not appear to have been covered specifically in the RAR (EC, 2001). No information from industry has been identified for the purposes of this study (only one company producing MDA-based adhesives has been identified and they did not provide information on releases from use) and no literature on releases from use in adhesives has been identified through the literature search undertaken.

4 Information on alternatives

4.1 *Identification of alternative substances and techniques*

4.1.1 Production of MDI

MDA is mainly used in the synthesis of MDI, which is itself used in the manufacture of polyurethanes.

Polyurethanes can be made from several diisocyanates. Diisocyanates are usually either based on MDI or on toluene diisocyanate (TDI). Therefore, TDI could potentially be considered as an alternative technique to the use of MDA in the synthesis of MDI and, further, of polyurethanes.

Similarly to MDI, TDI is synthesised through the reaction of phosgene on the corresponding diamine (meta-toluenediamine, meta-TDA). This represents the advantage of not using MDA in the manufacturing process, although it is not clear if polyurethanes using MDI can be all substituted by polyurethanes using TDI.

4.1.2 Non-MDI uses

Consultation with industry indicated that there was no known alternative to MDA in its use in the synthesis of high performance polymers.

As FEICA indicated that MDA used in adhesives has been phased out some time ago (8 – 15 years) by a number of their members, it is thought that alternatives have been developed. However, due to the short timescale to consult their members, and as this information is considered as commercially confidential by their members, FEICA only indicated that other 'amines' were used. They also revealed that each alternative was product or application-specific (i.e. there were a number of alternatives to MDA depending on the product and its application).

Information on alternatives to MDA used as a hardener in epoxy resins is presented in Annex 2 (confidential annex).

A literature search on alternatives to MDA when it is used as a hardener in epoxy resins revealed several possibilities, mainly aromatic or aliphatic amines[31]. Other possible alternatives included anhydride foams, however research was not conclusive[32].

Based on the literature review undertaken, it has not been possible to gain a good overview of the current status of development of alternatives for the remaining non-MDI uses (particularly epoxy resins and hardeners). Some promising alternatives have obviously been identified (as evidenced by a number of patents), although the actual market suitability of these alternatives is unknown.

[31] http://www.freepatentsonline.com/y2007/0244268.html
http://www.freepatentsonline.com/y2007/0244269.html
http://www.patentstorm.us/patents/7044324/description.html
[32] http://www.osti.gov/bridge/servlets/purl/10188734-StFggW/native/10188734.PDF

4.2 *Information on alternatives*

4.2.1 Human health and environmental effects

Production of MDI

Meta-toluenediamine (TDA) is classified as carcinogenic category 2 in the EU while toluene-2,4-diisocyanate is classified as carcinogenic category 3.

Therefore substitution of MDA with TDA in the synthesis of polyurethanes is not considered to be a valid option to decrease the risks.

Hardener in epoxy resins

A company (anonymous) suggested that the reduction of the hazardous potential was often the driver for R&D in this field. They indicated a concern that a number of possible alternatives are aromatic amines which may also have carcinogenic potential. For these alternatives, studies may take a number of years to confirm the hazards (i.e. switching to another aromatic amine may seem a safer alternative, but only because less is known about the toxicity of that alternative compared to MDA). However, no indication of the effort put into R&D has been communicated by this company.

Air Products provided information on alternatives for this application. This information is presented in Annex 3 (confidential annex).

Hardener in adhesives

As no specific alternatives to MDA for use in adhesives have been identified (see above), it has not been possible to present information on the health and environmental effects of alternatives for this application.

4.2.2 Technical and economical feasibility and availability

Hardener in epoxy resins

The same company referred to in Section 4.2.1, indicated that MDA was used as a hardener to fulfil many different applications. R&D conducted for more than 20 years had been successful in finding some suitable alternatives, but only where a small number of characteristics were essential for the use. However, the greater the number of characteristics demanded of the alternatives the more difficult it has been to find alternatives. They commented that where MDA remained in products it was because they could not find an alternative that fulfilled the technical criteria that were demanded of the product for particular applications.

