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Survey of *n*-hexane

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Survey of *n*-hexane

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Preface

Background and objectives

The Danish Environmental Protection Agency's List of Undesirable Substances (LOUS) is intended as a guide for enterprises. It indicates substances of concern whose use should 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 using computer models. 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 the environment, only substances which are used in an industrial context in large quantities in Denmark, i.e. over 100 tonnes per year, are included in the list.

Over the period 2012-2015 all 40 substances and substance groups on LOUS will be surveyed. The surveys include collection of available information on the use and occurrence of the substances, internationally and in Denmark, information on environmental and health effects, on alternatives to the substances, on existing regulation, on monitoring and exposure, and information regarding ongoing activities under REACH, among others.

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 *n*-hexane. The substance was included in the first list in 2000 within the group of simple hydrocarbons and has remained on the list since that time.

Hexane is included because of its problematic health properties, since it has been, amongst others, been classified as reproduction toxic and damaging to health by prolonged exposure.

The main objective of this study is, as mentioned, to provide background for the Danish EPA's consideration regarding the need for further risk management measures.

The process

The survey has been undertaken by COWI A/S and Syska Voskian Consulting from September 2013 to June 2014. The work has been followed by an advisory group consisting of:

- Peter Hammer Sørensen, Danish EPA, Chemicals
- Anne Louise Rønlev, Danish EPA, Aarhus
- Nikolai Nilsen, Confederation of Danish Industry
- Sonja Hagen Mikkelsen, COWI

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 International agreements from HELCOM, OSPAR, the Stockholm Convention, the PIC Convention, and 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 Danish ecolabel secretariat (Nordic Swan and EU Flower) and the German Angel.
- Pre-registered and registered substances from ECHA's website;
- Production and external trade statistics from Eurostat's databases (Prodcom and Comext);
- Export of dangerous substances from the Edexim database;
- Data on production, import and export of substances in mixtures from the Danish Product Register (confidential data, not searched via the Internet);
- Date on production, import and export of substances from the Nordic Product Registers as registered in the SPIN database;
- Information from Circa on risk management options (confidential, for internal use only, not searched via the Internet)
- Monitoring data from the National Centre for Environment and Energy (DCE), the Geological Survey for Denmark and Greenland (GEUS), the Danish Veterinary and Food Administration, the European Food Safety Authority (EFSA) and the INIRIS database.
- Waste statistics from the Danish EPA;
- Chemical information from the ICIS database;
- 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, IARC, IPCS, WHO, OSPAR, HELCOM, and the Basel Convention;
  - Environmental authorities in Norway (Klif), Sweden (KemI and Naturvårsverket), Germany (UBA), UK (DEFRA and Environment Agency), the Netherlands (VROM, RIVM), Austria (UBA). Information from other EU Member States was retrieved if quoted in identified literature.
  - US EPA, Agency for Toxic Substances and Disease Registry (USA) and Environment Canada.
- PubMed and Toxnet databases for identification of relevant scientific literature.

Besides, direct enquiries were made to Danish and European trade organisations and a few key market actors in Denmark.

Background and objectives

The Danish Environmental Protection Agency's List of Undesirable Substances (LOUS) is intended as a guide for enterprises. It indicates substances of concern whose use should 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 using computer models. 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 the environment, only substances which are used in an industrial context in large quantities in Denmark, i.e. over 100 tonnes per year, are included in the list.

Over the period 2012-2015 all 40 substances and substance groups on LOUS will be surveyed. The surveys include collection of available information on the use and occurrence of the substances, internationally and in Denmark, information on environmental and health effects, on alternatives to the substances, on existing regulation, on monitoring and exposure, and information regarding ongoing activities under REACH, among others.

On the basis of the surveys, the Danish EPA will assess the need for any further regulation, substitution/phase out, classification and labelling, improved waste management or increased dissemination of information.

Summary and conclusions

Over the period 2012-2015, all 40 substances and substance groups on the Danish Environmental Protection Agency's List of Undesirable Substances (LOUS) will be subject to survey and review. On the basis of the results, the Danish EPA will assess the need for any further regulation: substitution/phase out, classification and labelling, improved waste management or increased dissemination of information.

This survey concerns *n*-hexane. The substance was included in the LOUS in 1999.

