Danish Ministry of the Environment
Environmental Protection Agency

Survey of 1-methyl-2-pyrrolidone

Part of the LOUS review

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Survey of 1-methyl-2-pyrrolidone

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Preface

Background and objectives

The Danish Environmental Protection Agency's List of Undesirable Substances (LOUS) is meant as a guide for enterprises. It indicates substances of concern which uses are intended to be reduced or eliminated completely. The first list was published in 1998 and updated versions have been published in 2000, 2004 and 2009. The latest version, LOUS 2009 (Danish EPA, 2011) includes 40 chemical substances and groups of substances which have been documented as dangerous or which have been identified as problematic based on quantitative structure activity relationship (QSAR) modelling or otherwise been considered of concern or in political focus. For inclusion in the list, substances must fulfil several specific criteria. Besides the risk of leading to serious and long-term adverse effects on health or in the environment, only substances which are used in Denmark in industrial settings in large quantities i.e. over 100 tonnes per year are included in the list.

During the period 2012-2015 all 40 substances and substance groups on LOUS will be surveyed. The surveys include collection of available information on the uses and occurrences of the substances in Denmark and internationally, environmental and health effects, alternatives to the substances, monitoring and exposure data, and information regarding existing regulations.

The main objective of the surveys is to provide background for the Danish EPA's consideration regarding the need for further risk management measures. On the basis of the surveys, the Danish EPA will assess the need for any further information, regulation, substitution/phase out, classification and labelling, improved waste management or increased dissemination of information.

This survey concerns *1-methyl-2-pyrrolidone* (NMP) (CAS: 872-50-4) that has been included in the LOUS list due to its classification as Repr. 1B (H360D) and because NMP is placed on the Danish market in a quantity above 100 tonnes.

The process

The survey has been undertaken by DHI from April 2014 to October 2014. The work has been followed by an advisory group consisting of:

Frank Jensen, Danish EPA, Chair of advisory group
Lea Stine Tobiassen, Danish EPA
Toke Winther, Danish EPA
Anette Ravn Bharathan, AT
Nikolai Nissen, DI

Data collection

The survey and review is based on the available literature on the substances, information from databases and direct inquiries to trade organisations and key market actors.

The data search included (but was not limited to) the following:

- Legislation in force from Retsinformation (Danish legal information database) and EUR-Lex (EU legislation database);

- Ongoing regulatory activities under REACH and intentions listed on ECHA's website (incl. Registry of Intentions and Community Rolling Action Plan);
- Relevant documents regarding the Basel Convention.
- Data on harmonised classification (CLP) and self-classification from the C&L inventory database on ECHAs website;
- Data on ecolabels from the Ecolabelling Denmark (Nordic Swan and EU Flower) and the German Blue Angel.
- Pre-registered and registered substances from ECHA's website;
- Data on production, import and export of substances in mixtures from the Danish Product Register (confidential data, not searched via the Internet);
- Data on production, import and export of substances from the Nordic Product Registers as registered in the SPIN database;
- Data from the European Food Safety Authority (EFSA)
- Reports, memorandums, etc. from the Danish EPA and other authorities in Denmark;
- Reports published at the websites of:
  - The Nordic Council of Ministers, ECHA, the EU Commission, OECD, WHO, Scientific Committee on Consumer Safety (SCCS), Scientific Committee on Occupational Exposure Limits (SCOEL) and the Basel Convention;
  - Environmental authorities in Sweden (KemI and Naturvårsverket),
  - US EPA, Agency for Toxic Substances and Disease Registry (USA).
- PubMed and Toxnet databases for identification of relevant scientific literature.

This survey is mainly based on a compilation of existing reports and evaluations that has been made over time including data from the REACH system and from the common Nordic product register database, SPIN.

Summary and conclusions

NMP has a broad range of applications but is mainly used as a solvent for extraction in the petrochemical industry and as a reactive medium in polymeric and non-polymeric chemical reactions. NMP is used in cleaning products, as a remover of graffiti, as a paint stripper in the occupational setting, and for stripping and cleaning applications in the microelectronics fabrication industry. Furthermore, it is used as a formulating agent in pigments, dyes, and inks and as a formulating agent in insecticides, herbicides, and fungicides. NMP is also used as intermediate in the pharmaceutical industry and as a vehicle in the cosmetics industry.

Of a total global production of 100,000 to 150,000 tonnes, the estimated European production volume of NMP in 2003 was reported to be 30,000 to 50,000 tonnes. Thus, Europe accounted for about one third of global capacity in 2003. The European production was reported to be reduced from 30,000 to 20,000 tonnes by 2005.

When looking at the tonnage of NMP-containing preparations placed on the Nordic market, the reported tonnage for Denmark has been varying between 500 and 1000 tonnes through the last decade. From 2011 to 2012 there has been an increase from 995 to 1,352 tonnes with: solvents, raw materials for the production of pharmaceuticals and insecticides/herbicides as the dominating product groups.

Both the EU and Danish regulations specifically address the use of NMP. The current regulation of NMP includes registration under REACH and classification according to the CLP regulation. NMP is classified as a skin, eye and possible respiratory irritant (H315, H319 and H335) and is classified as a reproductive toxicant category 1B based on developmental toxicity (H360D). An opinion from European Chemicals Agency (ECHA)'s Risk Assessment Committee (RAC) to apply the generic concentration limits of 0.3% instead of the current limit of 5% was adopted by RAC in June 2014. The generic concentration limit is the concentration of NMP in mixtures that trigger classification of the mixture according to the classification of NMP. The change in the concentration limit means that mixtures containing NMP in concentrations from 0.3 % to 5% have to be reclassified. This also includes waste containing NMP.

NMP is listed on the Candidate list of substances of very high concern for authorisation.

NMP in the working environment is regulated by the directive (98/24/EC) on the protection of the health and safety of workers from the risk related to chemical agents at work (implemented in Denmark by the statutory order no. 292 of 26 April 2001). Furthermore, the exposure in the working environment is regulated through occupational exposure limits (OEL) for NMP stating the upper limit on the acceptable concentration of a hazardous substance in workplace air. In Denmark the OEL for NMP is 20 mg/m^3 (8 hour average). The EU has set indicative OEL-values of 40 mg/m^3 (8 hour average) and 80 mg/m^3 (15 minutes peak).

Currently, a proposal submitted by the Netherlands for REACH restriction of NMP at the workplace is discussed in The Committee for Socio-economic Analysis (SEAC). In the Annex XV restriction dossier, DNELs were derived and proposed for workers. An inhalation chronic systemic DNEL of 10 mg/m^3 is derived for workers and an inhalation developmental toxicity DNEL of 5.0 mg/m^3 is derived for pregnant workers. For dermal exposure, a dermal chronic systemic DNEL of 4.6 mg/kg

bw/day and a dermal developmental toxicity DNEL of 2.4 mg/kg bw/day are derived for pregnant workers.

The exposure of consumers is regulated through Annex XVII of REACH with restriction on the use to professional users. Furthermore, regulations and directives on specific products are setting limits for the content of NMP in consumer products, including the concentration in food contact material, medical devices, toys and cosmetics. Also Nordic and EU Eco-labeling criteria documents prohibit or set limits for NMP in labelled products due to its classification with H360D.

Waste with content of NMP has to be treated as hazardous waste if the content of NMP is 5% or more. The lower classification limit of 0.3% as proposed and agreed by the RAC means that the limit for treating NMP-containing waste as hazardous may change to 0.3% NMP. Several waste categories apply to NMP-containing waste. Industrial waste containing NMP is treated by incineration, whereas no information was found on treatment of waste from non-industrial use. NMP has been detected in industrial wastewater effluents and in domestic wastewater.

Overall, NMP does not possess environmental hazards leading to classification. Neither does NMP meet the criteria for being a PBT or a vPvB substance.

Releases into the environment may occur during production of NMP and during its use as solvent or cleaning agent. Especially, the release to air is high (up to 15,353 tonnes/year) compared to the releases to wastewater (353 tonnes/year). The calculated adsorption coefficient (Koc) of 9.6 demonstrates that NMP does not have a tendency to adsorb to sludge. Distribution to the terrestrial soil, for example through the application of sludge to agricultural soil, is therefore not expected. As the substance is mobile in soil, leaching from landfills may be a possible route of contamination of groundwater.

The toxicological properties of NMP indicate that NMP exposure can induce adverse developmental effects in foetuses during development. This is reflected in the classification as Repr. 1B, H360D. In addition to this classification, the harmonised classification for NMP further includes the classification as Skin Irrit. 2; H315, Eye Irrit. 2; H319 and STOT SE 3; H335.

In the Annex XV proposal for restriction of NMP submitted by the Netherlands, it is concluded that the risks are not sufficiently controlled for a number of industrial and professional uses, especially when it concerns processes under elevated temperatures, open processes and processes that require manual activities.

NMP was found in some consumer products in Denmark (porcelain colourant, textile colourant, coated tables, wood figurine, tooth brush, artificial grass, wood toys, cleaning product, iron, cosmetics and drugs) at relatively low levels but up to 5% in porcelain glass. No data on migration of NMP from porcelain glass are available.

For cleaning and coating products used by consumers, there could be a concern due to combined exposure and events of high exposure that could lead to irritation of the skin, eye and respiratory tract of the consumer.

No data concerning the concentration of NMP in cosmetic products and drugs were found, however, it is evaluated by the Scientific Committee on Consumer Safety (SCCS) that a concentration of 5% in cosmetic products is not safe for the consumer.

Replacement of NMP by other substances has been discussed for specific uses including coatings, electronics and cleaning products. For coatings it is noted that downstream users are gradually replacing solvent-based systems with multi-layer water based systems, which still contain a solvent fraction including NMP. The main alternative available on the market to NMP is N-ethylpyrrolidone

(NEP) (EC Number 220-250-6, CAS Number 2687-91-4). This substance is, however, being reviewed for a new classification as a substance toxic to reproduction. The conclusion in the Annex XV restriction dossier is that the solvent that mostly resembles NMP is DMSO.

Sammenfatning og konklusion

NMP har en lang række anvendelser men anvendes hovedsageligt som opløsningsmiddel til ekstraktion i den petrokemiske industri og som reaktionsmedie i polymere og ikke-polymere kemiske reaktioner. NMP anvendes i rengøringsmidler, som graffitifjerner, som malingsfjerner i erhvervsmæssig sammenhæng, og til stripping og renseprocesser i den mikroelektroniske industri. Endvidere anvendes det til formulering af pigmenter, farvestoffer og trykfarver samt af insekticider, herbicider og fungicider. NMP anvendes også som mellemprodukt i den farmaceutiske industri og som vehikel (bærestof) i kosmetikindustrien.

Af en samlet global produktion på 100.000 til 150.000 tons blev den estimerede europæiske produktionsvolumen af NMP rapporteret at være 30.000 til 50.000 tons i 2003. Således tegnede Europa sig for omkring en tredjedel af den globale kapacitet i 2003. Den europæiske produktion blev rapporteret at være reduceret fra 30.000 til 20.000 tons i 2005.

Når man ser på mængden af NMP-holdige præparater på det nordiske marked, har den rapporterede tonnage for Danmark varieret mellem 500 og 1000 tons gennem det sidste årti. Fra 2011 til 2012 har der været en stigning fra 995 til 1.352 tons med opløsningsmidler, råvarer til fremstilling af lægemidler og insekticider/herbicider som de dominerende produktgrupper.

Både EU's og den danske lovgivning adresserer specifikt brugen af NMP. Den nuværende regulering af NMP omfatter registrering i henhold til REACH og klassificering i henhold til CLP-forordningen. NMP er klassificeret som hud-, øjen- og muligvis åndedrætsirriterende (H315, H319 og H335) og er klassificeret som et reproduktionstoksisk stof i kategori 1B baseret på udviklingstoksicitet (H360D). En vurdering fra Det Europæiske Kemikalieagentur (ECHA)'s risikovurderingsudvalg (RAC) om at anvende de generiske koncentrationsgrænser på 0,3% i stedet for den nuværende grænse på 5% blev vedtaget af RAC i juni 2014. Den generiske koncentrationsgrænse er koncentrationen af NMP i blandinger, der udløser klassificering af blandingen i henhold til NMP's klassificering. Ændringen af koncentrationsgrænsen betyder, at blandinger indeholdende NMP i koncentrationer fra 0,3% til 5% skal omklassificeres. Dette omfatter også affald indeholdende NMP.

NMP er opført på kandidatlisten over meget problematiske stoffer til godkendelse.

NMP i arbejdsmiljøet er reguleret ved direktiv (98/24/EF) om beskyttelse af arbejdstagerens sikkerhed og sundhed under arbejdet med kemiske stoffer (implementeret i Danmark ved bekendtgørelse nr. 292 af 26. april 2001). Endvidere er eksponeringen i arbejdsmiljøet reguleret via Arbejdstilsynets grænseværdier (OEL) for NMP med angivelse af øvre grænse for den acceptable koncentration af et farligt stof i luften på arbejdspladsen. I Danmark er grænseværdien for NMP 20 mg/m^3 (gennemsnit 8 timer). EU har fastsat vejledende grænseværdier på 40 mg/m^3 (gennemsnit 8 timer) og 80 mg/m^3 (15 minutter).

I øjeblikket diskuteres i Udvalget for Socioøkonomisk Analyse (SEAC) et hollandsk forslag om begrænsning af NMP på arbejdspladsen gennem REACH. I Bilag XV begrænsningsdossieret blev DNEL afledt og foreslået for arbejdstagere. Der er afledt en inhalation kronisk systemisk DNEL på 10 mg/m^3 for arbejdstagere og en inhalation udviklingstoksicitet DNEL på 5,0 mg/m^3 for gravide arbejdstagere. For dermal eksponering er der afledt en dermal kronisk systemisk DNEL på 4,6 mg/kg legemsvægt/dag, og en dermal udviklingstoksicitet DNEL på 2,4 mg/kg legemsvægt/dag er afledt for gravide arbejdstagere.

Eksponering af forbrugere er reguleret ved Bilag XVII til REACH med begrænsning af anvendelse til erhvervsmæssige brugere. Desuden sætter forordninger og direktiver for specifikke produkter grænser for indholdet af NMP i forbrugerprodukter, herunder koncentrationen i materialer i kontakt med fødevarer, medicinsk udstyr, legetøj og kosmetik. Også de nordiske og EU's miljømærkekriteriedokumenter forbyder NMP som bestanddel på grund af dets klassificering med Repr. 1B, H360D.

Affald med indhold af NMP skal behandles som farligt affald, hvis indholdet af NMP er 5% eller derover. Den nedre klassificeringsgrænse på 0,3% som foreslået og vedtaget af RAC betyder, at grænsen, for hvornår NMP-holdigt affald behandles som farligt, kan ændres til 0,3% NMP. Adskillige affaldskategorier gælder for NMP-holdigt affald. Industriaffald indeholdende NMP behandles ved forbrænding, mens der ikke er fundet oplysninger om behandling af affald fra ikke-industriel brug. NMP er blevet påvist i industrispildevand og i husholdningsspildevand.

Alt i alt har NMP ingen miljøfarlige egenskaber, der fører til klassificering. NMP opfylder heller ikke kriterierne for at være et PBT eller et vPvB-stof.

Udslip til miljøet kan forekomme under produktion af NMP og, når det anvendes som opløsningsmiddel eller rengøringsmiddel. Der er især et højt udslip til luft (op til 15.353 tons/år) sammenlignet med udslip til spildevand (353 tons/år). Den beregnede adsorptionskoefficient (Koc) på 9,6 viser, at NMP ikke har tendens til at adsorbere til slam. Distribution til jord, for eksempel ved anvendelse af slam på landbrugsjord, forventes derfor ikke. Da stoffet er mobilt i jord, kan udvaskning fra lossepladser være en mulig rute til forurening af grundvandet.

NMP's toksikologiske egenskaber indikerer, at NMP-eksponering kan medføre negative udviklingsmæssige effekter hos fostre. Dette afspejles i klassificeringen som Repr. 1B, H360D. Ud over denne klassificering er den harmoniserede klassificering for NMP endvidere Skin Irrit. 2; H315, Eye Irrit. 2; H319 og STOT SE 3; H335.

I Bilag XV, forslag til begrænsning af NMP fremlagt af Holland, konkluderes det for en række industrielle og professionelle anvendelsesformål, at risici ikke er tilstrækkeligt kontrolleret, især når det drejer sig om processer ved høje temperaturer, åbne processer og processer, der kræver manuelle aktiviteter.

NMP er blevet fundet i forbrugerprodukter i Danmark (porcelæn-farvestof, tekstil-farvestof, belagte borde, træfigur, tandbørste, kunstgræs, trælegetøj, rengøringsprodukter, strygejern, kosmetik og lægemidler) på et relativt lavt niveau, men op til 5% i porcelænsglas. Der er ingen tilgængelige data om migration af NMP fra porcelænsglas.

For rengørings- og malingsprodukter, der anvendes af forbrugere, kan der være betænkelighed på grund af kombineret eksponering og episoder med høj eksponering, der kan medføre irritation af hud, øjne og luftveje.

Der blev ikke fundet data om koncentrationen af NMP i kosmetiske produkter og lægemidler. Den Videnskabelige Komité for Forbrugersikkerhed (VKF (SCCS)) har imidlertid vurderet, at en koncentration på 5% i kosmetiske produkter ikke er sikker for forbrugeren.

Substitution af NMP med andre stoffer diskuteres for specifikke anvendelser, herunder malingsprodukter, elektronik og rengøringsprodukter. For malingsprodukter skal det bemærkes, at downstream-brugere efterhånden erstatter opløsningsmiddelbaserede systemer med multi-lags vandbaserede systemer, som stadig indeholder en opløsningsmiddelfraktion, herunder NMP. Det primære alternativ, der er tilgængeligt på markedet, til NMP, er N-ethylpyrrolidon (NEP) (EF-nummer 220-250-6, CAS-nummer 2687-91-4). Dette stof er dog ved at blive undersøgt med henblik

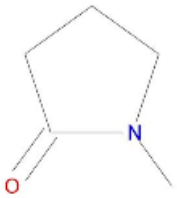
på en klassificering som reproduktionstoksisk. Konklusionen in Bilag XV begrænsningsdossieret er at det opløsningsmiddel, der mest minder om NMP, er DMSO.

1. Introduction to the substance

1.1 Identification of the substance

The substance identification is described in the Table 1-1 below.