Hardener in adhesives

The company using MDA in binders for sand forms used in the automotive industry (see 3.1.2), indicated that aliphatic amines were already used as an alternative to MDA for this use. However, they indicated that the lower durability of the sand forms manufactured using these alternatives (less than half when compared to using

MDA) was a cause for a higher cost to each part cast. This is especially important for complex casting forms where the costs for the forms are high.

5 References

BAuA (2000): Draft strategy for limiting risks, 4,4'-methylenedianiline, Bundesanstalt für Arbeitsschutz und Arbeitsmedizin

Brouwer DH, Hoogendoorn L, Bos PM, Boogaard PJ and van Hemmen JJ, (1998). Proposal for the assessment to quantitative dermal exposure limits in occupational environments: Part 2. Feasibility study for application in an exposure scenario for MDA by two different dermal exposure sampling methods. Occupational and Environmental Medicine 55(12):805-11.

EC (2001): European risk assessment report, 4,4'-methylenedianiline, European Commission.

ECHA (2008) Proposal for identification of a substance as a CMR cat 1 or 2, PBT, vPvB or a substance of an equivalent level of concern: 4,4'-Diaminodiphenylmethan MDA. Submitted by: Germany (Federal Institute for Occupational Safety and Health Division for Chemicals and Biocides Regulation)

Kirk Othmer (2000): AMINES, AROMATIC, METHYLENEDIANILINE, Kirk-Othmer Encyclopedia of Chemical Technology.

ISOPA (1999): Socio-economic data on the European Polyurethane Industry, European Diisocyanate and Polyol Producers Association.

ISOPA (2003): Socio-economic Information on the European Polyurethanes Industry, European Diisocyanate and Polyol Producers Association.

OECD (2005): SIDS Initial Assessment Report for 4,4´-Methylenedicyclohexyl diisocyanate, Organisation for the Economic Cooperation and Development.

6 Disclaimers

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Annex 1: Summary of information on manufacture, import, export, uses and releases

.

Table 1: Overview on manufacture, import and export of MDA

Manufacture, trade and formation	**Process** (narrative description)	**Locations** (number of M sites; spatial distribution) [2]	**Tonnage manufactured, imported, exported or formed**	**Releases to working environment** [3]	**Releases to environment** (t/y released to air, wastewater or to waste)
Manufacture	Reaction of aniline with formaldehyde	Possibly 11 sites across the EU (see section 2.1.1)	1,400,000t	Only exposure has been estimated	2.83t to water **
Total Manufacture			**1,400,000t***	**Only exposure has been estimated (see section 2.4.5)**	**2.83t ****
Import subst. on its own			Unknown		
Import subst. in preparations			Confidential		
Import subst. in articles [2]			Unknown or N/A		
Import into EU (total)			**Unknown or N/A**		
Export subst. on its own			Unknown		
Export subst. in preparations			Unknown or N/A		
Export subst. in articles [1]			Unknown or N/A		
Export from EU (total)			**Unknown or N/A**		
Global manufacture			unknown		
Unintentional formation during incineration (EU)	Unknown or N/A			Unknown or N/A	Unknown or N/A
Unintentional formation in processes (EU)	Unknown or N/A			Unknown or N/A	Unknown or N/A
Unintentional formation by transformation/degradation (EU)	Unknown or N/A			Unknown or N/A	Unknown or N/A
Total unintentional formation (EU)				∑ t/y; uncertainty; trends	∑ t/y; uncertainty; trends

1 A list of article types in which the substance is included shall be provided in addition.

2 In quantitative or geographical terms exact specifications are only required if the number of sites is low. If there are many sites a semi-quantitative or qualitative description of the manufacturing structure and spatial distribution of manufacturing sites (e.g. in which Member States, regions, etc.) may suffice.

3 In case a quantification of releases is not possible a qualitative description of the emission situation at the workplace(s) shall be given and a semi-quantitative estimate of the exposure situation provided (e.g. no exposure – very high exp.).

* This is an estimate. See section 2.1.1 for explanations.