***n*-Hexane**
n-Hexane is a highly volatile hydrocarbon and an ozone precursor. Pure *n*-hexane occurs in crude oil in small percentages and can be isolated from a number of oil fractions from the refinery process (e.g. light and heavy naphtha, light gasoline or BTX (benzene, toluene, and xylene). For example, *n*-hexane constitutes about 1 - 3% of unleaded gasoline. The content is less than 0.5 % in synthetic alkylate gasoline for two- and four stroke engines, sometimes named "environment petrol" according to safety data sheets on the Danish market.

Commercial hexane is a mixture that contains approximately 52% *n*-hexane. Other compounds in the mixture are e.g. varying amounts of structural isomers and related chemicals, such as methylpentane and methylcyclopentane.

Regulatory framework
n-Hexane is classified in the following hazard classes: flammable liquids, reproductive toxicity, aspiration toxicity, specific target organ toxicity after single and repeated exposure, and skin irritation, and furthermore as hazardous to the aquatic environment.

Hexane is prohibited for use in cosmetic products according to Annex II of the Cosmetic Regulation. *n*-hexane is allowed for use as an extraction solvent in production of foodstuffs and food ingredients with certain restriction regarding residue content and application in preparations of different food items. *n*-Hexane is a recognised ozone precursor which is recommended to be included in VOC measurement programmes according to the Statutory Order on management and control of air quality. Denmark has adopted the community indicative occupational 8-hour exposure limit value established for *n*-Hexane at 20 ppm or 72 mg/m^3.

In addition to the legislative instruments that specifically address *n*-hexane, other instruments are relevant for *n*-hexane due to generic classification criteria. The same is the situation in relation to the EU and the Nordic Eco-labelling schemes.

The substance is currently evaluated under CoRAP (eMSCA; Germany) due to concerns about human health and wide dispersive use.

Manufacture and uses
The total registered manufacture and import of *n*-hexane in the EU are indicated to be within the tonnage band 10,000-100,000 t/y.

In the trade statistics *n*-hexane is included in broader commodity codes and therefor no specific data on import/export for *n*-hexane or for the technical blends of hexanes have been identified.

Due to its technical properties *n*-hexane is used for a wide variety of products and processes. Except for its presence in fuels for engines, the major use in Denmark is as an extraction solvent used in manufacture of vegetable oils, and as a reaction solvent in manufacture of two intermediates in the production of organophosphorous pesticides. Hexane is recovered and recycled in both production processes. Manufacture of fish oils is based on a mixture of hexanes. According to information from the Product Register considerably smaller amounts are used in cleaning and washing agents, adhesives, lubricants, and corrosion inhibitors.

n-Hexane is present in a number of different consumer products such as glues, lubricants, water proofing sprays, spray paints, car care products, and certain scented products. Concentrations are typically below 1 % but higher concentrations up to ca. 25 % are seen in products for maintenance and repair of cars and machinery which may also be used by consumers.

n-Hexane has been the focus for substitution for many decades, but no statistical data have been identified to illustrate the development.

Waste management

n-Hexane is a highly volatile chemical which will tend to evaporate during production and use. It is therefore not likely to end up in the waste streams in any considerable amounts.

Environmental effects, fate and exposure

n-Hexane is classified as toxic to aquatic life with long lasting effects (cat. 2).

n-Hexane has a low water solubility (0.0098 g/L) and high vapour pressure (10 kPa). Atmospheric removal through reaction with hydroxyl radicals might therefore be the most important abiotic degradation process. By means of a read-across study on biodegradation of naphtha (mainly consisting of C4 - C11 alkanes), hexane was evaluated to be readily biodegradable.

Experimental data on bioaccumulation are not available. However, based on the log P (= log K_{OW} = 3.3 - 4), an estimated log K_{OC} of 2.9 – 3.6, and an estimated BCF of 453, *n*-hexane is not expected to bioconcentrate or bioaccumulate significantly in trophic food chains.

Some acute aquatic toxicity data are available, while there is a general lack of chronic and terrestrial data. The lowest acute toxic effect concentration of *n*-hexane was determined at 1.5 mg/L in a test with the small crustacean *Artemia salina*. However, for all aquatic organisms the reported effect concentrations cover several orders of magnitude, which is most likely related to methodological problems and requires very careful interpretation of the listed effect concentrations.