TABLE 1-1: NAME AND OTHER IDENTIFIERS OF 1-METHYL-2-PYRROLIDONE (NMP) (WHO, 2001; REACH REGISTRATION DATA, 2014; ANNEX XV SVHC DOSSIER, 2011)

1-methyl-2-pyrrolidone	
EC number	212-828-1
CAS number	872-50-4
Synonyms	1-methylpyrrolidin-2-one N-Methyl-2-pyrrolidone N-methylpyrrolidone 1-Methyl-5-pyrrolidinone 1-Methylazacyclopentan-2-one 1-Methylpyrrolidone AgsolEx 1 M-Pyrol Microposit 2001 N 0131 N-Methyl-α-pyrrolidinone N-Methyl-α-pyrrolidone N-Methyl-γ-butyrolactam N-Methyl-2-ketopyrrolidine N-Methyl-2-pyrrolidinone N-Methyl-2-pyrrolidone N-Methylbutyrolactam N-Methylpyrrolidone NMP NSC 4594 Pharmasolve Pyrol M SL 1332
Molecular formula	C_5H_9NO
Molecular weight	99.13
Structure	

1.1.1 Purity and impurities

The purity of NMP is in the range of 80-100% (Annex XV SVHC dossier, 2011).

According to the SCCS (2011), the impurities of NMP are described as follows:

Dimethyl pyrrolidones (mixtures of isomers) < 0.4 %
Methylamine < 0.005 %
γ-Butyrolactone < 0.05 %
Water < 0.05 %

1.2 Physical and chemical properties

NMP is a colourless liquid with a mild amine odor. It is a polar compound with high stability. It is slowly oxidised by air and is easily purified by fractional distillation. NMP is hygroscopic, which means it has an ability to attract and hold water molecules from the surrounding environment. The substance is completely miscible with water. It is highly soluble in lower alcohols, lower ketones, ether, ethyl acetate, chloroform, and benzene and moderately soluble in aliphatic hydrocarbons (WHO, 2001).

TABLE 1-2: PHYSICAL-CHEMICAL PROPERTIES FOR 1-METHYL-2-PYRROLIDONE (NMP) (WHO, 2001; ANNEX XV SVHC DOSSIER, 2011)

Property	
Physical state at 20°C and 101.3 kPa	Liquid
Density	1.028 g/cm^3
Viscosity	1.796 mPa s at 20 °C
Freezing/Melting point	23 to 24.4 °C
Boiling point	202°C at 101.3 Pa
Flash point	91 °C
Vapour pressure	39 Pa at 20 °C 45 Pa at 25 °C
Water solubility (mg/L)	Miscible
Log Kow (octanol/water)	0.38

2. Regulatory framework

This chapter gives an overview of how NMP is addressed in existing and forthcoming EU and Danish legislation, international agreements, eco-label criteria etc. The overview reflects the findings from the data search.

For readers not used to dealing with legislative issues, Appendix 1 provides a brief overview of and connections between legislative instruments in EU and Denmark. The appendix also gives a brief introduction to chemicals legislation, explanation of lists referred to in chapter 2, as well as a brief introduction to international agreements and the aforementioned eco-label schemes.

2.1 Existing legislation

The Danish EPA has included NMP on the LOUS list (2009) based on its classification as Repr. 1B (H360D) and because NMP is placed on the Danish market in a quantity above 100 tonnes.

Both the EU and Danish regulations specifically address the use of NMP. The current regulation of NMP, which is listed in Table 2-1 below, includes registration under REACH and classification according to the CLP.

The exposure to workers is regulated through the regulation of the use of chemicals in the working environment, i.e. the exposure to chemicals agents at work places in addition to indicative occupational exposure limits (OEL). In EU the OEL for NMP is 40 mg/m^3 (8 hour average). This value is also recommended by Scientific Committee on Occupational Exposure Limits (SCOEL, 2007). In Denmark an OEL of 20 mg/m^3 (8-hour average) applies.

The exposure of consumers is regulated through Annex XVII of REACH and directives addressing and setting limits for the content of NMP in specific consumer products such as food contact material, medical devices, toys and cosmetics.

TABLE 2-1: LEGISLATION ADRESSING 1-METHYL-2-PYRROLIDONE (NMP) (CAS: 872-50-4)

Legal instrument	EU/DK	Requirement as concerns NMP and national implementation
Regulation on chemical substances and mixtures		
REACH Regulation Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)	EU	Registration for manufacture and import above 1 tonnes per year. Registered tonnage band 10,000-100,000 tonnes per year NMP is listed on the Candidate List of Substances of Very High Concern for Authorisation NMP is included in Appendix 6 to Annex XVII, entry 30 (Toxic to reproduction: category 1B) with restriction on the use of NMP to professional users
CLP Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures	EU	EU harmonised classification. Please refer to Table 2-2
Environment and waste regulation		
Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy	EU	As a consequence of the classification as Repr. 1B, NMP is included in Annex VIII of Directive 2000/60/EC (Indicative list of main pollutants)
Directive 2008/98/EC of the European Parliament and of the Council of 19 November 2008 on waste and repealing certain directives	EU	As a consequence of the classification as Repr. 1B, NMP is included in Annex III: Properties of waste which render it hazardous.
Danish Statutory Order No. 1309 of 18/12/2012 (Statutory Order on waste)	DK	As a consequence of the classification as Repr. 1B, NMP is included in Annex 4: Properties and weight % which classifies waste as hazardous
Basel Convention on the control of transboundary movements of hazardous wastes and their disposal	Global	As a consequence of the classification, NMP is covered by Annex III of the Basel Convention regarding the control of transboundary movements of hazardous wastes and their disposal.

Legal instrument	EU/DK	Requirement as concerns NMP and national implementation
Working environment		
Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work and amended by Directive 2014/27/EU of 26 February 2014. Implemented in Denmark by Statutory Order No. 292 of 26. April 2001 with later amendments on work with substances and materials (chemical agents).	EU	On the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC). 'Hazardous chemical agent' means: any chemical agent which meets the criteria for classification as hazardous within any physical and/or health hazard classes laid down in Regulation (EC) No 1272/2008 of the European Parliament and of the Council. NMP meets this criterion due to the classification as Repr. 1B.
Directive 2009/161/EU establishing a third list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC and amending Directive 2000/39/EC	EU	Indicative occupational exposure limits for chemical agents: The OELs of 40 mg/m^3 (8 hour average) and 80 mg/m^3 (15 minutes peak exposure) apply for NMP
Danish Statutory Order No. 1134 of 01/12/2011 amending the Order on limit values for substances and materials in the working environment	DK	The OEL of 20 mg/m^3 (8 hour average) applies for NMP with a skin notation (H) and a notation E, which indicate that there is an indicative European occupational exposure limit.
Danish Executive Order on the Performance of Work No. 559 of 17 June 2004	DK	Section 16. Any unnecessary effect of substances and materials shall be avoided. Therefore, the effect of substances and materials during work shall be reduced to the lowest level reasonably practicable taking account of technical progress, and any limit values fixed shall be complied with. Section 8. (2) Particularly sensitive risk groups, including pregnant employees and employees who are breastfeeding, shall be protected against the dangers which specifically affect them.

Legal instrument	EU/DK	Requirement as concerns NMP and national implementation
Consumer products regulation		
REACH regulation Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)	EU	NMP is included in Appendix 6 to Annex XVII, entry 30. NMP shall not be placed on the market, or used, — as substances, — as constituents of other substances, or, — in mixtures, for supply to the general public when the individual concentration in the substance or mixture is equal to or greater than: — either the relevant specific concentration limit specified in Part 3 of Annex VI to Regulation (EC) No 1272/2008, or, — the relevant concentration specified in Directive 1999/45/EC where no specific concentration limit is set out in Part 3 of Annex VI to Regulation (EC) No 1272/2008
Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products	EU	As a consequence of the classification as Repr. 1B, the use of NMP in cosmetic products shall be prohibited. NMP is not included in Annex II of the regulation: "List of substances prohibited in cosmetic products"
Directive 2009/48/EC of the European Parliament and of the Council of 18 June 2009 on the safety of toys	EU	As a consequence of the classification as Repr. 1B, NMP is not allowed in toys in components of toys or in micro-structurally distinct parts of toys.
Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food	EU	As a consequence of the classification as Repr. 1B, NMP should not be used in food contact materials or articles without previous authorisation. Plastic materials and articles shall not transfer their constituents to foods in quantities exceeding the specific migration limits (SML) set out in Annex I. NMP is included on Annex I of the regulation. No SML is set for NMP therefore the limit of 60mg/kg applies.

Legal instrument	EU/DK	Requirement as concerns NMP and national implementation
Council Directive 93/42/EEC of 14 June 1993 concerning medical devices	EU	The devices must be designed and manufactured in such a way as to reduce to a minimum the risks posed by substances leaking from the device. Special attention shall be given to substances which are carcinogenic, mutagenic or toxic to reproduction, in accordance with the CLP Regulation (EC) No 1272/2008.
Other regulation		
The Danish EPA´s guidance document No. 2 on B-values.	DK	B-value (contribution value) of 0.5 mg/m^3, as a limit value for each company's contribution to the air pollution in the environment.

2.2 Classification and labelling

2.2.1 Harmonised classification in the EU

A harmonised classification and labelling is appointed to NMP according to Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation). NMP is classified as presented in Table 2-2.

TABLE 2-2: HARMONISED CLASSIFICATION OF 1-METHYL-2-PYRROLIDONE (NMP) (CAS: 872-50-4)

Chemical identification (CAS No)	Classification	
	Hazard Class and Category Code(s)	Hazard statement Code(s)
NMP (872-50-4)	Skin Irrit. 2	H315
	Eye Irrit. 2	H319
	STOT SE 3	H335
	Repr. 1B	H360D

H315: Causes skin irritation; H319: Causes serious eye irritation; H335: May cause respiratory irritation; H360D: May damage the unborn child.

The specific concentration limits to be applied for NMP are:

Repr. 1B; H360D: C ≥ 5 %

STOT SE 3; H335: C ≥ 10 %

See Section 2.2.4 for proposal for classification and labelling.

NMP shall be labelled with the signal word: Danger
and the warning pictograms:

2.2.2 Notified classification in the EU

The classifications notified by the companies placing NMP on the EU-market are found in the C&L Inventory database (2014). There are 2,261 notified classifications for NMP. In total, 2,128 of these notified classifications are in accordance with the harmonised classification presented above.

2.2.3 Classification from the REACH registration

The classification of NMP in the lead registration dossier in REACH reflects the harmonised classification (REACH registration data, 2014).

2.2.4 Proposal for classification and labelling

A proposal for change in specific concentration limit has been submitted by the Netherlands (Bureau REACH, 2013). In June 2014, the Risk Assessment Committee (RAC) agreed to the proposal by the Netherlands to remove the specific concentration limit (SCL) relating to the classification as presumed reproductive toxicant (Repr. 1B; H360D) so that the generic concentration limit (GCL) of 0.3% applies (ECHA, 2014a). The generic concentration limit is the concentration of NMP in mixtures that trigger classification of the mixture according to the classification of NMP. The change in the concentration limit means that mixtures containing NMP in concentrations from 0.3 % to 5% have to be reclassified.

2.3 REACH

NMP has been registered under REACH at a tonnage band of 10,000- 100,000 tonnes per year. One lead registration dossier has been submitted.

Because of the classification as Repr. Category 1B, NMP has been identified as a Substance of Very High Concern (SVHC) and included in the Candidate List for Authorisation in 2011 (Decision ED31/2011). The inclusion was according to REACH Articles 57 and 59 and based on an Annex XV SVHC dossier (2011) prepared by ECHA.

2.3.1 Proposal for restriction

An Annex XV proposal for restriction of NMP (Annex XV Restriction dossier, 2013) was submitted by the Netherlands in August 2013. The proposal addresses the reproductive toxicity of NMP and it concludes that risks are not sufficiently controlled for a number of industrial and professional uses: Especially when the use is related to processes under elevated temperatures, open processes, and processes that require manual activities and where additional implementation of risk management measures (RMMs) are not possible. The restriction proposal includes a limit of 5 mg/m^3 to the 8-hour OEL-value in order to adequately control exposure from the manufacture and use of NMP.

The proposal has been discussed by RAC in June 2014 (ECHA, 2014b). According to the opinion of RAC, manufacturers, importers and downstream users of NMP on its own or in mixtures in a concentration equal or greater than 0.3% shall use a long-term Derived No Effect Level (DNEL) of 10 mg/m^3 for inhalation and 4.6 mg/kg bw/day for dermal exposure in their chemical safety assessments and safety data sheets for workers. The Committee for Socio-economic Analysis (SEAC) agrees on the proposal and has prepared a draft opinion on the above mentioned restriction dossier. SEAC considers that the proposed restriction on NMP, as modified by RAC, is the most appropriate EU wide measure to address the identified risks in terms of cost-effectiveness. SEAC is

however unable to determine if the restriction is an appropriate EU-wide measure to address the identified risks in terms of providing a net gain in socioeconomic welfare to society (SEAC, 2014).

2.3.2 Notification of substances in articles

A total of 6 notifications have been done for NMP in articles in concentrations above 0.1 % (W/W). However, no article categories or types have been reported and no consumer use of articles has been indicated.

2.4 Other legislation/initiatives

2.4.1 Eco labels

The European Flower Eco label and the Nordic Swan Eco label generally address substances by their classification when evaluating products; excluding substances with a specific classification or setting concentration limits for the content of these substances within the product. The specific requirements are dependent on the product in question and the corresponding criteria document.

Due to NMP's classification as Repr. 1B; H360D, the European Flower Eco label prohibits NMP as an ingredient in concentrations greater than 0.01% in labelled products such as paint and coatings, cleaning products and detergents. The Nordic Swan Eco-label prohibits NMP as an ingredient in the labelled products and only allows NMP as a residue from the production in concentrations below 0.01%.

2.5 Summary and conclusions

Both the EU and Danish regulations specifically address the use of NMP. The current regulation of NMP includes registration under REACH and classification according to the CLP regulation. NMP is classified as a skin, eye and possible respiratory irritant (H315, H319 and H335) and is classified as a reproductive toxicant category 1B based on developmental toxicity (H360D). An opinion from RAC to apply the generic concentration limits of 0.3% instead of the current limit of 5% was adopted by RAC in June 2014.

Furthermore, there is a regulation addressing the use of NMP in the working environment and there are occupational exposure limits (OEL) for NMP stating the upper limit on the acceptable concentration of a hazardous substance in workplace air. In Denmark the OEL for NMP is 20 mg/m^3 (8 hour average). The EU has set OEL-values of 40 mg/m^3 (8 hour average) and 80 mg/m^3 (15 minutes peak).

The exposure of consumers is regulated through Annex XVII of REACH and directives addressing and setting limits for the content of NMP in consumer products, including the concentration in food contact material, medical devices, toys and cosmetics. Also Nordic and EU Eco-labeling criteria documents prohibit or set limits for NMP in labelled products due to its classification with H360D.

3. Manufacturing

3.1 Manufacturing processes

NMP is a synthesised organic substance. The manufacturing process is described as part of the Annex XV SVHC dossier (2011) as follows:
The precursor for the synthesis of NMP is γ-Butyrolacton, which is manufactured in a catalytic process from formaldehyde and acetylene. Adding methylamine, the γ-Butyrolacton is transformed into NMP.

3.2 Manufacturing sites and volumes

The annual world production capacity of NMP in 2003 was estimated at 100,000 to 150,000 tonnes, subdivided into 30,000 – 50,000 tonnes/year for Europe (3 production sites), 60,000 – 80,000 tonnes/year for USA (3 production sites), and 10,000 – 20,000 tonnes/year for Asia/Pacific (4 production (Table 3-1). This indicates that Europe accounted for about one third of global capacity in 2003. During 2005, the estimated European production capacity was about 20,000 – 30,000 tonnes (OECD SIDS, 2007). It is likely that Europe's global share of capacity has reduced in recent years, as Asian chemical production capacity and demand has increased.

TABLE 3-1: GLOBAL AND EU 1-METHYL-2-PYRROLIDONE (NMP) (CAS: 872-50-4) PRODUCTION SITES AND CAPACITY (OECD SIDS, 2007)

Geographical region	Number of production sites	Capacity (t/a) [year]
Europe	3	30.000 – 50.000 [2003] 20.000 – 30.000 [2005]
USA	3	60.000 – 80.000 [2003]
Asia	4	10.000 – 20.000 [2003]
Global	10	100.000 – 150.000 [2003]

3.3 Import and export

The total amount of NMP placed on the EU market is between 10,000 tonnes and 50,000 tonnes (Annex XV SVHC dossier, 2011). Based on data reported in registration dossiers, there does not seem to be a significant trend in imports over the last 3-4 years, with some importers increasing quantities and others decreasing quantities imported (Annex XV SVHC dossier, 2011).

According to information in the Annex XV restriction dossier (2013), the share accounted for by imports into the EU as pure substance or in a mixture is estimated around 50% of the total tonnage used. It appears that several hundred tonnes of the imports are in the form of mixtures. Export of NMP was reported to be 1,000 to 2,000 tonnes per year, although it should be noted that this is

based on a limited response to a questionnaire and which was not considered to represent the EU as a whole. The export of NMP in mixtures is unknown (Annex XV Restriction dossier, 2013).

3.4 Use

3.4.1 Identified uses in the EU

NMP has a broad range of applications. NMP is used as a solvent for extraction in especially the petrochemical industry for extraction of aliphatic and aromatic hydrocarbons, natural and manufactured gases, lubricant oils, coals and tars and compounds containing oxygen, nitrogen and/or halogens. NMP has a strong and selective solvent power and dissolves most mono- and polymers. NMP is used as a reactive medium in polymeric and non-polymeric chemical reactions. Furthermore, NMP is used in cleaning products, as a remover of graffiti, as a paint stripper in the occupational setting, and for stripping and cleaning applications in the microelectronics fabrication industry. NMP is also used as a formulating agent in pigments, dyes, and inks and as a formulating agent in insecticides, herbicides, and fungicides. NMP is used in surface coatings and binders in road and construction activities including paving, manual mastic and in the application of roofing and water-proofing membranes. NMP is further used as intermediate in the pharmaceutical industry, as a penetration enhancer for topically applied drugs, and as a vehicle in the cosmetics industry (Åkesson, B, 1994; WHO, 2001, Annex XV SVHC Dossier, 2011).

The registered uses of NMP according to ECHA's database of REACH registered substances are shown below.