** Tentative value; not based on recent site-specific information.

Table 2: Overview on uses of MDA

Uses	**Use Process** (description: narrative and by use descriptor system)	**Amount used** (t/y)	**Number of sites of use** [1] (#)	**Spatial distribution of emission sites** [1]	**Releases to working environment** [3]	**Releases to environment** (t/y released to air, wastewater or to waste)
Formulation						
Hardener in epoxy resins		confidential	unknown	Potentially across all the EU	Only exposure has been estimated	Not significant
Hardener in adhesives		unknown	unknown	Potentially across all the EU		
∑ Formulation		**confidential**	**unknown**	**Potentially across all the EU**	**Only exposure has been estimated (see section 3.4.5)**	**Not significant**
End uses						
End Use 1						
End Use 2						
……..						
End Use *n*						
∑ End Uses		∑ t/y; uncertainty; trends	∑#, trend	Overall geographical pattern; trend	∑ t/y; uncertainty; trends	∑ t/y; uncertainty; trends
Consumer use						
Substance in articles [2]						
Substance in preparations						

∑ consumer use of subst. in articles and preparations		∑ t/y; uncertainty; trends				∑ t/y; uncertainty; trends

1 In quantitative or geographical terms exact specifications are only required if the number of sites is low. If there are many sites a semi-quantitative or qualitative description of the use structure and spatial distribution of sites of release (e.g. in which Member States, regions, etc.) may suffice.

2 A list of article types with the substance included and used by consumers shall be provided as well.

3 In case a quantification of releases is not possible a qualitative description of the emission situation at the workplace(s) shall be given and a semi-quantitative estimate of the exposure situation provided (e.g. no exposure – very high exp.).

Table 3: Overview of quantitative information requested at Member State level for individual years.

YEAR n	**Manufacturing** (t/y)	**Manufacturing** # sites	**Formulation** (t/y)	**Formulation** # sites	**Use 1** (t/y)	**Use 1** # sites	**Use n** (t/y)	**Use n** # sites
Member state								
Austria								
Belgium								
…								
Total								

YEAR n+1	**Manufacturing** (t/y)	**Manufacturing** # sites	**Formulation** (t/y)	**Formulation** # sites	**Use 1** (t/y)	**Use 1** # sites	**Use n** (t/y)	**Use n** # sites
Member state								
Austria								
Belgium								
…								
Total								

ANNEX 2: LITERATURE SEARCH

A literature search was conducted on exposure and alternatives to MDA, interrogating the databases available via Chemical Abstracts and CIN (Chemical Industry Notes) including APOLLIT (Applied Polymers Literature), CIN (Chemical Industry Notes) and RAPRA (rubber, plastics, adhesives and polymeric composites).

Search terms and key words used were:

4-4' diaminodiphenylmethane
MDA
(other synonyms are: bis(4-aminophenyl)methane; 4,4'-methylenedianiline; 4,4'-diaminodiphenylmethane; 4,4'-diphenylmethane diamine; 4,4'-methylendibenzolamine; 4,4'-methylenebisbenzeneamine; 4-(4'-aminobenzyl)aniline).

hardener/s
plastics
epoxy resins
adhesives
epoxy resin adhesives
glues

alternatives
substitutes
replacements

exposure
professional use
skilled use

Search results on exposure papers are in the table below:

Author	Journal	Title of paper
Liippo J, Lammintausta K.	Contact Dermatitis. 2008 Aug; 59(2):109-14.	Contact sensitization to 4,4'-diaminodiphenylmethane and to isocyanates among general dermatology patients.
Wellner T, Lüersen L, Schaller KH, Angerer J, Drexler H, Korinth G.	Food Chem Toxicol. 2008 Jun; 46(6):1960-8. Epub 2008 Feb 2.	Percutaneous absorption of aromatic amines - a contribution for human health risk assessment.
Kenyon SH, Bhattacharyya J, Benson CJ, Carmichael PL.	Toxicology. 2004 Mar 1; 196(1-2):65-75.	Percutaneous penetration and genotoxicity of 4,4'-methylenedianiline through rat and human skin in vitro.
Dugas TR, Kanz MF, Hebert VY, Hennard KL, Liu H, Santa Cruz V, Conklin D, Boor PJ.	Cardiovasc Toxicol. 2004; 4(1):85-96.	Vascular medial hyperplasia following chronic, intermittent exposure to 4,4'-methylenedianiline.
Fortina AB, Piaserico S, Larese F, Recchia GP, Corradin MT, Gennaro F, Carrabba E, Peserico A.	Contact Dermatitis. 2001 May; 44(5):283-8.	Diaminodiphenylmethane (DDM): frequency of sensitization, clinical relevance and concomitant positive reactions.
***Brouwer DH, Hoogendoorn L, Bos PM,**	**Occup Environ Med. 1998 Dec; 55(12):805-11.**	**Proposal for the assessment to quantitative dermal exposure limits in occupational environments: Part 2.**

Boogaard PJ, van Hemmen JJ.		**Feasibility study for application in an exposure scenario for MDA by two different dermal exposure sampling methods.**
Kanerva L, Estlander T, Jolanki R.	**Int J Dermatol. 1996 Dec; 35(12):852-6.**	**Occupational allergic contact dermatitis caused by 2,4,6-tris-(dimethylaminomethyl)phenol, and review of sensitizing epoxy resin hardeners.**
Schütze D, Sagelsdorff P, Sepai O, Sabbioni G.	Chem Res Toxicol. 1996 Oct-Nov; 9(7):1103-12.	Synthesis and quantification of DNA adducts of 4,4'-methylenedianiline.
***Skarping G, Dalene M, Svensson BG, Littorin M, Akesson B, Welinder H, Skerfving S.**	**Occup Environ Med. 1996 Mar; 53(3):180-7.**	**Biomarkers of exposure, antibodies, and respiratory symptoms in workers heating polyurethane glue.**
#Schütze D, Sepai O, Lewalter J, Miksche L, Henschler D, Sabbioni G.	**Carcinogenesis. 1995 Mar; 16(3):573-82.**	**Biomonitoring of workers exposed to 4,4'-methylenedianiline or 4,4'-methylenediphenyl diisocyanate.**
Brunmark P, Dalene M, Skarping G.	Analyst. 1995 Jan; 120(1):41-5.	Gas chromatography-negative-ion chemical ionization mass spectrometry of hydrolysed human urine and blood plasma for the biomonitoring of occupational exposure to 4,4'-methylenebisaniline.
Dalene M, Skarping G, Brunmark P.	**Int Arch Occup Environ Health. 1995; 67(2):67-72.**	**Assessment of occupational exposure to 4,4'-methylenedianiline by the analysis of urine and blood samples.**
Liss GM, Guirguis SS.	Am J Ind Med. 1994 Jul; 26(1):117-24.	Follow-up of a group of workers intoxicated with 4,4'-methylenedianiline.
Jolanki R, Kanerva L, Estlander T, Tarvainen K.	Contact Dermatitis. 1994 Jan; 30(1):12-5.	Concomitant sensitization to triglycidyl isocyanurate, diaminodiphenylmethane and 2-hydroxyethyl methacrylate from silk-screen printing coatings in the manufacture of circuit boards.
Seldén A, Berg P, Jakobsson R, de Laval J.	Int Arch Occup Environ Health. 1992; 63(6):403-8.	Methylene dianiline: assessment of exposure and cancer morbidity in power generator workers.
Gunderson EC, Anderson CC.	Am Ind Hyg Assoc J. 1988 Oct; 49(10):531-8.	A sampling and analytical method for airborne m-phenylenediamine (MPDA) and 4,4'-methylenedianiline (MDA).
#Bastian PG.	**Med J Aust. 1984 Oct 13; 141(8):533-5.**	**Occupational hepatitis caused by methylenedianiline.**
#Robert A, Ducos P, Francin JM.	**Cahiers de notes documentaries, 1996.**	**Assessment of occupational exposure to 4,4'-methylenedianiline (MDA) in France.**
Sepai O, Sabbioni G.	**Adv Exp Med Biol. 1996; 387:451-5.**	**Biomonitoring workers exposed to arylamines. Application to hazard assessment.**
Boeniger MF.	Report number: PB-91-212662/XAB; IWS-143.21. National Inst. for Occupational Safety and Health, Cincinnati, OH (United States). Div. of Surveillance, Hazard Evaluation and Field Studies	Industrial hygiene survey report to General Electric Company. Albuquerque, New Mexico, April 18-24, 1989.
		Industrial hygiene survey report of Arion Electric Substrates Division, Rancho Cucamonga, California, September 21-23, 1988.
Vaudine M, Lery N, Diter JN, Droin M, Chamaillard C.	J de Toxicol Medicale. 1982; 2(3):207-13.	Diaminodiphenylmethane: an example of toxicovigilance in the workplaces of Rhone-Poulenc Industrie.