TABLE 3-2: REGISTERED USES OF NMP ACCORDING TO REACH REGISTRATION DATA (2014)

Industrial uses	Manufacture of other substances, Polymer processing, Formulation of preparations, Use in industrial chemical processes, Dip Coating, Use in Functional Fluids, Use as a solvent, Uses in Coatings, Use as binders and release agents, Use in Construction Chemicals, Use in Cleaning Agents, Water treatment chemicals, Use in laboratories, Use in Oil field drilling and production operations
Professional uses	Formulation of preparations, Polymer processing, Use in Functional Fluids, Use in Coatings, Roller coating, Use as binders and release agents, Use in Cleaning Agents, Use in laboratories, Agrochemical uses, Road and construction applications, Use in Oil field drilling and production operations
Consumer uses	Use in ink for consumer

The corresponding Sectors of End-Use categories (SU) are the following:
SU 0: Other
SU 1: Agriculture, forestry and fishing
SU 3 Industrial Manufacturing (all)
SU 8: Manufacture of bulk, large scale chemicals (including petroleum products)
SU9: Manufacture of fine chemicals
SU 10: Formulation [mixing] of preparations and/or re-packaging (excluding alloys)
SU 22 Professional Uses (all)
SU 24: Scientific research and development

There is only one identified use for consumers (non-professional uses): consumers use of printing ink (PC 18: Ink and toners). No subsequent “service life" is declared for the identified uses (REACH registration data, 2014).

3.4.2 Uses according to available safety datasheets

An internet search was done on material safety data sheets in order to identify products containing NMP and to identify to which user groups, professionals or consumers, the products are available. The search was done based on substance name and CAS number.

In general, most safety data sheets are not stating whether the products are for professional and/or consumers (Table 3-3). As the brand names of the products are not very expressive, the products are considered to be products meant for professional and industrial users. Only the product named “Yellow printing ink” does have a name indicating that the product is meant to be used by consumers. The products may be globally available as the safety data sheets do not state that they are intended for a specific market. The products containing NMP are representing paints, coatings, printing ink, insecticide, herbicide, paint stripper and sealants. The concentration of NMP in the products varies from only a few percentages and up to 85 %.

TABLE 3-3: MATERIAL SAFETY DATA SHEETS FOR PRODUCTS CONTAINING NMP

Product type (name)	User	Form	Content of NMP [%]	Further information	Reference
Coating (Agrotain® Ultra Fertilizer Coating)	NA	Green Liquid	10-30	NA	KOCH Agronomic Services, LLC, MSDS 10.06.2011
Coating (Macekote 5545 Waterborne polyurethane dispersion)	NA	Milky - translucent liquid	NA	NA	Mace company (no year)
Coating (MOBIHEL HYDRO Clear base Coating, based on Polyurethane water dispersions with solvents content)	NA	Liquid	1-2.5	NA	Helios SDS, Revision Date: 07/07/06
Coating (MIL-DTL-64159B, Type II Coating, Water Dispersible Aliphatic Polyurethane, CARC, Black 37038)	NA	NA	4	NA	THE SHERWIN-WILLIAMS CO. MSDS, 16.09.2013
Paint (A-4100 SERIES Aerosol acrylic)	Industrial	NA	1-5	NA	Cardinal industrial finishes MSDS, 01.04.2005
Paint Stripper/Stripper. (Peel Away 5 Soy Based)	NA	NA	25-35	Organic solvent mixture	Dumond, SDS version 1 12.12.2012

Product type (name)	User	Form	Content of NMP [%]	Further information	Reference
Pesticide (MERIDIAN 0.33G Neonicotinoid Insecticide)	NA	Brown granules	<5	NA	Syngenta MSDS (no year)
Pesticide (Agri west aw invest 240EC selective herbicide)	NA	Liquid	<10	NA	Agri West, MSDS 13.04.2010 CHEMWATCH 23-4474
Printing ink (CN816Series Inkjet printing Yellow printing ink)	NA	NA	<5	NA	Hewlett-Packard Company, MSDS Revision date: 14.11.2013
Product type not stated X-Gal - IPTG Ready Solution	NA	Liquid	75-85	For Further Manufacturing Use Only	AMRESCO, LLC SDS 24.01.2012
Sealant (TURTLE WAX Headlight restoration kit – headlight base coat sealant)	NA	Slightly Viscous Thin Liquid	1-5	NA	Turtle wax MSDS (no year)
Solder (TSF 6521C Tacky Solder Flux)	Professionals only	NA	1-2.5	NMP is not present in the finished part	Kester safety data sheet Revision: 20.11.2013

According to the Household Product Database, which is part of the US-Department of Health and Human Services (2014), NMP is contained in several consumer products on the US market. Appendix 2 summarises the results from the database (search based on CAS number). From the database it can be seen that NMP is applied in arts and crafts, auto products, home maintenance products, and in pesticides in various concentrations. Arts & crafts products may contain up to 45%, auto products up to 40% and home maintenance products may consist of 100% NMP. A similar European database for consumer products was not found, but it is noted here that printing ink is the only consumer use of NMP registered in REACH.

3.4.3 Use in the Nordic countries

The Nordic SPIN database ("Substances in Preparations in the Nordic Countries") is the result of a common Nordic initiative to gather non-confidential data. The database summarises information from the Nordic product registers on the common use of chemical substances in different types of products and industrial areas. Information on use volumes and the tonnage of preparations in the Nordic countries has been retrieved for the period 2006-2012 and presented in Figure 3.1 and Figure 3.2 (Nordic SPIN Database, 2014).

From 2006 to 2008, the number of preparations containing NMP was constant (770-786) where after the number has been declining. In 2012 the numbers of preparations reported was 585. A decline in the number of products should be considered in parallel with the tonnage of preparations (Figure 3.2) as the decline may be an indication of one or few preparations dominating the market. In Sweden there has been a steady increase, and especially from 2010 to 2011, the numbers increased markedly, however, without a corresponding increase in the tonnage reported. Norway

and Finland have had a quite constant numbers of NMP-containing preparations fluctuating around 150 to 200 from year 2006 to 2012 (Nordic SPIN Database, 2014).

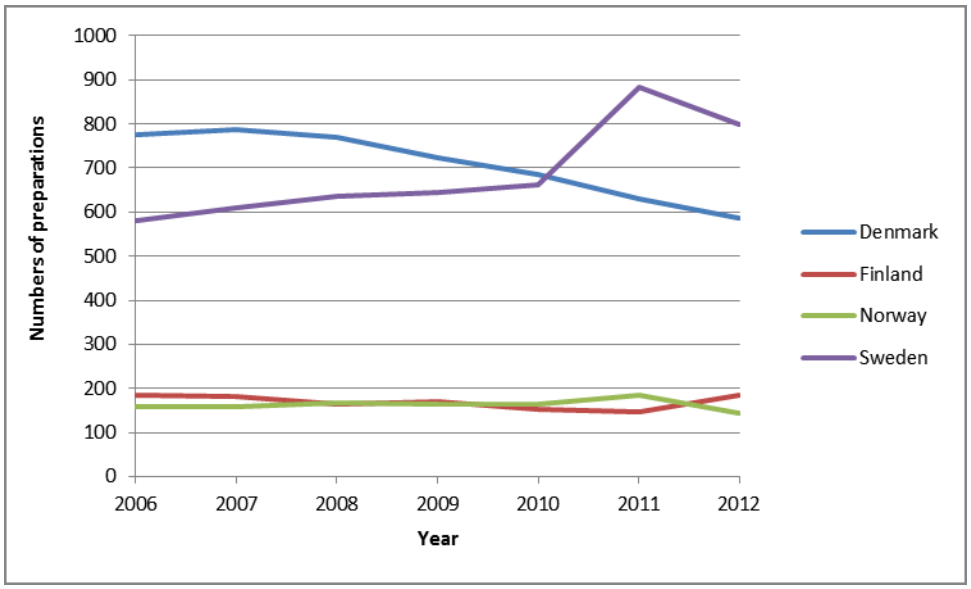


FIGURE 3.1: NUMBERS OF NMP-CONTAINING PREPARATIONS PLACED ON THE NORDIC MARKET (NORDIC SPIN DATABASE, 2014).

Regarding the tonnage of NMP contained in preparations placed on the Nordic market, the reported tonnage for Denmark has been at a level of 500 tonnes with a peak to above 850 tonnes in 2008. In 2011 the tonnage increased to 995 tonnes and further to 1,352 tonnes in 2012. In Sweden the tonnage has been declining since 2006. The Swedish Chemical Agency (KemI) states on their home page that the decline was due the reassessment of the hazard of NMP at that time. Norway is the country with the lowest tonnage reported even though there was an increase from 2010 (23.1 t) to 2011 (188.5 t). However, the reported tonnage for 2012 (23.4 t) is corresponding to the reported level in 2010. For Finland there has also been a decline since 2006 where there were 1,213 tonnes on the market compared to 106.6 tonnes in 2012 (Nordic SPIN Database, 2014).

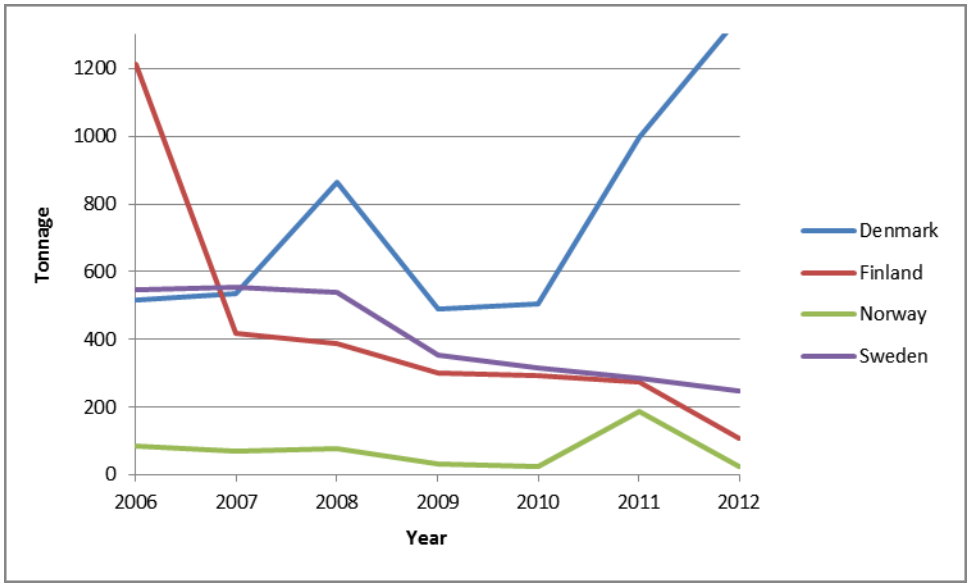


FIGURE 3.2: TOTAL TONNAGE OF NMP-CONTAINED IN PREPARATIONS PLACED ON THE NORDIC MARKET (NORDIC SPIN DATABASE, 2014).

In Denmark paint, lacquers and varnishes accounted for more than half of the numbers of preparations, i.e. 311 preparations in 2012 which therefore was the largest product category containing NMP. Second was Cleaning and washing agents with 70 different preparations (Table 3-4). It must be noted that the total numbers of NMP-containing products reported in the table below is not identical with the number (585) reported above, even though data are from the same data source (Nordic SPIN Database). It has not been possible to find an explanation for this deviation.

TABLE 3-4: NUMBERS OF NMP-CONTAINING PREPARATIONS PLACED ON THE DANISH MARKET IN 2006 AND 2012 (NORDIC SPIN DATABSE, 2014)

Category	2006	2012
Solvents	23	17
Cleaning/washing agents	125	70
Adhesives, binding agents	46	27
Paints, laquers and varnishes	358	311
Surface treatment	27	31
Impregnation materials	9	-
Pesticides, agricultural	13	-
Fillers	19	14
Viscosity adjustors	5	-
Reprographic agents	62	33
Non-agricultural pesticides and preservatives	9	4
Colouring agents	25	-
Process regulators	8	-
Lubricants and additives	7	-
Surface-active agents	6	-
Construction materials	9	31
Total	**751**	**538**

According to information from the Danish Product Registry, solvents in general are representing the highest volume registered followed by raw materials for the production of pharmaceuticals and insecticides and herbicides (Danish Product Registry, 2014).

Reports on measurements of NMP in different types of consumer products have been prepared from the Danish EPA. NMP was found in consumer products such as porcelain glass, textile

colourant, coated tables, wood figurine, tooth brush, artificial grass, wood toys, iron and cleaning products (paint and lacquer remover) (see section 6.2.1.1).

3.5 Trends in use

Based on information retrieved from the Annex XV Restriction dossier, several companies have indicated that they have ceased use of NMP in recent years, particularly due to regulatory concerns following its classification as a reproductive toxicant (Repr. 1B) in 2010 (Annex XV Restriction dossier, 2013).

The major categories of preparations, in Denmark, containing NMP, are presented in Table 3-4. From this table it can be seen that both in 2006 and in 2012 it has mainly been preparations such as "paints, lacquers and varnishes" which contain NMP followed by "cleaning and washing agents". The use in cleaning and washing agent has, however, gone down from125 to 70. Also the use in reprographic agents has gone down from 62 to 33. According to data in the Nordic Spin Database, several types of preparations are no longer including NMP. These include pesticides (agricultural), colouring agents and impregnation agents. Based on the volumes of NMP in products on the Danish market, the product groups: solvents, raw materials for the production of pharmaceuticals and insecticides/herbicides are dominating.

The lower classification limit of 0.3%, as proposed and agreed by the RAC, means that NMP-containing products will only be allowed for consumers use if concentration of NMP is lower than 0.3% according to the restriction in REACH (Annex XVII entry 30).

3.6 Summary and conclusions

NMP is mainly used as a solvent for extraction in the petrochemical industry and as a reactive medium in polymeric and non-polymeric chemical reactions. NMP is used in cleaning products, as a remover of graffiti, as a paint stripper in the occupational setting, and for stripping and cleaning applications in the microelectronics fabrication industry. Furthermore it is used as a formulating agent in pigments, dyes, and inks and as a formulating agent in insecticides, herbicides, and fungicides. NMP is also used as intermediate in the pharmaceutical industry and as a vehicle in the cosmetics industry. Of a total global production of 100,000 to 150,000 tonnes, the estimated European production volume of NMP in 2003 was reported to be 30,000 to 50,000 tonnes. Europe accounted for about one third of global capacity in 2003. The European production was reported to be reduced from 30,000 to 20,000 tonnes by 2005.

In Denmark paint, lacquers and varnishes accounted for 311 preparations containing NMP in 2012, which therefore was the largest product category containing NMP. Second was Cleaning and washing agents with 70 different preparations. When looking at the tonnage of NMP-containing preparations placed on the Nordic market, the reported tonnage for Denmark has been varying between 500 and 1000 tonnes through the last decade. However, from 2011 to 2012 there has been an increase from 995 to 1,352 tonnes with: solvents, raw materials for the production of pharmaceuticals and insecticides/herbicides as the dominating product groups.

4. Waste management

4.1 Waste from manufacture and use of NMP

Waste generated during manufacturing or from industrial use has according to the EU and Danish legislation on waste to be treated as hazardous waste if the waste contains substances in an amount that according to classification rules for chemical substances and preparations would result in classification for either physical-chemical, toxicological or environmental properties (Danish Ministry of Environment, 2012; Directive 2008/98/EC). Waste is considered hazardous if it exhibits one or more of the characteristics listed in Table 1 of the Danish Statutory Order on waste (No. 1309 of 18/12/2012), as indicated by the %-limits in Table 2 of the Statutory Order unless a specific classification limit exists.

Below is indicated the various concentration limits for the various classifications that are applied for NMP, which has a specific classification limit:

Repr. 1B (H360D) ≥ 5%
STOT SE 3 (H335) ≥ 10%

Thus, the limit for classification of NMP-containing waste as hazardous waste is a content of 5% NMP in the waste. However, as mentioned in section 2.2.4 the Risk Assessment Committee (RAC) agreed to the proposal by the Netherlands to remove the specific concentration limit (SCL) relating to the classification as reproductive toxicant (Repr. 1B; H360) so that the generic concentration limit (GCL) of 0.3% applies.

Furthermore, the following waste categories (EAK codes) described in the Danish Statutory Order may be especially relevant for NMP-containing waste: 07 - - -- (several categories addressing NMP all starting with the code 07; "waste from various organic chemicals industrial processes" this includes manufacture of medicines); 140603 (Other solvents and mixtures of solvents) and 160506 (Laboratory chemical made of or containing hazardous substances including mixtures of laboratory chemicals). These categories shall be applied when handling waste and for handling waste correctly.

4.2 Waste treatment

NMP may occur in industrial waste together with other organic solvents and other hazardous constituents. The waste may not be considered as suitable for recycling, but due to the high energy content of organic solvents these waste fractions constitute an energy source and they are typically subjected to incineration and energy production.

In semiconductor processes, in which NMP is used as a key process aid in the manufacture of semiconductor devices, it is described that about 90-95% of the solvent used is collected for offsite incineration, <5% evaporates and <0.5% is discharged to waste water (Annex XV Restriction dossier, 2013).

Under the US Emergency Planning and Community Right-to-Know Act (EPCRA) quantities of routine releases of chemicals to the environment and the quantities of treated chemicals (treated, recycled or combusted for energy recovery) on-site or sent off-site for that purpose are reported.

IBM has extended this reporting requirement to cover their worldwide operations and for 2013, the reported quantity of NMP related to IBM's activities was a total of 143 tonnes (IBM, 2013).

According to the literature, NMP can be recycled by distillation and extraction with water (Abolghasem *et al.*, 2010). No information was available on whether this method has been applied.

No information has been identified for waste treatment of non-industrial waste.

Information on NMP in wastewater streams has been reported in a survey of 46 US industrial effluent samples of which NMP was detected in one of the samples (detection limit not reported) and in a German investigation of three different biologically treated wastewater effluents (domestic waste water, wastewater from a lubricating oil refinery, and wastewater from an oil reclaiming facility) NMP was qualitatively identified in the domestic wastewater (WHO, 2001).
NMP was also detected at concentrations of 66.3 and 33.7 µg/L in wastewaters from a petrochemical plant and detected in the raw effluent from a textile finishing plant in North Carolina, US but no concentrations were provided (HSDB, 2014).