Dunn GW, Guirguis SS.	Arh Hig Rada Toksikol. 1979; 30(suppl):639-45.	p,p'-Methylene dianiline (MDA) as an occupational health problem. A suggested time-weighted average exposure level and medical program.
Boeniger M.	U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Division of Surveillance, Hazard Evaluation, and Field Studies, Cincinnati, Ohio. pp. 1-52, 1984	Protocol for urine monitoring study of workers exposed to 4,4'-methylene dianiline.
Marshall H Chin, MD, MPH.	J Gen Intern Med. 2005 May; 20(5):448–449.	Populations at risk.
E Kusters.	Br J Ind Med. 1992 January; 49(1):72.	Biological monitoring of MDA.

Titles highlighted in bold were considered for retrieval for further information. Those marked '#' in the above table were already considered by the RAR (EC, 2001) and were therefore not retrieved as information on exposure was already reported in the RAR (EC, 2001). Those marked '*' were retrieved after consideration of the abstract.

Preliminary results on alternatives papers are in the table below:

Author	**Journal**	**Title of paper**
		Two-phase epoxy coatings. Morphology and physicomechanical properties.
Garin J, Melendez J, Tejero T.	J Heterocyclic Chem. 1990; 27(5):1341-1344.	Diheterocyclic compounds from dithiocarbamates and derivatives thereof. III. 3,3'Arylenebis(2,4-dioxo-1,2,3,4-tetrahydroquinazolines).
Boeniger, MF.	Report number: PB-89-164701/XAB; IWS-143.23. National Inst. for Occupational Safety and Health, Cincinnati, OH (USA).	Industrial hygiene survey report, Wabash Magnetic Company, Huntingdon, Indiana, May 24-26, 1988.
Wu K, Bonin AM, Leslie CL, Baker RS, Stacey NH.	**Carcinogenesis. 1989 Nov; 10(11):2119-22.**	**Genotoxicity and effects on rat liver drug-metabolizing enzymes by possible substitutes for 4,4-methylene bis(2-chloroaniline).**
Young PR, Sykes GF.	**NASA Technical Report. 1980. Langley Research Centre. Document ID: 19810059236.**	**Analysis of aromatic polyamine mixtures for formulation of LARC-160 resin.**
McManus KP, Kaiser EA, Burt S, Bresler F.	National Institute for Safety and Health report HETA 91-251-2218. 1992.	Health hazard evaluation report HETA 91-251-2218, New Hampshire Ball Bearing, Laconia, New Hampshire.
		Use of factice in ethylene-propylene terpolymers.
Aboobucker Sithique M, Ramesh S, Alagar M.	Int J Polymeric Materials. 2008 May; 57(5):480-93.	Mechanical and morphological behaviour of bismaleimide-modified soy-based epoxy matrices.

Titles highlighted in bold are those considered for retrieval for further information. After consideration of the abstracts, none were considered to be relevant for retrieval of the full paper.

In addition to searches of the scientific/technical literature, searches on the internet were conducted using the search engine 'Google' with relevant combinations of key words. Information gathered on alternatives is presented, were relevant, in the main document.

ANNEX 3: CONFIDENTIAL INFORMATION