4.3 Summary and conclusions

Waste with content of NMP has to be treated as hazardous waste if the content of NMP is 5% or more. The lower classification limit of 0.3% as proposed and agreed by the RAC means that the limit for treating NMP-containing waste as hazardous may change to 0.3% NMP. Several waste categories apply to NMP-containing waste. Industrial waste containing NMP is treated by incineration. No information has been found on treatment of waste from non-industrial use. NMP has been detected in industrial wastewater effluents and in domestic wastewater.

5. Environmental effects and exposure

5.1 Environmental hazard

The information reported in this section is based on public available information from a WHO report from 2001 as well as the information registered under REACH (2014). Furthermore, information has been retrieved from the US-EPA's database AQUIRE and from IUCLID.

Overall, NMP does not possess environmental hazards leading to classification.

5.1.1 Toxicity to aquatic organisms

Several studies on the toxicity of NMP (CAS No. 872-50-4) are available. Studies include acute and chronic data on algae, crustacean and fish. Effect concentrations are reported in the range of hundreds mg/L or more with only one EC50 (48h) value of 1 mg/L and a NOEC of 12.5 mg/L for *Daphnia magna*. The results are presented in Table 5-1 below.

TABLE 5-1: AQUATIC TOXICITY DATA FOR 1-METHYL-2-PYRROLIDONE (NMP) (CAS NO. 872-50-4) (IUCLID DATASHEET, 2000; WHO, 2001; AQUIRE DATABASE, DATA RETRIEVED APRIL 2014; REACH REGISTRATION DATA, 2014)

Organism	Name	Duration	Endpoint	Effect (mg/L)	Reference
Fish	*Oncorhynchus mykiss* (fw)	96 h	LC50	>500	WHO, 2001; REACH registration data, 2014
Fish	*Lepomis macrochirus* (fw)	96 h	LC50	724	US-EPA AQUIRE database, 2014
Fish	*Lepomis macrochirus* (fw)	96 h	LC50	832	IUCLID Datasheet, 2000
Crustacean	*Daphnia magna* (fw)	24 h	EC50	>1,000	REACH registration data, 2014 IUCLID Datasheet, 2000
Crustacean	*Daphnia magna* (fw)	48 h	EC50	1.0	US-EPA AQUIRE database, 2014

Organism	Name	Duration	Endpoint	Effect (mg/L)	Reference
Crustacean	*Palaemonetes vulgaris* (sw)	96 h	EC50	1,107	REACH registration data, 2014 IUCLID Datasheet, 2000
Crustacean	*Daphnia magna* (fw)	21 d	NOEC	12.5	REACH registration data, 2014
Algae	*Desmodesmus subspicatus* (fw)	72 h	EC50 (growth)	600.5	REACH registration data, 2014
Algae	*Desmodesmus subspicatus* (fw)	72 h	NOEC (biomass)	125	REACH registration data, 2014

5.1.2 Predicted No Effect Concentration (PNEC) – Aquatic organisms

No information on the Predicted No Effect Concentration (PNEC) has been reported in the WHO report (WHO, 2001). REACH registration data report a PNEC = 0.25 mg/L for freshwater and a PNEC = 0.025 mg/L for marine water based on the NOEC value (12.5 mg/L) obtained during the test with *Daphnia magna* and applying an assessment factor of 50 and 500 for the fresh water and marine compartment respectively (REACH registration data, 2014).

5.1.3 Toxicity to sediment living organisms

The substance is not expected to adsorb to sediment particles (Log Kow = 0.38). No information is available for sediment living organisms.

5.1.4 Predicted No Effect Concentration (PNEC) – sediment organisms

The PNEC for freshwater sediment and PNEC for marine sediment reported in the REACH registration data for NMP is 1.42 mg/kg dw and 0.142 mg/kg dw, respectively. These values are based on the equilibrium partition method (REACH registration data, 2014).

5.1.5 Toxicity to microorganisms

The results from two studies on the toxicity of NMP to microorganisms are reported in the REACH registration data. The endpoint reported in one of the studies is stated as “similar” to EC10 and is reported as 100 mg/L (respiration rate, guideline not specified). The second study reports an EC50 (30 min.) > 600 mg/L and was conducted according to ISO 8192 (Test for Inhibition of Oxygen Consumption by Activated Sludge). Furthermore, a PNEC for microorganism of 10 mg/L is reported (REACH registration data, 2014).

5.1.6 Toxicity to terrestrial organisms

No data on terrestrial toxicity are reported in the REACH registration data, where the argument “scientifically unjustified” is stated (REACH registration data, 2014).

5.2 Environmental fate

As the substance is completely miscible in water, it is not expected to adsorb to soil, sediments, or suspended organic matter or to bioconcentrate (Log Kow = 0.38) (WHO; 2001).

5.2.1 Bioaccumulation

No data on bioaccumulation are available. Based on the Log Kow = 0.38, no bioaccumulation is expected.

5.2.2 Environmental degradation

Water

Atmospheric NMP may be transported from air into surface water or soil pore water during rain events. In surface water biodegradation appears to be the primary degradation process. NMP is readily biodegradable under aerobe conditions shown in an OECD Guideline 301 test where 73% of an initial concentration of 100 mg NMP/L was degraded within 28 days of incubation by the non-adapted activated sludge (REACH registration data, 2014).

No data on anaerobic biodegradability were available.

NMP is not degraded by chemical hydrolysis since this compound lacks functional groups that hydrolyse under environmental conditions (pH 5 to 9) (WHO, 2001).

Sediment

No available information on degradation half-lives in sediment is available. When released to water, NMP is not expected to be adsorbed to suspended solids or sediment in the water column based upon a calculated adsorption coefficient (Koc) of 9.6 (WHO, 2001).

Soil

A calculated adsorption coefficient (Koc) of 9.6 indicates that NMP is highly mobile in soil. Soil thin-layer chromatography also indicates a high mobility in soil, retention (R*f*) values being 0.65–1.0 in four different soils. The dissipation of NMP showed half-lives of about 4 days in clay, 8 days in loam, and 12 days in sand (WHO, 2001).

Air

In air, NMP is expected to be removed by wet deposition or by photochemical reactions with hydroxyl radicals.

When released to the atmosphere NMP is expected to undergo rapid gas-phase reaction with photo-chemically produced hydroxyl radicals. The half-life for this process is estimated to be 5.2 hours (IUCLID Datasheet, 2000; WHO, 2001). NMP does not absorb light at wavelengths >290 nm and, therefore, is not expected to be susceptible to direct photolysis by sunlight (PubChem, 2014).

Table 5-2 summarises the reported half-lives for NMP.

TABLE 5-2: SUMMARY ON REPORTED HALF-LIVES FOR 1-METHYL-2-PYRROLIDONE (NMP)

Compartment	Half-life	Source
Water and sediment	NA	-
Air	5.2 hours	(IUCLID Datasheet, 2000; WHO, 2001)
Soil	4 days (clay) 8 days (loam) 12 days (sand)	(WHO, 2001)

5.2.3 PBT

Based on the results of a test according to OECD 301, the substance is readily biodegradable. Hence, the substance is not persistent (not P) and not very persistent (not vP).

No data on bioaccumulation are available, however due to the low log Kow (0.38), accumulation in organisms is not expected (not B or vB).

NMP is meeting the criteria for toxicity (T) due to the classification as Repr. 1B

These conclusions are in accordance with the information submitted under the REACH registrations (REACH registration data, 2014).

5.3 Environmental exposure

5.3.1 Sources of release

Releases into the environment may occur during production of NMP and during its use as solvent or cleaning agent.

NMP may enter the environment as emissions to the atmosphere, when used as a solvent, since the substance is volatile, or it may be released to water as a component of municipal and industrial wastewaters (WHO, 2001).

The calculated adsorption coefficient (Koc) of 9.6 (WHO, 2001) demonstrates that NMP will not adsorb to sludge. Distribution to the terrestrial soil, for example through the application of sludge to agricultural soil, is therefore not expected. The substance is mobile in soil, leaching from landfills is therefore a possible route of contamination of groundwater.

In the Annex XV SVHC dossier (2011), the emissions of NMP to the environment have been estimated based on an overall usage in the EU of 10,000 to 50,000 tonnes and the breakdown between use areas. Emission factors applied in the dossier have been taken from the Specific Environmental Release Categories[1]. Results of the emission estimates from the dossier are presented in Table 5-3. From these calculations, it can be seen that the yearly tonnage of NMP released to air is much higher (up to 15,353 tonnes/year) than the release to wastewater (up to 352 tonnes/year). Especially the application areas: coating (professional), cleaning, agrochemical and electric equipment contribute to high releases to air. When NMP is released to air it is expected to be removed by wet deposition or by photochemical reactions with hydroxyl radicals.

TABLE 5-3: ENVIRONMENTAL RELEASE ESTIMATES (ANNEX XV SVHC DOSSIER, 2011)

Application	Fraction	Release to air (t/year)	Release to wastewater (t/year)
Coatings (industrial)	10%	98 - 490	20 - 100
Coatings (professional)	10%	980 – 4,900	10 - 50
Cleaning	20%	600 – 3,000	0.2 - 1
Agrochemicals	15%	750 – 3,750	0 - 0

[1] See http://www.cefic.be/en/reach-for-industries-libraries.html.

Application	Fraction	Release to air (t/year)	Release to wastewater (t/year)
Electrical equipment	20%	600 – 3,000	0.2 - 1
Petrochemical processing	10%	5 - 25	10 - 50
Pharmaceuticals	15%	37.5 - 187.5	30 - 150
Total		**3,071-15,353**	**70 - 352**

5.3.2 Monitoring data

Effluent
In a survey of 46 US industrial effluent samples, NMP was detected in one of the samples (detection limit not reported) (WHO, 2001).

The compound was detected at concentrations of 66.3 and 33.7 µg/L in wastewaters from a petrochemical plant sampled in January and March 1997, respectively. Furthermore, NMP was detected in the raw effluent from a textile finishing plant in North Carolina but no concentrations were provided (HSDB, 2014).

A German investigation of three different biologically treated wastewater effluents (domestic waste water, wastewater from a lubricating oil refinery, and wastewater from an oil reclaiming facility) NMP was qualitatively identified in the domestic waste water (WHO, 2001).

Sediment
No information on concentrations in sediment was available.

Air
No monitoring data for NMP have been found.

Soil
NMP was detected in concentrations of 0.2 and 3.9 µg/L in leachate from an industrial landfill sampled in December 1996 and March 1997, respectively; locations not specified; limit of detection was 0.2 µg/L. Also, NMP was detected at 68.9 µg/L in leachate from a municipal waste landfill in Japan (HSDB, 2014).

The substance was identified in leachate from a municipal landfill in Ontario USA. No information on the measured concentration was reported (WHO, 2001).

Groundwater
No data for contamination of groundwater with NMP have been found. However, as the substance is mobile in soil, leaching from landfills is a possible route of contamination of groundwater.

5.4 Environmental impact

Overall, NMP does not possess environmental hazards leading to classification. Based on the inherent properties of the substance (readily biodegradable, low log Kow) it is not expected to accumulate in the environment nor lead to any toxic effects.

Neither monitoring data nor information on the predicted environmental concentration (PEC) are available for NMP to make a qualitative risk assessment.

5.5 Summary and conclusions

Overall, NMP does not possess environmental hazards leading to classification.

Several studies on the aquatic toxicity of NMP are available. The results do not indicate a high toxicity. No information on the toxicity towards sediment living organism and soil organisms is available. However, NMP is not expected to adsorb to sediment and soil.

NMP is readily biodegradable. Hence, the substance is not persistent (not P) and not very persistent (not vP). Based on the low log Kow (0.38) accumulation in organisms is not expected (not B). Due to the classification as Repr. 1B, NMP does meet the criteria for toxicity (T).

Releases into the environment may occur during production of NMP and during its use as solvent or cleaning agent. Especially, the release to air is high (up to 15,353 tonnes/year) compared to the releases to wastewater (353 tonnes/year).

The calculated adsorption coefficient (Koc) of 9.6 demonstrates that NMP will not adsorb to sludge. Distribution to the terrestrial soil, for example through the application of sludge to agricultural soil, is therefore not expected. The substance is mobile in soil, leaching from landfills is therefore a possible route of contamination of groundwater.

No monitoring data are available.

6. Human health effects and exposure

6.1 Human health hazard

The information reported in this section is based on the following reports that are publicly available: WHO (2001), OECD SIDS (2007), SCCS (2011), SCOEL (2007), Annex XV Restriction dossier (2013) as well as the information registered under REACH (2014). Furthermore, information has been retrieved from the Danish EPA's database on chemical substances in consumer products.

6.1.1 Classification

As described in section 2.2.1, NMP (CAS No. 872-50-4) has a harmonised classification ((EC) No 1272/2008) for the following hazard statements:

Skin Irrit. 2; H315: Causes skin irritation
Eye Irrit. 2; H319: Causes serious eye irritation
STOT SE 3; H335: May cause respiratory irritation
Repr. 1B; H360D: May damage the unborn child

6.1.2 Absorption, Distribution, Metabolism and Excretion of NMP

Available data from studies in animals and humans show that NMP is rapidly absorbed after oral, dermal and inhalation exposure.

In rats, the percutaneous absorption, expressed as the total excretion in urine, faeces, and expired air, was 69% in males and 78% in females. The percutaneous absorption of NMP may differ when NMP is applied as pure NMP or as an NMP solution. In a dermal absorption study in the rat, the absorbed amounts of applications of pure NMP, 30% NMP in water, and 30% NMP in (R)-(+)-limonene were 31%, 3.5%, and 72%, respectively (WHO, 2001).
An uptake, calculated as the difference between inhaled and exhaled NMP concentrations, of about 90% by the inhalation route was found (WHO, 2001).
After intravenous administration to rats, there is a rapid distribution to all major organs. The plasma NMP level declined 5–30 min after administration and was only slightly decreased from then on up to 2 hr. Six hours after administration of radiolabelled NMP, the highest accumulation of radioactivity occurred in the liver, small and large intestines, testes, stomach, and kidneys, although the thymus and bladder had the highest concentrations when expressed per gram of tissue. After 24 hrs, the radioactivity was still measurable in the liver and intestines. The rapid distribution phase is followed by a slow terminal elimination phase (WHO, 2001). Following intravenous administration in rats, the main pathway for biotransformation of NMP is by hydroxylation. The major metabolite excreted in urine, 70–75% of the dose, is identified as 5-hydroxy-N-methyl-2-pyrrolidone (5-HNMP). The almost identical metabolism for NMP administered by dermal and oral routes indicates that little first-pass metabolism occurs. Twelve hours after an orally or percutaneously administered dose, all of the NMP in plasma was in the form of the polar metabolites (WHO, 2001).
All studies of NMP exposure of rats report discolouration (yellow-orange-brownish) of urine. The colouration, noted at 100 mg/m^3 and higher concentrations, was probably dose related, but has not

been studied further. It may be due to a coloured unidentified metabolite or to an effect in the body (e.g. in the liver). The half-life of NMP in plasma is 7–10 h. The urinary excretion of NMP and NMP metabolites accounted for about 70% of the dose within 12 hrs and 80% within 24 hrs (WHO, 2001).
Studies in humans show comparable results. Dermal penetration through human skin has been shown to be very rapid. NMP is rapidly biotransformed by hydroxylation to 5-hydroxy-N-methyl-2-pyrrolidone, which is further oxidised to N-methylsuccinimide; this intermediate is further hydroxylated to 2-hydroxy-N-methylsuccinimide. These metabolites are all colourless. The excreted amounts of NMP metabolites in the urine after inhalation or oral intake represented about 100% and 65% of the administered doses, respectively (WHO, 2001).

6.1.3 Acute toxicity

NMP has a low toxicity by oral, dermal, inhalational, intraperitoneal, and intravenous routes of exposure. Oral LD50 values range from 3605 - 7725 mg/kg bw in rats and mice and dermal LD50 values range from 5000 - 7000 mg/kg in rats. Reliable inhalation exposure studies were generally conducted with a vapour/aerosol mixture. The valid LC50 was >5.1 mg/l/4h. Low toxicity was also observed after intraperitoneal and intravenous injection in rats and mice (OECD SIDS, 2007).

Uptake of oral, dermal, or inhaled acutely toxic doses causes functional disturbances and depressions in the central nervous system (OECD SIDS, 2007).

6.1.4 Irritation

Within a 3 months inhalation toxicity study in male and female Wistar rats to concentrations of 0, 500, 1000 and 3000 mg/m^3 for 6h/day and 5 times/week, respiratory tract irritation was observed at ≥1000 mg/m3. The no observed adverse effect concentration (NOAEC) for local irritation was 500 mg/m3 (Annex XV restriction report).

The SCCS Panel evaluated the irritation potential of NMP in animals and humans.
Skin irritation tests in New Zealand White rabbits (n = 6) exposed to 0.5 ml NMP (100%) were performed according to Draize. Only slight erythema was observed. When the examination was repeated 72 hrs and 7 days after the start of exposure, no effects were observed. The tests showed a low potential for skin irritation and resulted in a primary irritation index of 0.5 (out of a maximum 8).
Repeated daily dermal application of 450 mg/kg bw to rabbits caused painful and severe haemorrhage and eschar formation after four doses; the reaction to a dose of 150 mg/kg bw per day was less marked.
Aqueous solutions of NMP were tested for primary skin irritation in 10 male albino guinea pigs. Twenty-four hours after application, slight erythema was observed in two guinea-pigs with the 50% solution and in zero with the 5% solution. After 48 hrs, no effects were registered. It was concluded that in rabbits and guinea-pigs, slight or moderate irritation has been reported. Primary eye irritation tests according to Draize were performed in New Zealand White rabbits (n = 9). The tests in the rabbits indicated a moderate potential for eye irritation (SCCS, 2011).

In humans, skin irritation was reported in several workers after a few days of working with NMP. Irritation of the skin has been reported by workers with prolonged or repeated exposure (dermatitis, oedema, redness, blister or cracking). Six volunteers (human males) were exposed by inhalation to 0, 10, 25, or 50 mg NMP/m^3 for 8 hours on one single day. No discomfort of the eyes was reported by the subjects (SCCS, 2011). Besides, it was reported that the volunteers displayed no respiratory tract irritation symptoms (WHO, 2001).

In the REACH registration dossier, it was concluded that although the dermal response was rated as minimal in a primary dermal irritation study with albino rabbits dermally exposed to undiluted NMP not leading to classification, the EU has classified NMP as irritating to the skin. It was also

concluded from the ocular effects rated as moderate observed in a primary irritation study where New Zealand White rabbits received a single intraocular application of 0.1 mL neat NMP into the conjunctival sac of one eye, the other served as untreated control, that NMP has to be classified as irritating according to the European Commission (REACH registration, 2014).

Based on a volunteer study undertaken in order to investigate possible chemosensory effects of NMP under workplace conditions, a NOEC of 80 mg/m^3 can be derived based on the moderate annoyance reported by the subjects exposed to NMP at the peak exposures to 160 mg/m^3, whereas the volunteers at 80 mg/m^3 for longer periods noted no effects (Annex XV Restriction dossier, 2013).

NMP is classified as Skin Irrit. 2; H315: Causes skin irritation, Eye Irrit. 2; H319: Causes serious eye irritation and STOT SE 3; H335: May cause respiratory irritation.

6.1.5 Sensitisation

No valid animal data on skin sensitisation exist. Information from secondary literature sources suggests that NMP is not a skin sensitiser in animals or humans (OECD SIDS, 2007).

In the REACH registration dataset based on the results of a study performed on a structurally analogue substance (Ethyl pyrrolidone, CAS nr 2687-91-4), read across to NMP is indicating that NMP is not sensitising (REACH registration, 2014).

6.1.6 Repeated dose toxicity

6.1.6.1 Inhalation

Rats (Crl:CD) were exposed to 100, 500, and 1000 mg/m^3 NMP (aerosol vapour mixture) with an additional control (air) (> 95% of the droplets below 10 µm in diameter) 6 hrs/day, 5 days/week for 4 weeks. At all levels, all rats showed signs of lethargy and irregular respiration after approximately 3-4 hrs of exposure. These signs persisted until the end of exposure. Rats at 100 and 500 mg/m^3 recovered within 30-45 minutes post-exposure, but only a few rats recovered by 18 hrs post-exposure at the high dose. At 1000 mg/m^3: Out of 30 rats, 8 rats died and 5 rats were euthanised within the first 9 days of exposure. Histopathological examination of the dead animals revealed focal pneumonia, hypoplasia and haemorrhage in the bone marrow, and atrophy of the lymphoid tissue in the spleen and thymus. At 100 and 500 mg/m^3: There were no changes in body weight, blood and urinary analysis, and no pathological lesions after 4 weeks of exposure or 2 weeks post-exposure (SCCS, 2011). Derivation of a NOAEC was not part of the study, but based on the results, a NOAEC of 500 mg/m^3 can be established.

In a medium-term exposure study, rats were exposed (head only) to 0, 500, 1000, or 3000 mg NMP/m^3 for 6 hrs/day, 5 days/week, for 13 weeks. The generated NMP atmospheres consisted of a large proportion (82–92%) of respirable aerosol particles (MMAD 2.1–3.5 µm; relative humidity 52–61%). Dark yellow discolouration of the urine was found at all levels, and nasal irritation as shown by crust formation on nasal edges at 1000 mg/m^3 was observed at the end of the exposure period. At 3000 mg/m^3, non-specific clinical symptoms and irritation of the respiratory tract were registered. In male rats, body weight was significantly decreased (34%) and absolute testes weight was decreased. Cell loss in germinal epithelium of testes in 4 out of 10 male rats was noted. Slight increases in erythrocytes, haemoglobin, haematocrit, and mean corpuscular volume were observed. In female rats, the number of polymorphonuclear neutrophils increased and the number of lymphocytes decreased. Examination of the satellite group at the end of the 4-week post-exposure observation period showed a significant lower body weight gain in males compared with the controls. The testes effects registered in the 3000 mg/m^3 group sacrificed at the end of exposure were also registered in the satellite group at the end of the 4-week post-exposure observation period. The NOAEL was 500 mg NMP/m^3 for both male and female rats (SCCS, 2011).

6.1.6.2 Oral

In a repeated-dose toxicity study, rats (Orl:CD.BR) were given 0, 2000, 6000, 18 000, or 30 000 mg NMP/kg diet for 28 days. The mean daily NMP doses were 0, 149, 429, 1234, and 2019 mg/kg bw/day in males and 0, 161, 493, 1548, and 2268 mg/kg bw/day in females. Lower body weights and body weight gains were noted at ≥ 1234 mg/kg bw/day in males and at 2268 mg/kg bw/day in females. Males showed degeneration and/or atrophy of the testicular seminiferous tubules at the two highest doses. The weight of testes was also altered (not detailed). The NOAEL was 429 mg/kg bw/day (6000 ppm) for males and 1548 mg/kg bw/day (18000 ppm) for females (SCCS, 2011).

In a repeated-dose toxicity study, mice (B6C3F1/CrlBR) were given 0, 500, 2500, 7500, or 10 000 mg NMP/kg diet for 28 days. The mean daily NMP dose was 0, 130, 720, 2130, and 2670 mg/kg bw/day in males and 0, 180, 920, 2970, and 4060 mg/kg bw/day in females. The NOAEL was 720 mg/kg bw/day (2500 mg/kg) in males and 2970 mg/kg bw/day (7500 mg/kg) in females, based on the kidney histopathology (SCCS, 2011).

Rats (Crl:CD) were administered 0, 3000, 7500, or 18 000 mg NMP/kg diet for 90 days (Malley LA et al, 1999 cited in SCCS, 2011). The mean daily NMP doses were 0, 169, 433, and 1057 mg/kg bw/day in males and 0, 217, 565, and 1344 mg/kg bw/day in females. The NOAEL was 169 mg/kg bw/day in males and 217 mg/kg bw/day in females (3000 mg NMP/kg for both sexes) based on body weight effects and changes in three neurobehavioral parameters in males only (increase in foot splay, a higher incidence of low arousal and slight palpebral closure) at higher doses (SCCS, 2011).

Mice (B6C3F1) were administered 0, 1000, 2500, or 7500 mg NMP/kg diet for 90 days. The mean daily NMP dose was 0, 277, 619, and 1931 mg/kg bw/day. The NOAEL was set at 277 mg/kg bw/day (1000 mg/kg) based on the liver responses at higher doses. (Transient changes in biochemical parameters were also observed at > 1000 mg/kg) (SCCS, 2011).

Dogs (Beagle) that were administered NMP (purity: 99.9%) at doses of 0, 25, 79, or 250 mg/kg bw/day in the diet for 90 days showed no statistically significant adverse effects. The NOAEL for dietary exposure in dogs in this study is 250 mg/kg bw/day (SCCS, 2011).

6.1.6.3 Dermal

Repeated dermal exposure to rabbits resulted in mortality at high dose levels without other signs of systemic toxicity in a study from 1963 (Cited in Annex XV Restriction dossier, 2013). The NOAEL is 826 mg/kg bw. For local irritation, the LOAEL is 413 mg/kg bw. It is noted that the study from 1963 has some limitations as to the information provided on the vehicle used, the method of application and the dilutions of the substance (Annex XV Restriction dossier, 2013).
In the Annex XV restriction dossier it is mentioned that alternatively, the overall NOAEL from the oral repeated dose toxicity using route-to-route extrapolation could be used to determine the POD (Point of departure) for risk assessment. The Dossier Submitter assumed absorption percentages of 100% for the oral and dermal route because NMP is absorbed readily via the oral and dermal route. It is noted that the assumption is conservative as the oral absorption is likely to be higher and faster compared to the dermal absorption (Annex XV Restriction dossier, 2013). This results in an external dermal NOAEL of 169 mg/kg bw/d, based on the oral rat 90-d study (Annex XV Restriction dossier, 2013). The oral rat 90-d study (Malley LA et al, 1999 cited in SCCS, 2011) is mentioned in the chapter 6.1.6.2.

6.1.7 Mutagenicity

NMP was tested both in *in vitro* and *in vivo* genotoxic studies.

The results available indicate that NMP can cause aneuploidy in a fungal test *in vitro*. However, NMP does not express a genotoxic effect in a standard bacterial assay and in two well-conducted *in vivo* assays (bone marrow chromosome aberration assay and micronucleus assay). NMP is not considered to have *in vivo* genotoxic potential (SCCS, 2011)

6.1.8 Carcinogenicity

The potential carcinogenicity of NMP has been investigated in two long-term studies with rats and one with mice. No oncogenic potential of NMP in rats was found after oral administration (highest dose 678 mg/kg bw/day) or inhalation exposure (highest dose 400 mg/m^3; about 100 mg/kg bw/day). Chronic nephropathy, especially in males, was the main toxic effect recorded. In the oral mice study at the highest dose, an increased frequency of liver adenomas (males and females) and carcinomas (males) was found. No evidence of an increase incidence of malignant tumours was seen at lower doses and there were no NMP related neoplastic or non-neoplastic changes in other organs (SCCS, 2011).
NMP was not found to be carcinogenic, although the results in the feeding study in B6C3F1 mice showed liver adenomas and carcinomas at the top dose of 7200 ppm in the liver. The specific strain of mice (B6C3F1) is very sensitive to induction of non-genotoxic liver tumours and these are normally not considered relevant for humans. Since NMP is not mutagenic and the rat carcinogenicity studies showed no carcinogenic response, NMP is not considered to be carcinogenic (Annex XV Restriction dossier, 2013).

6.1.9 Reproduction and Developmental toxicity

Two oral reproduction toxicity studies in line with the requirements of OECD 416 were performed in Sprague Dawley and Wistar rats using dietary dose levels of 0, 50 160 and 500/350 mg/kg bw/day. In both studies, the high dose level was reduced to 350 mg/kg bw/day due to severe pup mortality in the first litter. Both rat strains were very similar with respect to the observed findings. All F0 and F1 parental rats proved to be fertile at least after one of the two mating intervals. The NOAEL for reproductive performance/fertility was 350 mg/kg bw/day in both strains. The NOAEL for developmental toxicity in both oral studies was 160 mg/kg bw/day. The NOAEL for maternal toxicity was 160 mg/kg bw/day for the oral route.

The inhalation route was tested in a two generation study where a NOAEC for reproduction toxicity was 478 mg/m^3 (the top dose) and the NOAEC for maternal systemic and developmental toxicity was observed to be 206 mg/m^3 (Solomon et al. (1995) cited in Annex XV Restriction dossier, 2013).

The developmental toxicity of NMP was investigated in 7 studies of which three by the oral route, and two by the dermal and inhalation route.

Two oral exposure studies were evaluated in the rat (Sprague-Dawley). In the first study, rats were exposed by oral gavage to NMP doses of 0, 125, 250, 500, 750 mg/kg bw/day during the gestation day (GD) 6 to 20. In the second study rats were exposed by oral gavage to NMP doses of 0, 40, 125, 400 mg/kg bw/day during GD 6-15. In both studies, decreased body weight in dams and fetus were observed at doses above 125mg/kg bw/day. A NOAEL for maternal toxicity and developmental toxicity of 125 mg/kg bw/day was established for both oral studies in rats (Annex XV Restriction dossier, 2013). In a developmental study, rabbits were exposed by oral gavage to NMP doses of 0, 55, 175, 540 mg/kg bw/day during GD 6-18. From this study, a NOAEL maternal toxicity of 55 mg/kg bw/day and a NOAEL teratogenicity and developmental toxicity: 175 mg/kg bw/day were established (Annex XV Restriction dossier, 2013). Remarkably, the NOAEL in the rabbit study for developmental toxicity was higher, i.e. 175 mg/kg bw/day. For the oral route it was decided to use the NOAEL from the rat study for maternal and developmental effects of 125 mg/kg bw/day since the rat NOAEL lies between the rabbit NOAEL and rabbit LOAEL of 55 and 175 mg/kg bw/day, respectively, and the observed effects were of a similar nature.

For the dermal route the study on rats exposed to doses of 0, 75, 237, 750 mg/kg bw/day during GD 6-15 for 8h/day, 1x/day were considered as starting point for the DNEL derivation, i.e. the NOAEL for maternal and developmental effects of 237 mg/kg bw/day (Annex XV Restriction dossier, 2013). In a study where rabbits were exposed dermally (semi-occlusive) to doses of 0, 100, 300, 1000 mg/kg bw/day 6h/day, 1x/day, a NOAEL maternal toxicity: 1000 mg/kg bw/day and a NOAEL developmental toxicity: 300 mg/kg bw/day were established (Annex XV Restriction dossier, 2013).

Regarding maternal effects, the NOAEL from the rat study was chosen over the NOAEL from the rabbit study, because the effects in the rat were more severe (decrease body weight gain and increase resorption) at the LOAEL of 750 mg/kg bw/day compared to the effects observed in the rabbit at 1000 mg/kg bw/d, indicating that for the dermal route the rat is more sensitive to NMP exposure. With regard to developmental effects, the developmental toxicity study with rabbits provides a NOAEL of 300 mg/kg bw/day which is in the same range as the NOAEL of 237 mg/kg bw/day in the rat (Annex XV Restriction dossier, 2013).

Two developmental inhalation studies were performed, one with rats and one with rabbits. In addition, one 2-generation study included a cohort for developmental toxicity. As POD for developmental effects, the NOAEC of 206 mg/m^3 was chosen. This NOAEC was derived from the 2-generation study by Solomon et al. (1995) (cited in Annex XV Restriction dossier, 2013). The NOAEC is based on a decrease in foetal and pup weight in the F1 offspring. As POD for maternal toxicity, the NOAEC of 206 mg/m^3 was taken from the same study (Solomon et al. 1995 cited in Annex XV Restriction dossier, 2013).

In humans, it was reported in one case report that a pregnant woman suffered from stillbirth at 31 weeks after she was (dermally) exposed at work to a spill of NMP at about 16 weeks of gestation. The human case description supports the effects observed in the animal studies but cannot be used for risk assessment (Annex XV Restriction dossier, 2013).

Based on the NOAELs and NOAECs determined in the animal studies, DNELs were derived for workers (Annex XV restriction dossier, 2013). An inhalation chronic systemic DNEL of 10 mg/m^3 is derived for workers and an inhalation developmental toxicity DNEL of 5.0 mg/m^3 is derived for pregnant workers. For dermal exposure, a dermal chronic systemic DNEL of 4.6 mg/kg bw/day and a dermal developmental toxicity DNEL of 2.4 mg/kg bw/day are derived for pregnant workers (Annex XV Restriction dossier, 2013).

NMP is classified as Repr. 1B; H360D: May damage the unborn child.

6.1.10 Overall conclusions for NMP

NMP is classified as a skin, eye and possible respiratory irritant and is classified reproductive toxicity category 1B based on developmental toxicity. NMP has been studied extensively in the past decades showing not a complete but a rather comprehensive dataset of toxicological studies.

Regarding sensitising properties of NMP, no data are available on NMP. However, results from the read across on a substance (Ethyl pyrrolidone, CAS nr 2687-91-4) indicates that the read across substance is not sensitising.

The systemic effects of NMP observed in oral studies were changes in body weight, liver weight, testicular atrophy, thymic atrophy, swelling of distal kidney tubuli, where the critical effects were generally seen in terms of reduced body weight (gain) and food consumption.
Repeated dermal exposure of rabbits resulted in mortality at high dose levels without other signs of systemic toxicity. An external dermal NOAEL of 169 mg/kg bw/day, based on an oral rat 90-d study was estimated.

The inhalation studies show a consistent NOAEC. It should be noted that the pattern of exposure and environmental conditions could have a major influence on the toxicity of NMP at high concentrations. The overall NOAEC was set at 500 mg/m^3 for both local and systemic effects (local respiratory tract irritation and at higher concentrations systemic effects including testicular atrophy) resulting from inhalation exposure (Annex XV Restriction dossier, 2013).

Since NMP is not mutagenic and the rat carcinogenicity studies showed no carcinogenic response, NMP is not considered to be carcinogenic.

In the prenatal developmental toxicity studies and 2-generation studies, effects on maternal body weights and foetus weights were most critical. Notably, the body weight changes of the dams occurred at lower concentrations than observed in general animals. At higher concentrations, clear effects on the foetuses were observed such as variations and malformations, reduced litters, stillborn and resorptions amongst other. Despite effects observed on testes and spermatogenesis (slight effects) no reduction in fertility was observed in any of the reproduction toxicity studies (Annex XV Restriction dossier, 2013).

In the Annex XV restriction dossier (2013) DNEL were derived for workers. An inhalation chronic systemic DNEL of 10 mg/m^3 is derived for workers and an inhalation developmental toxicity DNEL of 5.0 mg/m^3 is derived for pregnant workers. For dermal exposure, a dermal chronic systemic DNEL of 4.6 mg/kg bw/day and a dermal developmental toxicity DNEL of 2.4 mg/kg bw/day are derived for pregnant workers (Annex XV Restriction dossier, 2013).

6.2 Human exposure

6.2.1 Direct exposure

6.2.1.1 Consumers

Reports on measurements of NMP in different types of consumer products such as porcelain colourant, textile colourant, coated tables, wood figurine, tooth brush, artificial grass, wood toys, cleaning product and iron were prepared from the Danish EPA (MST).

NMP was measured to a concentration of 1-5% in porcelain glass, where NMP is used as a colourant (MST, 2005b).

NMP was found in one textile sample at a concentration of 740 mg/kg (0.074%), where NMP is used as a transfer colourant in textile (MST, 2005a).

Migration levels of NMP from a coated table of rubber tree (Hevea brasiliensis) and ink figure made of wood type Belalu (Albizia falcata) into artificial saliva were measured. The measured migration levels of NMP were 4.0 µg/g and 41 µg/g, respectively (MST, 2004b) corresponding to 0.0004% and 0.0041%, respectively.

NMP was found in toothbrushes, and the highest migration level measured was 200µg/toothbrush (MST, 2004a).

NMP was found in infill materials of artificial grass at a concentration of 3.5 µg/g (approximately 0.00035%). Extraction measurements of NMP in dichloromethane show a concentration of 80 µg/g (approx. 0.008%) in pad and infill materials, and leaching of organic substances from elastic infill show a concentration of NMP in 2 infill materials gl. of 613 µg/l and 847 µg/l (approx. 0.0000613 % and 0.0000847% considering that 1L is equivalent to 1 kg) (MST, 2008).

NMP was found in extracts from wooden toys. The measured migration levels are 28-59 µg/g (approx. 0.0028-0.0059%). It was evaluated that at this concentration, NMP is not of concern regarding the use of wooden toys containing NMP (MST, 2005c).

NMP was found in one cleaning product corresponding to a paint and lacquer remover. There is no information on the concentration (MST, 2007).

It was measured that emissions from iron give a concentration of NMP of 4.4 µg/iron/hour for 7 hours (MST, 2005d).

NMP is also used as a solvent in drugs (Abolghasem *et al.*, 2010).

NMP is used as a solvent and a surfactant in cosmetic products. The final concentration of NMP in cosmetic products is not known (SCCS, 2011).

In the Annex XV SVHC dossier, it is mentioned that NMP can be used in various types of paints and coatings, including writing ink that are used by consumers. NMP can be used by consumers in certain cleaning products such as paint removers, cleaners and degreasers. NMP content of the consumer product has been assumed to be a maximum of 5% by weight (i.e. 0.05 g/g), in line with the existing Annex XVII restriction based on the classification as toxic to reproduction category 1B (Annex XV SVHC dossier, 2011). The consumer exposure estimates from the Annex XV SVHC dossier (2011) are presented in Appendix 3.

6.2.1.2 Occupational exposure

Although NMP does not have a high vapour pressure, the pattern and wide range of uses results in some potential for occupational exposure by inhalation. Exposure may be to NMP as a vapour, as an aerosol or as a mixture of both, the relative proportions being dependent on temperature and relative humidity. At normal room temperature and humidity (60% relative humidity) and concentrations of NMP below 80 mg/m^3, aerosol formation is unlikely; however, aerosol formation is potentiated at higher humidity and with increasing concentrations of NMP. Levels of up to 10 mg/m^3 NMP have been measured in the breathing zone of workers involved in the removal of graffiti, while workers in the microelectronics industry have been exposed to up to 6 mg/m^3. Much higher exposures (up to 280 mg/m^3) were reported in the microelectronics industry when NMP was used at a temperature of 80°C. Exposures of up to 64 mg/m^3 have been measured in the breathing zone of paint-strippers, with peak exposures of up to 280 mg/m^3.

Dermal exposure to NMP in the occupational setting is also likely, given the pattern and wide range of uses. NMP is readily absorbed through the skin, and dermal exposure thus is considered to contribute significantly to the internal NMP dose. There are several older reports in the literature of toxic effects resulting from skin contamination through spills, inhalation of fumes may however have contributed to the toxicity seen. Additionally, Bader and co-workers have reported dermal absorption of NMP from the vapour phase, equivalent to approximately 30% of the total inhalation dose in an experimental study in human volunteers, the design of which included a phase in which inhalational uptake was prevented by face shields (Bader et al., 2007 cited in SCOEL, 2007) (SCOEL, 2007).

In the Annex XV restriction dossier, reference is made to the REACH registration dossier in which the registrant estimated exposure to NMP at the workplace using the EasyTRA tool. Similarly, it uses the same default values for each PROC (Process Category) to determine the exposure to NMP during that process taking into account any RMMs (risk management measures) and OCs (operational conditions) assigned to the process. According to the information obtained from the registrant, the most common RMMs applied are LEV (local exhaust ventilation), gloves and reduction in exposure time and/or concentrations of NMP used in the process. Detailed information on RMMs typically applied in workplaces where NMP is used is not available to the Dossier Submitter.
The exposure was calculated for the following industrial uses: manufacture, importers and suppliers, chemical industry processes (generic use for synthesis processes), formulators (generic

use for production of mixtures and articles), coaters, cleaners, laboratory use, functional fluids, and use in construction industry.
Professional uses considered are: importers and suppliers, formulators, coaters, laboratory use, agrochemical use and use in functional fluids. Charging and discharging of NMP is a generic process applied in both industrial and professional settings.
In general, exposures resulting from high energy processes (e.g. under elevated temperatures and processes requiring intensive manual applications) and from open processes are relatively high, despite of RMMs taken into account. In industrial settings, processes can be more enclosed and RMM options are better compared to processes and RMM options available in professional settings. Moreover, most open and high energy processes are not supported anymore by the lead registrant as it was indicated that such uses, e.g. professional cleaning with NMP, will diminish in a few years. Therefore, the exposure levels that were calculated by the registrant did not differ much between the industrial and professional uses. The exposure levels ranged from 0.04 to 20.65 mg/m^3 for the inhalation exposure for industrial uses. Dermal exposure ranged from 0.03 to 5.49 mg/kg bw/day for industrial uses, where it is noted that RMMs are taken into account. The exposure levels ranged from 2.97 to 20.65 mg/m^3 for the inhalation exposure for professional uses. Dermal exposure ranged from 0.14 to 5.38 mg/kg bw/day for professional uses, where it is noted that RMMs are taken into account (Annex XV Restriction dossier, 2013).

6.2.2 Indirect exposure

6.2.2.1 Air

In air, NMP is expected to be removed by wet deposition or by photochemical reactions with hydroxyl radicals (WHO, 2001).

No information of human indirect exposure to NMP via air.

6.2.2.2 Soil

The substance is mobile in soil, and leaching from landfills is thus a possible route of contamination of groundwater. As the substance is completely miscible in water, it is not expected to adsorb to soil, sediments, or suspended organic matter or to bioconcentrate. NMP is not degraded by chemical hydrolysis. Data from screening tests on the biodegradability of NMP show that the substance is rapidly biodegraded (WHO, 2001).

No information of human indirect exposure to NMP via soil.

6.2.2.3 Drinking water

NMP has been qualitatively detected in US drinking-water supplies (WHO, 2001).
No other information of human indirect exposure to NMP via drinking water.

6.2.2.4 Food

NMP was identified in certain food products like roasted nuts (filberts) as volatile component as well as in the water soluble part of cigarette smoke condensate. These data are about 30 years old and may not be representative of, or comparable to, today's conditions (OECD SIDS, 2007).

NMP is used as an additive (as a solvent) during the production of polysulfone or polyethersulfone. These polymers are used for production of articles intended for heating in a microwave oven. Maximum residual content of NMP in the polymer is <100 mg/kg (EFSA, 2005).

6.2.2.5 Indoor climate

The chemical and sensory emissions from five building materials (carpet, PVC flooring, sealant, floor varnish and wall paint) were tested under different combinations of temperature and relative humidity (RH). NMP emission was detected in floor varnish ranging from 167.7 µg/m^2 at 18°C/ 30% RH to 2081 µg/m^2 at 28°C/70% RH.

Between November 1988 and October 1999, 744 indoor air analyses were performed in the metropolitan area of Berlin, Germany. The majority of the analysed rooms were private homes, but some public rooms as offices, schools and hospitals were also included. NMP was detected at an arithmetic mean concentration of 15 µg/m³; the median was < 2 µg/m³ and the maximum value was 302 µg/m³ (OECD SIDS, 2007).

Thirty target VOCs (volatile organic compounds) were analysed in personal 48-hr exposure samples and residential indoor, residential outdoor and workplace indoor microenvironment samples as a part of the EXPOLISHelsinki study (Finland). NMP was not detected in 99% of the samples. Maximum outdoor and indoor values were 4.84 and 90.62 µg/m³, respectively. The maximum workplace and personal exposure concentration was determined to be 135.78 and 42.49 µg/m³, respectively.
Between 1998 and 2000 simultaneous personal exposure and micro environmental measurements (home indoor, home outdoor, and work indoor) of fine particulate matters (PM) and VOCs including NMP were carried out in Oxford, U.K. once per person among 50 adults over a 48-hour period. NMP was found above the detection limit in 2% of samples from personal exposure and 5% of residential indoor samples. NMP was not found in residential outdoor and workplace indoor samples.
Nilsson et al. (2004, cited in OECD SIDS, 2007) analysed airborne indoor dust samples from damp and control residences for microorganisms, bacterial markers, and adsorbed volatile compounds (VOCs) including NMP. VOCs were determined qualitatively, but not quantitatively. NMP was found in airborne dust of 1 out of 6 damp (17%) and 2 out of 9 control (22%) residences.

6.3 Bio-monitoring data

Measurement of non metabolised NMP in plasma or urine has been proposed as a biological monitor, reflecting exposure from both the inhalation and dermal routes, but has several disadvantages, including the comparatively short half-life of NMP and the low concentrations in urine.

The metabolites of NMP are more appropriate biological indicators of exposure, and measurement of the major metabolite 5-HNMP, with a half-life of 6-7 hours, in urine or plasma has been proposed as a suitable method for biological monitoring. The same group has also suggested measurement of MSI, given the readily-available analytical method for this metabolite. However, MSI has a somewhat larger volume of distribution and levels in urine are low (SCOEL, 2007).

Due to the significant dermal uptake of NMP, biological monitoring is also recommended. 5-HNMP and 2-hydroxy-N-methylsuccinimide (2-HMSI), two key metabolites of NMP, are appropriate biological indicators of exposure, and monitoring of either of these metabolites can be undertaken. The optimum sampling time for 5-HNMP is the first 2-4 hrs post-exposure, while in the case of the longer half-life metabolite 2-HMSI a urine collection 16 hrs post-exposure (i.e. on the morning after an 8-hr work-shift) is advised. Both parameters should be corrected for urinary creatinine to compensate for diuretic variations. The delayed peak maximum of 16-24 hrs post-exposure and the long biological half-life makes urinary HMSI especially suitable for the surveillance of accumulative effects during a working week.
For the longer half-life metabolite 2-HMSI, an 8-hr TWA of 10 ppm (40 mg/m³) corresponds to a biological value of approximately 16 mg/g creatinine, 16 hr post exposure for a work scenario without workload and approximately 22 mg/g creatinine for a work scenario with moderate workload (75 Watt). A Biological Limit Value (BLV) of 20 mg/g creatinine is recommended for 2-HMSI, measured on the morning after an 8-hr work-shift. For 5-HNMP, an 8-hr TWA of 10 ppm (40 mg/m³) corresponds to a biological value of approximately 60 mg/g creatinine, 2-4 hrs post exposure for a work scenario without workload and approximately 75 mg/g creatinine for a work

scenario with moderate workload (75 Watt). A Biological Limit Value (BLV) of 70 mg/g creatinine is recommended for 5-HNMP, measured 2-4 hours after the end of exposure (SCOEL, 2007).

In conclusion, humans can be exposed directly and indirectly to NMP. The direct exposure can be via consumer products such as porcelain colourant, textile colourant, coated tables, wood figurine, tooth brush, artificial grass, wood toys, cleaning product, iron, cosmetics and drugs. The direct exposure can also be via occupational exposure. For professional uses, the exposure levels ranged from 2.97 to 20.65 mg/m^3 for the inhalation whereas dermal exposure ranged from 0.14 to 5.38 mg/kg bw/day. Industrial workers exposure levels ranged from 0.04 to 20.65 mg/m^3 for the inhalation from 0.03 to 5.49 mg/kg bw/day for dermal exposure. It is noted that RMMs are taken into account in these calculations (Annex XV Restriction dossier, 2013). Humans can also be exposed indirectly via indoor climate at concentrations of <2 µg/m^3 to 302 µg/m^3. Few data are available on the indirect exposure of human to NMP via air, soil, water and food. For biological monitoring, the metabolites of NMP (5-HNMP and 2-HMSI) are more appropriate biological indicators of exposure.

6.4 Human health impact

6.4.1 Workers

This paragraph is based on the Annex XV Restriction dossier (2013) making reference to the REACH registration where the exposure data are based on modelling data using the EasyTRA tool and not on measured exposures. Data on measured values for exposure in the working environment are described in section 6.2.1.2 above. The measured values are ranging from 6 mg/m^3 up to 64 mg/m^3 with peak exposures of up to 280 mg/m^3 showing that the measured values may be much higher than the modelled data which are up to 20.65 mg/m^3 for professional workers and industrial workers.

Industrial uses show relatively high levels of containment and good RMM options. Processes conducted in closed systems generally do not give reason for concern, unless processes are conducted under elevated temperatures. Generally it can be concluded that processes under elevated temperatures give reason for concern. Industrial use that involve more open processes are typically performed using LEV and gloves, which may be sufficient to control the risks for general workers, but in most cases are insufficient to control the risks for pregnant workers. It is considered by the Dossier Submitter that risks resulting from dermal exposure may be controlled if very strict conditions are applied to ensure minimal contact with NMP (Annex XV Restriction dossier, 2013).

The same or slightly higher Risk Characteristic Ratios (RCR) as industrial uses were calculated for the professional user (see Appendix 4). Notably, the lead registrant no longer supported high exposure and risk uses, such as working with NMP at elevated temperatures, spraying processes and manual applications. Nevertheless, especially for inhalation exposure there may be insufficiently controlled risks for all workers for a number of activities. Dermal exposure does not seem to present risks that cannot be controlled, although in some cases through requiring training of the use of protective wear to reach higher protection factors (Annex XV Restriction dossier, 2013).

The RCRs were in most cases for workers and pregnant workers >1 indicating that there is a risk. A qualitative appraisal of the RCR was made as for some exposure estimates additional RMMs were possible. It is therefore concluded that risks are not sufficiently controlled for a number of industrial and professional uses, especially when it concerns processes under elevated temperatures, open processes and processes that require manual activities (Annex XV Restriction dossier, 2013). The overview of the RCR calculated in the Annex XV Restriction dossier, 2013 is presented in Appendix 4.

According to the Danish Working Environment Authority it is not known to which extent this conclusion can be transferred to Danish conditions, since in Denmark an employer has an obligation to ensure that exposure to hazardous substances is as low as possible – even below the OEL if possible.

6.4.2 Consumers

In the Annex XV SVHC dossier (Annex XV SVHC dossier, 2011), the consumer exposure to coatings and cleaning products containing NMP was evaluated. NMP can be used in various types of paints and coatings that are used by consumers. The consumer exposure estimates from the Annex XV SVHC dossier (2011) presented in Appendix 3 show that the chronic exposure to NMP is relatively low, and the acute exposure can be high for some activities that can lead to irritation of the skin, eye and respiratory tract. It is important to note that consumers can be exposed to NMP from several products at the same time, for example paints and coatings, and combined exposure could lead to higher exposure for the consumer.

The Danish EPA has found NMP in some consumer products such as cleaning products, but no concentration level was given. NMP was also found in articles for consumers at relatively low levels but up to 5% in porcelain glass. Data on migration from porcelain glass are lacking.

Regarding the presence of NMP in cosmetic products, the SCCS is of the opinion that the presence of NMP with a maximum use concentration of 5% in cosmetic products is not safe for the consumer (SCCS, 2011). No information on the acceptable NMP concentration in cosmetic products is provided in the SCCS opinion.

Regarding the presence of NMP in drugs, it is noted that the safety of substances present in medicinal products safety are assessed under the relevant legislation for medicinal products.

6.5 Summary and conclusions

The toxicological properties of NMP described above show that NMP exposure can induce adverse developmental effects in foetuses during development. This is reflected in the classification as Repr. 1B, H360D.

In addition to this classification, the harmonised classification for NMP also includes the classification as Skin Irrit. 2; H315, Eye Irrit. 2; H319 and STOT SE 3; H335.

Based on the data from the Annex XV restriction dossier submitted by the Netherlands, the risk for workers for industrial and professional uses of NMP was evaluated. It was concluded that the risks are not sufficiently controlled for a number of industrial and professional uses, especially when it concerns processes under elevated temperatures, open processes and processes that require manual activities.

The Danish EPA has found NMP in some consumer products such as cleaning products, but no concentration level was given. NMP was also found in articles for consumers at relatively low levels but up to 5% in porcelain glass. Data on migration from porcelain glass are lacking.

For cleaning and coating products used by consumers, there could be a concern due to combined exposure and events of high exposure that could lead to irritation of the skin, eye and respiratory tract of the consumer.

There were no data concerning the concentration of NMP in cosmetic products and drugs, however the SCCS evaluated that a concentration of 5% in cosmetic products is not safe for the consumer.

7. Information on alternatives

In the Annex XV SVHC dossier (2011) for NMP, replacement of NMP is discussed for specific uses including coatings, electronics and cleaning products. Information on alternatives included in the Annex XV SVHC dossier was provided by companies who responded to a questionnaire. The majority of companies providing information were importers of the substance, although information was also provided by EU manufacturers. Approximately 80% (28 companies out of 34) of the downstream users responding to the questionnaire use NMP in formulations (mixtures/preparations) of which the majority (approximately 91%) uses NMP as a solvent in coatings (Annex XV SVHC dossier, 2011).

Coatings:
It is noted that downstream users are gradually replacing solvent-based systems with multi-layer water based systems. These can be of higher quality and longer lasting but more difficult to apply. However, they still are containing a solvent fraction including NMP. In some cases, this trend has been driven by local and regional regulations and by environmental considerations (Annex XV SVHC dossier, 2011).

The main alternative available on the market to NMP is N-ethylpyrrolidone (NEP) (EC Number 220-250-6, CAS Number 2687-91-4). Most of the downstream users noted that NEP is currently being reviewed for reproduction toxicity and pending upcoming initiative for a possible new classification and labelling of NEP as a substance toxic to reproduction (Annex XV SVHC dossier, 2011).

Further alternatives which have been considered or are being considered include (Annex XV SVHC dossier, 2011):

- Water borne coatings: methyl diproxitol butyldiglycol
- Dimethyl sulfoxide (DMSO)
- Hydrocarbon solvent
- Ketone solvents
- Glycolethers (DPM)
- Dimethylformamide (DMF) and dimethylacetamide (DMAC)
- Alcoxy alkyl amide
- Gamma butyrolactone (CAS 96-48-0)
- 1,3-Dimethyl-2-imidazolidinone (CAS 80-73-9)
- 2-Pyrrolidone (CAS 616-45-5)

Electronics:
Alternatives which have been or are considered for the use of NMP in electronics include (Annex XV SVHC dossier, 2011):

- Dimethyl sulfoxide DMSO
- Sulfolane
- Gamma butyrolactone (CAS 96-48-0)
- Propylene Glycol Methyl Ether Acetate (PGMEA)
- Ethyl lactate
- glycol ethers

Within the semi-conductor industry the following alternatives are listed for use in polyimide precursor coatings:

N-formyl piperidine (CAS 2591-86-8);
Dimethylpropionamide (CAS 758-96-3);
1,3 dimethyl-2-imidazolidinone (CAS 80-73-9);
1,1,3,3 Tetramethylurea (CAS 632-22-4).

Cleaning products:
Alternatives which have been considered or are being considered for use of NMP in cleaning products include (Annex XV SVHC dossier, 2011):

N-ethylpyrrolidone (NEP, CAS 2687-91-4).

In the Annex XV SVHC dossier prepared for the similar substance *N,N*-dimethylacetamide (DMAC) (Annex XV SVHC dossier DMAC, 2011) a list of alternatives considered for DMAC has been included. NMP is included in this list and therefore these alternatives including DMAC are considered as alternatives to NMP as well.

Table 7-1 lists these substances including their harmonised classifications, risk phrases and application areas.

According to the Directive on the protection of the health and safety of workers from the risks related to chemical agents at work (98/24/EC) it is a requirement that alternatives should be less hazardous than the substance being substituted. For several of the proposed alternatives listed in Table 7-1 this is not the case and therefore they will not be useful from a working environment point of view.

TABLE 7-1: ALTERNATIVES FOR DMAC ALSO CONSIDERED ALTERNATIVES FOR NMP. INCLUDING HARMONISED CLASSIFICATIONS (ANNEX XV SVHC DOSSIER DMAC, 2011)

Abbr./ name	Chemical name	EC no. CAS no.	Classification	Risk phrases	Area of application
DMAC	N,N-Dimethylacetamide	204-826-4 127-19-5	Repr. 1B (H360D) Acute Tox. 4 (H312/H332)	May damage the unborn child Harmful by inhalation and in contact with skin	
DMF	N,N-Dimethylformamide	200-679-5 68-12-2	Repr. 1B (H360D) Acute Tox. 4 (H312/H332) Eye Irrit. 2 (H319)	May damage the unborn child Harmful by inhalation and in contact with skin Causes serious eye irritation	Fibres Pharmaceuticals Polyimid films

Abbr./ name	Chemical name	EC no. CAS no.	Classification	Risk phrases	Area of application
DMPU	Tetrahydro-1,3dimethyl-1H-pyrimidin2-one	230-625-6 7226-23-5	Acute Tox. 4 (H302) Eye Dam. 1 (H318) Repr. 2 (H361f)	Harmful if swallowed Causes serious eye damage Suspected of damaging fertility	Pharmaceuticals
DCM	Dichloro-methane	200-838-9 75-09-2	Carc. 2 (H351)	Suspected of causing cancer	Pharmaceuticals
NEP*	1-ethyl-pyrrolidin-2-one	220-250-6 2687-91-4	Repr. 1B (H360D)	May damage the unborn child	Fibres
DMI	1,3-dimethylimidazolidin-2-one	201-304-8 80-73-9	Not classified	-	Fibres Pharmaceuticals
DMSO	Dimethyl sulfoxide	200-664-3 67-68-5	Not classified	-	Pharmaceuticals Polyimid films
TMU	Tetramethyl urea	211-173-9 632-22-4	Not classified-	-	Pharmaceuticals
Sulfolane	Tetrahydrothiophene 1,1-dioxide	204-783-1 126-33-0	Acute Tox. 4 (H302)	Harmful if swallowed	Pharmaceuticals
Acetone	Acetone	200-662-2 67-64-1	Flam. Liq. 2 (H225) Eye Irrit. 2 (H319) STOT SE 3 (H336)	Highly flammable liquid and vapour Causes serious eye irritation May cause drowsiness or dizziness	Pharmaceuticals

Abbr./ name	Chemical name	EC no. CAS no.	Classification	Risk phrases	Area of application
Acetoni-trile	Acetonitrile	200-835-2 75-05-8	Flam. Liq. 2 (H225) Acute Tox. 4 (H302) Acute Tox. 4 (H312) Eye Irrit. 2 (H319) Acute Tox. 4 (H332)	Highly flammable liquid and vapour Harmful if swallowed Harmfull in contact with skin Causes serious eye irritation Harmful if inhaled	Pharmaceuticals

* France has submitted a proposal for classification of NEP as toxic to reproduction, Repr. 1B H360 (2011)

An internet search furthermore revealed the esteramide “Rhodiasolv Polarclean” (or a blend of the diester “Rhodiasolv IRIS” and dimethyl sulphoxide (DMSO)) as a proposed alternative for solvents of concern such as N-methyl pyrrolidone (NMP), dimethyl formamide (DMF), dimethyl acetamide (DMAC), or flammable solvents such as acetone, in various applications (http://ip.com/IPCOM/000202894).

Also part of the Annex XV restriction dossier alternatives to NMP has been evaluated. A technical equally good alternative for NMP in the major applications (like wire-coatings and membranes) seems to be lacking. For other applications (like non-wire coatings and cleaners) alternatives are already available. Although the availability of alternatives may vary per use category and depends on the type of application, the restriction dossier focused on the possible selection of alternatives for NMP with a broad range of applications. In total about 70 alternative solvents have been identified for the whole spectrum of applications for which NMP is being used. Some of these are very specific for a certain use and therefore not in focus. There are about 20 alternative solvents that are used in various applications for which NMP is also used. From these 20 alternatives specifically the polar aprotic solvents (i.e. not able to donate a hydrogen, H^+) NEP, DMF, DMAC, DMSO, THF and acetone are often mentioned as alternatives to NMP, as well as sulfolane, and DMI. For the protic solvents (i.e. contains labile H^+), ethyl lactate, methyl ethyl ketone and propylene carbonate are mostly mentioned. After a selection based on toxicity characteristics only DMSO, acetone, MEK, ethyl lactate, DMI and 2-(2aminoethoxy)ethanol were selected as possible alternatives. In practice these solvents are already applied in a number of applications. For DMI and 2-(2aminoethoxy)ethanol, no harmonised classification is available and only limited information is available on toxicity. The conclusion in the restriction dossier is that of the remaining alternatives, it is supposed that DMSO mostly resembles NMP as it is also a polar aprotic solvent (Annex XV Restriction dossier, 2013).

7.1 Summary and conclusions

Replacement of NMP by other substances is addressed for specific uses including coatings, electronics and cleaning products. Information on alternatives for other applications than these is not available.

For coatings it is noted that downstream users are gradually replacing solvent-based systems with multi-layer water-based systems. However, they are still containing a solvent fraction including NMP. The main alternative available on the market to NMP is N-ethylpyrrolidone (NEP) (EC Number 220-250-6, CAS Number 2687-91-4). This substance is being reviewed for a new classification as a substance toxic to reproduction. NEP is also an alternative which has been considered for cleaning products.

In the Annex XV SVHC dossier prepared for the similar substance *N,N*-dimethylacetamide (DMAC) NMP is included as a possible alternative for DMAC. Therefore DMAC and the other substances included in the dossier are also considered as alternatives for NMP.

The conclusion in the Annex XV restriction dossier is that DMSO mostly resembles NMP.

Several of the proposed alternatives will not be useful alternatives to NMP from a working environment point of view as it is required by the Directive on the protection of the health and safety of workers from the risks related to chemical agents at work (98/24/EC) that alternatives should be less hazardous than the substance being substituted.

References

Abolghasem Jouyban, Mohammad A. A. Fakhree, and Ali Shayanfar (2010). Review of Pharmaceutical Applications of N-Methyl-2-Pyrrolidone. J Pharm Pharmaceut Sci (www.cspsCanada.org) 13(4) 524 - 535, 2010

Annex XV SVHC dossier DMAC (2011). Proposal for identification of N,N-Dimethylacetamide (DMAC) as SVHC. ECHA, August 2011

Annex XV SVHC dossier (2011). Proposal for identification of 1-methyl-2-pyrrolidone as SVHC. ECHA, February, 2011

Annex XV Restriction dossier (2013). Proposal for a restriction. N-Methylpyrrolidone (NMP) Version 2.0, 9 AUGUST 2013

AQUIRE Database (2014). Data retrieved April, 2014. http://www.epa.gov/med/Prods_Pubs/ecotox.htm (CAS no. 872-50-4)

Bureau REACH (2013). CLH report for 1-methyl-2-pyrrolidone. Proposal for Harmonised Classification and Labelling. Version 2, August 2013.

Danish Product Registry (2014). Confidential information retrieved May 2014.

ECHA C&L Inventory (2014). Data retrieved April, 2014 (CAS no. 872-50-4): http://echa.europa.eu/information-on-chemicals/cl-inventory

ECHA (2014a). Committee for Risk Assessment RAC Opinion proposing harmonised classification and labelling at EU level of 1-methyl-2-pyrrolidone (NMP), Adopted 6 June 2014.

ECHA (2014b). Committee for Risk Assessment RAC Opinion on an Annex XV dossier proposing restrictions on 1-methyl-2-pyrrolidone (NMP), Adopted 5 June 2014.

EFSA (2005). Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on a request from the Commission related to a 7th list of substances for food contact materials. The EFSA Journal (2005)201, 1-28.

HSDB (2014). Data retrieved April, 2014. CAS no. 872-50-4 http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@DOCNO+5022

IBM (2013): Pollution Prevention http://www.ibm.com/ibm/responsibility/2013/environment/pollution-prevention.html

IUCLID Datasheet (2000): CAS no. 872-50-4 http://esis.jrc.ec.europa.eu/doc/IUCLID/data_sheets/872504.pdf

KemI: Swedish Chemical Agency http://apps.kemi.se/flodessok/floden/kemamne_eng/nmetyl2p_eng.htm

MST, 2004a. Nanna Svendsen, Søren F. Pedersen, Ole Chr. Hansen, Jakob Toft Mossing, Nils Bernth (Teknologisk Institut). Kortlægning af kemiske stoffer i Tandbørster. Kortlægning af kemiske stoffer i forbrugerprodukter nr. 42, 2004.

MST, 2004b. Thomas Witterseh (Teknologisk Institut). Afgivelse af kemiske stoffer fra produkter af eksotisk træ. Kortlægning af kemiske stoffer i forbrugerprodukter, Nr. 49 2004

MST, 2005a. Ole Christian Hansen (Teknologisk Institut). Screening af sundhedseffekter fra kemiske stoffer i tekstilfarver. Kortlægning af kemiske stoffer i forbrugerprodukter, Nr. 57 2005

MST, 2005b. Sonja Hagen Mikkelsen, Sven Havelund, Anders Skibsted Mogensen, Frank Stuer-Lauridsen (COWI). Kortlægning og vurdering af kemiske stoffer i porcelænsfarver. Kortlægning af kemiske stoffer i forbrugerprodukter, Nr. 59 2005

MST, 2005c. Ole Christian Hansen and Eva Pedersen (Teknologisk Institut). Kortlægning og sundhedsmæssig vurdering af kemisk stoffer i overfladebehandlet trælegetøj. Kortlægning af kemiske stoffer i forbrugerprodukter, Nr. 60 2005.

MST, 2005d. Peter B. Mortensen (Eurofins A/S). Afgivelse og vurdering af kemiske stoffer fra udvalgte elektriske og elektroniske produkter – del 2. Kortlægning af kemiske stoffer i forbrugerprodukter, Nr. 66 2005.

MST, 2007. Lone Wibroe and Christian Libak Pedersen (JobLiv Danmark as). Kortlægning af kemiske stoffer i rengøringsmidler til brug ved rengøring efter ildebrand eller røgskade i private hjem. Kortlægning af kemiske stoffer i forbrugerprodukter, Nr. 83 2007.

MST, 2008. Nils H. Nilsson, Bjørn Malmgren-Hansen and Uffe Sognstrup Thomsen (Teknologisk Institut). Kortlægning, emissioner samt miljø- og sundhedsmæssig vurdering af kemiske stoffer i kunstgræs. Kortlægning af kemiske stoffer i forbrugerprodukter, Nr. 100 2008.

Nordic SPIN Database (2014): http://195.215.202.233/DotNetNuke/default.aspx. (Data search on CAS number)

OECD SIDS (2007) SIAM 24, 19-20 April 2007, 1-methyl-2-pyrrolidone SIDS INITIAL ASSESSMENT PROFILE (CAS no. 872-50-4).

PubChem (2014). Data retrieved April 2014: http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=13387#x351

WHO (2001). Concise International Chemical Assessment Document 35, N-METHYL-2-PYRROLIDONE. World Health Organization Geneva, 2001

REACH registration data (2014): Public data retrieved April 2014: http://echa.europa.eu/information-on-chemicals/registered-substances (CAS no. 872-50-4)

SCCS (2011): Scientific Committee on Consumer Safety. OPINION ON N-Methyl-2-pyrrolidone (NMP), March 2011

SCOEL (2007): Recommendation from the Scientific Committee on Occupational Exposure Limits for N-Methyl-2-Pyrrolidone (August 2007).

SEAC (2014): The Committee for Socio-economic Analysis (Opinion on an Annex XV dossier proposing restrictions on 1-Methyl-2-pyrrolidone (NMP)) Draft 10. September 2014 http://echa.europa.eu/documents/10162/111d5ef1-7d4c-475c-a8e7-e6d2b9b26c4a

U.S. Department of Health and Human Services (2014), National Library of Medicine, Household Products Database. Data retrieved August 2014: http://householdproducts.nlm.nih.gov/cgi-bin/household/brands?tbl=chem&id=171

Åkesson, B. (1994): Nordic Expert Group for Criteria Documentation of Health Risk from Chemicals. 115 N-Methyl-2-pyrrolidone (NMP); Arbete och Hälsa, 1994:40, Appendix 1

Appendix 1: Background information to chapter 2 on legal framework

The following annex provides some background information on subjects addressed in Chapter 3. The intention is that the reader less familiar with the legal context may read this concurrently with chapter 3.

EU and Danish legislation

Chemicals are regulated via EU and national legislations, the latter often being a national transposition of EU directives.

There are four main EU legal instruments:

- Regulations (DK: Forordninger) are binding in their entirety and directly applicable in all EU Member States.
- Directives (DK: Direktiver) are binding for the EU Member States as to the results to be achieved. Directives have to be transposed (DK: gennemført) into the national legal framework within a given timeframe. Directives leave margin for manoeuvering as to the form and means of implementation. However, there are great differences in the space for manoeuvering between directives. For example, several directives regulating chemicals previously were rather specific and often transposed more or less word-by-word into national legislation. Consequently and to further strengthen a level playing field within the internal market, the new chemicals policy (REACH) and the new legislation for classification and labelling (CLP) were implemented as Regulations. In Denmark, Directives are most frequently transposed as laws (DK: love) and statutory orders (DK: bekendtgørelser).

The European Commission has the right and the duty to suggest new legislation in the form of regulations and directives. New or recast directives and regulations often have transitional periods for the various provisions set-out in the legal text. In the following, we will generally list the latest piece of EU legal text, even if the provisions identified are not yet fully implemented. On the other hand, we will include currently valid Danish legislation, e.g. the implementation of the cosmetics directive) even if this will be replaced with the new Cosmetic Regulation.

- Decisions are fully binding on those to whom they are addressed. Decisions are EU laws relating to specific cases. They can come from the EU Council (sometimes jointly with the European Parliament) or the European Commission. In relation to EU chemicals policy, decisions are e.g. used in relation to inclusion of substances in REACH Annex XVII (restrictions). This takes place via a so-called comitology procedure involving Member State representatives. Decisions are also used under the EU ecolabelling Regulation in relation to establishing ecolabel criteria for specific product groups.
- Recommendations and opinions are non-binding, declaratory instruments.

In conformity with the transposed EU directives, Danish legislation regulate to some extent chemicals via various general or sector specific legislation, most frequently via statutory orders (DK: bekendtgørelser).

Chemicals legislation

REACH and CLP

The REACH Regulation[2] and the CLP Regulation[3] are the overarching pieces of EU chemicals legislation regulating industrial chemicals. The below will briefly summarise the REACH and CLP provisions and give an overview of 'pipeline' procedures, i.e. procedures which may (or may not) result in an eventual inclusion under one of the REACH procedures.

(Pre-)Registration

All manufacturers and importers of chemical substance > 1 tonne/year have to register their chemicals with the European Chemicals Agency (ECHA). Pre-registered chemicals benefit from tonnage and property dependent staggered dead-lines:

- 30 November 2010: Registration of substances manufactured or imported at 1000 tonnes or more per year, carcinogenic, mutagenic or toxic to reproduction substances above 1 tonne per year, and substances dangerous to aquatic organisms or the environment above 100 tonnes per year.
- 31 May 2013: Registration of substances manufactured or imported at 100-1000 tonnes per year.
- 31 May 2018: Registration of substances manufactured or imported at 1-100 tonnes per year.

Evaluation

A selected number of registrations will be evaluated by ECHA and the EU Member States. Evaluation covers assessment of the compliance of individual dossiers (dossier evaluation) and substance evaluations involving information from all registrations of a given substance to see if further EU action is needed on that substance, for example as a restriction (substance evaluation).

Authorisation

Authorisation aims at substituting or limiting the manufacturing, import and use of substances of very high concern (SVHC). For substances included in REACH annex XIV, industry has to cease use of those substance within a given deadline (sunset date) or apply for authorisation for certain specified uses within an application date.

Restriction

If the authorities assess that that there is a risk to be addressed at the EU level, limitations of the manufacturing and use of a chemical substance (or substance group) may be implemented. Restrictions are listed in REACH Annex XVII, which has also taken over the restrictions from the previous legislation (Directive 76/769/EEC).

Classification and Labelling

The CLP Regulation implements the United Nations Global Harmonised System (GHS) for classification and labelling of substances and mixtures of substances into EU legislation. It further specifies rules for packaging of chemicals.

Two classification and labelling provisions are:

1. **Harmonised classification and labelling** for a number of chemical substances. These classifications are agreed at the EU level and can be found in CLP Annex VI. In addition to newly agreed harmonised classifications, the annex has taken over the harmonised classifications in

[2] Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

[3] Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures

Annex I of the previous Dangerous Substances Directive (67/548/EEC); classifications which have been 'translated' according to the new classification rules.
2. **Classification and labelling inventory**. All manufacturers and importers of chemicals substances are obliged to classify and label their substances. If no harmonised classification is available, a self-classification shall be done based on available information according to the classification criteria in the CLP regulation. As a new requirement, these self-classifications should be notified to ECHA, which in turn publish the classification and labelling inventory based on all notifications received. There is no tonnage trigger for this obligation. For the purpose of this report, self-classifications are summarised in Appendix 2 to the main report.

Ongoing activities - pipeline
In addition to listing substance already addressed by the provisions of REACH (pre-registrations, registrations, substances included in various annexes of REACH and CLP, etc.), the ECHA web-site also provides the opportunity for searching for substances in the pipeline in relation to certain REACH and CLP provisions. These will be briefly summarised below:

Community Rolling Action Plan (CoRAP)
The EU member states have the right and duty to conduct REACH substance evaluations. In order to coordinate this work among Member States and inform the relevant stakeholders of upcoming substance evaluations, a Community Rolling Action Plan (CoRAP) is developed and published, indicating by who and when a given substance is expected to be evaluated.

Authorisation process; candidate list, Authorisation list, Annex XIV
Before a substance is included in REACH Annex XIV and thus being subject to Authorisation, it has to go through the following steps:

1. It has to be identified as a SVHC leading to inclusion in the candidate list4
2. It has to be prioritised and recommended for inclusion in ANNEX XIV (These can be found as Annex XIV recommendation lists on the ECHA web-site)
3. It has to be included in REACH Annex XIV following a comitology procedure decision (substances on Annex XIV appear on the Authorisation list on the ECHA web-site).

The candidate list (substances agreed to possess SVHC properties) and the Authorisation list are published on the ECHA web-site.

Registry of intentions
When EU Member States and ECHA (when required by the European Commission) prepare a proposal for:

- a harmonised classification and labelling,
- an identification of a substance as SVHC, or
- a restriction

this is done as a REACH Annex XV proposal.

The 'registry of intentions' gives an overview of intensions in relation to Annex XV dossiers divided into:
- current intentions for submitting an Annex XV dossier,
- dossiers submitted, and
- withdrawn intentions and withdrawn submissions

for the three types of Annex XV dossiers.

[4] It should be noted that the candidate list is also used in relation to articles imported to, produced in or distributed in the EU. Certain supply chain information is triggered if the articles contain more than 0.1% (w/w) (REACH Article 7.2 ff).

International agreements

OSPAR Convention

OSPAR is the mechanism by which fifteen Governments of the western coasts and catchments of Europe, together with the European Community, cooperate to protect the marine environment of the North-East Atlantic.

Work to implement the OSPAR Convention and its strategies is taken forward through the adoption of decisions, which are legally binding on the Contracting Parties, recommendations and other agreements. Decisions and recommendations set out actions to be taken by the Contracting Parties. These measures are complemented by other agreements setting out:

- issues of importance
- agreed programmes of monitoring, information collection or other work which the Contracting Parties commit to carry out.
- guidelines or guidance setting out the way that any programme or measure should be implemented
- actions to be taken by the OSPAR Commission on behalf of the Contracting Parties.

HELCOM - Helsinki Convention

The Helsinki Commission, or HELCOM, works to protect the marine environment of the Baltic Sea from all sources of pollution through intergovernmental co-operation between Denmark, Estonia, the European Community, Finland, Germany, Latvia, Lithuania, Poland, Russia and Sweden. HELCOM is the governing body of the "Convention on the Protection of the Marine Environment of the Baltic Sea Area" - more usually known as the Helsinki Convention.

In pursuing this objective and vision the countries have jointly pooled their efforts in HELCOM, which is works as:

- an environmental policy maker for the Baltic Sea area by developing common environmental objectives and actions;
- an environmental focal point providing information about (i) the state of/trends in the marine environment; (ii) the efficiency of measures to protect it and (iii) common initiatives and positions which can form the basis for decision-making in other international fora;
- a body for developing, according to the specific needs of the Baltic Sea, Recommendations of its own and Recommendations supplementary to measures imposed by other international organisations;
- a supervisory body dedicated to ensuring that HELCOM environmental standards are fully implemented by all parties throughout the Baltic Sea and its catchment area; and
- a co-ordinating body, ascertaining multilateral response in case of major maritime incidents.

Stockholm Convention on Persistent Organic Pollutants (POPs)

The Stockholm Convention on Persistent Organic Pollutants is a global treaty to protect human health and the environment from chemicals that remain intact in the environment for long periods, become widely distributed geographically, accumulate in the fatty tissue of humans and wildlife, and have adverse effects to human health or to the environment. The Convention is administered by the United Nations Environment Programme and is based in Geneva, Switzerland.

Rotterdam Convention
The objectives of the Rotterdam Convention are:

- to promote shared responsibility and cooperative efforts among Parties in the international trade of certain hazardous chemicals in order to protect human health and the environment from potential harm;
- to contribute to the environmentally sound use of those hazardous chemicals, by facilitating information exchange about their characteristics, by providing for a national decision-making process on their import and export and by disseminating these decisions to Parties.
- The Convention creates legally binding obligations for the implementation of the Prior Informed Consent (PIC) procedure. It built on the voluntary PIC procedure, initiated by UNEP and FAO in 1989 and ceased on 24 February 2006.

The Convention covers pesticides and industrial chemicals that have been banned or severely restricted for health or environmental reasons by Parties and which have been notified by Parties for inclusion in the PIC procedure. One notification from each of two specified regions triggers consideration of addition of a chemical to Annex III of the Convention. Severely hazardous pesticide formulations that present a risk under conditions of use in developing countries or countries with economies in transition may also be proposed for inclusion in Annex III.

Basel Convention
The Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal was adopted on 22 March 1989 by the Conference of Plenipotentiaries in Basel, Switzerland, in response to a public outcry following the discovery, in the 1980s, in Africa and other parts of the developing world of deposits of toxic wastes imported from abroad.

The overarching objective of the Basel Convention is to protect human health and the environment against the adverse effects of hazardous wastes. Its scope of application covers a wide range of wastes defined as “hazardous wastes” based on their origin and/or composition and their characteristics, as well as two types of wastes defined as “other wastes” - household waste and incinerator ash.

The provisions of the Convention center around the following principal aims:

- the reduction of hazardous waste generation and the promotion of environmentally sound management of hazardous wastes, wherever the place of disposal;
- the restriction of transboundary movements of hazardous wastes except where it is perceived to be in accordance with the principles of environmentally sound management; and
- a regulatory system applying to cases where transboundary movements are permissible.

Eco-labels
Eco-label schemes are voluntary schemes where industry can apply for the right to use the eco-label on their products if these fulfil the ecolabelling criteria for that type of product. An EU scheme (the flower) and various national/regional schemes exist. In this project we have focused on the three most common schemes encountered on Danish products.

EU flower
The EU ecolabelling Regulation lays out the general rules and conditions for the EU ecolabel; the flower. Criteria for new product groups are gradually added to the scheme via 'decisions'; e.g. the Commission Decision of 21 June 2007 establishing the ecological criteria for the award of the Community eco-label to soaps, shampoos and hair conditioners.

Nordic Swan
The Nordic Swan is a cooperation between Denmark, Iceland, Norway, Sweden and Finland. The Nordic Ecolabelling Board consists of members from each national Ecolabelling Board and decides on Nordic criteria requirements for products and services. In Denmark, the practical implementation of the rules, applications and approval process related to the EU flower and Nordic Swan is hosted by Ecolabelling Denmark "Miljømærkning Danmark" (http://www.ecolabel.dk/). New criteria are applicable in Denmark when they are published on the Ecolabelling Denmark's website (according to Statutory Order No. 447 of 23/04/2010).

Blue Angel (Blauer Engel)
The Blue Angel is a national German eco-label. More information can be found on: http://www.blauer-engel.de/en.

Appendix 2: Information on NMP in consumer products on the US market

USES AND CONCENTRATIONS (%) OF NMP WITHIN PRODUCTS LISTED IN THE HOUSEHOLD PRODUCT DATABASE (2014)

Category	Number of products	Form	Content of NMP [%]
Arts & Crafts	1	liquid	40-45
Auto Products	2	aerosol	3.0-5.0
Auto Products	6	liquid	0.1-1; 1-5; 30-40
Home maintenance	5	aerosol	<5.0; 15-25; 30-60; 65-70
Home maintenance	1	gel	30-60
Home maintenance	1	paste	1
Home maintenance	1	Kit	0.1-0.3
Home maintenance	22	liquid	1.0-10; 25-30; 40-45; 65-100
Inside the Home	1	liquid	1.0-5.0
Inside the Home	1	pump spray	1
Landscape/Yard	1	liquid	-
Pesticides	2	aerosol	-
Pesticides	3	liquid	<7

Appendix 3: Information on consumer exposure

Table 19: Summary of consumer exposure estimates

Scenario	Calculation method	Exposure route	Estimated exposure dose (internal)	
			Acute (on day of event) (mg kg^{-1})	Chronic (mg kg^{-1} d^{-1})
Coatings	ECHA (2010a) – Tier 1 (no ventilation)	Inhalation	138-516 (females) 203-761 (males)	0.38-1.4 (females) 0.56-2.1 (males)
		Dermal	6 (females) 6 (males)	0.016 (females) 0.016 (males)
		Oral	Negligible	Negligible
		Total	144-522 (females) 209-767 (males)	0.40-1.4 (females) 0.58-2.1 (males)
Coatings – brush/roller application, solvent rich paint	ConsExpo v4 (includes ventilation)	Inhalation	67.9	0.19
		Dermal	2.77-11.1	0.0076-0.030
		Oral	Negligible	Negligible
		Total	70.7-79	0.18-0.22
Coatings – brush/roller application, high solid paint	ConsExpo v4 (includes ventilation)	Inhalation	88.3	0.24
		Dermal	2.77-11.1	0.0076-0.030
		Oral	Negligible	Negligible
		Total	91.0-99.4	0.25-0.27
Coatings – brush/roller application, waterborne paint	ConsExpo v4 (includes ventilation)	Inhalation	84.9	0.23
		Dermal	2.77-11.1	0.0076-0.030
		Oral	Negligible	Negligible
		Total	87.7-96.0	0.24-0.26
Coatings – brush/roller application, waterborne wall paint	ConsExpo v4 (includes ventilation)	Inhalation	255	1.39
		Dermal	2.77-11.1	0.0076-0.030
		Oral	Negligible	Negligible
		Total	258-266	1.40-1.42
Writing inks	ECHA (2010a) – Tier 1 (no ventilation)	Inhalation	Negligible	Negligible
		Dermal[a]	0.008 (females) 0.007 (males)	0.008 (females) 0.007 (males)
		Oral[a]	0.008 (females) 0.007 (males)	0.008 (females) 0.007 (males)
		Total	0.008 (females) 0.007 (males)	0.008 (females) 0.007 (males)

Scenario	Calculation method	Exposure route	Estimated exposure dose (internal)	
			Acute (on day of event) (mg kg^{-1})	Chronic (mg kg^{-1} d^{-1})
Cleaning products	ECHA (2010a) – Tier 1 (no ventilation)	Inhalation	38-333 (females) 55-491 (males)	0.10-0.91 (females) 0.15-1.3 (males)
		Dermal	6 (females) 6 (males)	0.016 (females) 0.016 (males)
		Oral	Negligible	Negligible
		Total	44-339 (females) 61-497 (males)	0.12-0.93 (females) 0.17-1.3 (males)
Cleaning products – paint remover	ConsExpo v4 (includes ventilation)	Inhalation	41.8	0.11
		Dermal	0.39	0.0011
		Oral	Negligible	Negligible
		Total	42.2	0.11
Cleaning products – glue remover	ConsExpo v4 (includes ventilation)	Inhalation	49.3	0.034
		Dermal	5.54	0.0038
		Oral	Negligible	Negligible
		Total	54.8	0.038
Cleaning products – sealant/foam remover	ConsExpo v4 (includes ventilation)	Inhalation	5.54	0.076
		Dermal	0.077	0.0011
		Oral	Negligible	Negligible
		Total	5.6	0.077

a) The scenario of ink may lead to either dermal exposure or oral exposure and therefore the two routes should not be added to avoid double counting.

The table is taken from the Annex XV SVHC dossier (2011).

Appendix 4: Overview of the RCR for workers and pregnant workers

Table B.116: *Overview of RCRs for workers in the different uses.*

Use	PROC	RCR inhalative	RCR dermal	RCR combined	Conclusion of risk
RCRs industrial uses					
- Manufacturers	3	1.24	0.15	1.39	Measurement data of air concentrations of NMP at the production plants where NMP or other chemicals are produced (see section B.9.3.2.) suggest that the EasyTRA output is indeed a conservative estimate and therefore support the Dossier Submitter's conclusion that risks are expected to be sufficiently controlled
Generic uses: *charging and discharging* - All use categories as defined in table B.03 with industrial use	8a	1.74	0.60	2.33	Inhalation exposure to NMP may be too high if proper RMMs are not in place. Risks may not be sufficiently controlled when processes take place under elevated temperatures even with RMMs.
Generic uses: *chemical industry processes (elevated temp)* - Petrochemical industries - Agricultural chemical industry (synthesis) - Pharmaceutical industry	3	2.07	0.15	2.22	Inhalation exposure to NMP may be too high if proper RMMs are not in place. Risks may not be sufficiently controlled when processes take place under elevated temperatures even with RMMs.
Generic use: *formulation (up to 60)* - Formulators - Non-wire coaters - Wire coaters - Cleaners - Battery industries - Membrane manufacturers - High performance polymer producers - Agricultural chemical industry (synthesis) - Pharmaceutical industry - Functional fluids - Construction industry	5	2.07	0.60	2.66	Risks of NMP can be controlled at room temperature with proper RMMs in place. At elevated temperatures the risks may not be sufficiently controlled even with RMMs.
Coatings process: - Non-wire coaters - Wire coaters - Battery industries	7	1.87	0.38	2.25	Risks may not be sufficiently controlled
Cleaning process: - Cleaners - Electronics and semiconductor industries	7	1.87	0.38	2.25	Risks may be sufficiently controlled (measurement data and EasyTRA calculation are in the same range)
Laboratory use	15	0.21	0.07	0.28	Risks are sufficiently controlled

Use	PROC	RCR inhalative	RCR dermal	RCR combined	Conclusion of risk
Functional fluids	17	0.83	1.19	2.02	Risks are sufficiently controlled (EasyTRA calculations conservative)
Construction chemicals	10	0.41	1.19	1.61	Risks are sufficiently controlled (EasyTRA calculations conservative)
Professional uses					
Generic uses: *charging and discharging* - All use categories as defined in table B.03 with professional use	8b	1.74	0.60	2.33	Inhalation risks may not be sufficiently controlled
Generic uses: *Formulation* - Formulators - Non-wire coaters - Agricultural chemical industry (formulation) - Functional fluids Construction industry	5	1.74	0.60	2.33	Inhalation risks may not be sufficiently controlled
Coating process: Non-wire coaters	13	1.45	0.30	1.74	Inhalation risks may not be sufficiently controlled
Agricultural chemical industry (formulation)	11	0.53	1.17	1.70	Risks can be sufficiently controlled (if proper RMMs are taken)
Laboratories	15	0.41	0.07	0.49	Risks are sufficiently controlled
Functional fluids	20	2.07	0.37	2.44	Activities that fall under PROC20 will lead to insufficiently controlled risks from inhalation of NMP for all workers if no proper RMMs are considered due to the high energy processes.

Table B.117: *RCRs for pregnant worker.*

Use	PROC	RCR inhalative	RCR dermal	RCR combined	Conclusion on risk
RCRs industrial uses					
- Manufacturers	3	2.48	0.29	2.77	Measurement data of air concentrations of NMP at the production plants where NMP or other chemicals are produced (see section B.9.3.2.) suggest that the EasyTRA output is indeed a conservative estimate and therefore support the Dossier Submitter's conclusion that risks are expected to be sufficiently controlled
Generic uses: *charging and discharging* - All use categories as defined in table B.03 with industrial use	8a	3.47	1.14	4.61	Inhalation exposure to NMP may be too high if proper RMMs are not in place. Risks may not be sufficiently controlled when processes take place under elevated temperatures even with RMMs.
Generic uses: *chemical industry processes (elevated temp)* - Petrochemical industries - Agricultural chemical industry (synthesis) - Pharmaceutical industry	3	4.13	0.29	4.42	Inhalation exposure to NMP may be too high if proper RMMs are not in place. Risks may not be sufficiently controlled when processes take place under elevated temperatures even with RMMs.

Use	PROC	RCR inhalative	RCR dermal	RCR combined	Conclusion on risk
Generic use: *formulation (up to 60)* - Formulators - Non-wire coaters - Wire coaters - Cleaners - Battery industries - Membrane manufacturers - High performance polymer producers - Agricultural chemical industry (synthesis) - Pharmaceutical industry - Functional fluids - Construction industry	5	4.13	1.14	5.27	Risks of NMP can be controlled at room temperature with proper RMMs in place. At elevated temperatures the risks may not be sufficiently controlled even with RMMs.
Coatings process: - Non-wire coaters - Wire coaters - Battery industries	7	3.74	0.72	4.46	Risks may not be sufficiently controlled
Cleaning process: - Cleaners - Electronics and semiconductor industries	7	3.74	0.72	4.46	Risks may not be sufficiently controlled
Laboratory use	15	0.41	0.14	0.56	Risks are sufficiently controlled
Functional fluids	17	1.65	2.29	3.94	Risks may not be sufficiently controlled
Construction chemicals	14	2.89	0.29	3.18	Risks may not be sufficiently controlled
Professional uses					
Generic uses: *charging and discharging,* - All use categories as defined in table B.03, with professional use	8b	3.47	1.14	4.61	Inhalation risks may not be sufficiently controlled
Generic uses: *Formulation* - Formulators - Non-wire coaters - Agricultural chemical industry (formulation) - Functional fluids Construction industry	5	3.47	1.14	4.61	Inhalation risks may not be sufficiently controlled
Coating process: Non-wire coaters	13	2.89	0.57	3.46	Inhalation risks may not be sufficiently controlled
Agricultural chemical industry (formulation)	11	1.05	2.24	3.30	Risks can be sufficiently controlled (if proper RMMs are taken)
Laboratories	15	0.83	0.14	0.97	Risks are sufficiently controlled
Functional fluids	20	4.13	0.71	4.84	Risks cannot be excluded

The two tables in Appendix 4 are extracted from Annex XV Restriction dossier, 2013.

Survey of 1-methyl-2-pyrrolidone (NMP)

This survey is part of the Danish EPA's review of the substances on the List of Undesirable Substances (LOUS). The survey concerns the substance 1-methyl-2-pyrrolidone (NMP). This substance was included in the LOUS list in 2009 due to its reproductive toxic effects. The report defines the substance and present information on the use and occurrence of NMP internationally and in Denmark, information on existing regulation, on environmental and health effects, on monitoring and exposure, on waste management and on alternatives to the substance.

Denne kortlægning er et led i Miljøstyrelsens kortlægninger af stofferne på Listen Over Uønskede Stoffer (LOUS). Kortlægningen omhandler stoffet 1-methyl-2-pyrrolidon (NMP). Rapporten definerer stoffet og indeholder blandt andet en beskrivelse af brugen og forekomsten af NMP internationalt og i Danmark, om eksisterende regulering, en beskrivelse af miljø- og sundhedseffekter af stoffet, af moniteringsdata, af affaldsbehandling samt alternativer til stoffet.

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