There is considerable potential for releases of *n*-hexane to environmental media through the use of fuels for heating or transportation. Atmospheric emissions of *n*-hexane are due to evaporation during processing of the substance or due to incomplete combustion of fuels. Other releases include industrial discharges, effluents from municipal wastewater treatment plants, and nonpoint-source runoff, spills, sludge and other waste deposition. Quantitative data on emissions to environmental compartments in Denmark or Europe could not be identified. Consumer products that contain small amounts of *n*-hexane are expected primarily to result in releases to air.

In Denmark, urban background concentrations of *n*-hexane have been measured in Copenhagen since 2009, because of the substance's identification as an ozone precursor. The measurements have been relatively stable over this period with an average of 0.15 to 0.19 µg/m^3.

Human health effects and exposure

n-Hexane is absorbed rapidly through the lungs in experimental animals and is widely distributed in the body with an affinity for tissues high in lipid content. Particularly high levels have been found in peripheral nerves. Dermal absorption is limited, but may be enhanced by other solvents. In humans, *n*-hexane is absorbed more slowly via the lung and very slowly through the skin.

n-Hexane has low acute toxicity. The critical effects of chronic exposure to *n*-hexane appear to be testicular toxicity and neurotoxicity both to the central and peripheral nervous systems. Peripheral neuropathy is well described after industrial exposure to *n*-hexane, particularly in shoemakers. The testicular effects observed in rats have not been well documented in humans.

2,5-Hexanedione is the main metabolite found in humans exposed to *n*-hexane and the substance suspected of being responsible for the neurotoxicity of the substance and toxic effects in the testes. The first symptoms of neurotoxicity are usually sensory and consist of tingling, numbness, burning, or prickling sensations in the feet or toes followed by progressive muscle weakness first in the lower and then upper extremities. Distal nerves are more commonly affected.

There is a large number of studies linking occupational exposure to *n*-hexane to the incidence of peripheral neuropathy in humans particularly among shoemakers. However, few of these report air concentrations, and where exposures are quoted it is not clear whether they refer to *n*-hexane or to commercial hexane. Also workers were exposed to mixtures of volatile solvents, and the proportions of *n*-hexane are not reported.

No information on exposure levels relevant for Danish industrial uses is available. However, the major applications of the substance as an extraction or reaction solvent take place in closed systems and are less likely to result in significant workplace exposures.

Very limited data are available regarding consumer exposure in Denmark. As *n*-hexane is present in several spray products and taking the volatility of the substance into account, consumers may be exposed to relatively high concentrations on a short term basis. However, in general the consumers are not expected to be exposed on frequent basis or for long periods of time, and are thereby not expected to be at risk in relation to the long-term effects of *n*-hexane.

Indirect exposure can occur through air, drinking water and food. Urban air concentrations measured in Copenhagen of on average 0.16-0.19 $\mu g/m^3$ do not give grounds for major health concerns. No data on *n*-hexane in drinking water or food have been identified for the Danish situation. Data from Canada estimating the total contribution from *n*-hexane containing food, in particular refined vegetable oils, do not indicate any risk for the consumer. Based on the limited database, combined exposures illustrating the Danish situation are not expected to be a concern in relation to the critical effects of *n*-hexane.

There is little information on how Danish consumers are exposed to *n*-hexane and if certain product types with a high content of *n*-hexane, e.g. for car repair and maintenance, may result in unacceptable exposures.

Alternatives to *n*-hexane

The high volume uses in Denmark are based on *n*-hexane rich blends of hexane isomers and it does not seem likely that the *n*-hexane will be replaced for these applications in the near future. For solvent extraction of edible oils, only solvents that are allowed according to the legislation in this area can be used.

Many large companies have developed solvent selection and replacement guides where *n*-hexane often is listed as a substance to avoid or restrict where technical requirements makes it possible.

With regard to consumer products, *n*-hexane has been substituted in many products before the turn of the millennium and *n*-hexane is mostly found in smaller concentrations in the majority of the products. For most types of consumer product alternatives will be available without hexane.

Most of the identified alternatives are also highly flammable and are not safer than *n*-hexane with respect to flammability. Heptane, which is often suggested as an alternative has a stronger environmental classification and may therefore be a concern in relation to uses such as cleaning and washing. From a health perspective several of the alternatives share some of the less critical health effects of *n*-hexane. Ethanol, which is the least toxic of the alternatives, has been tested as an extraction solvent, but a technological solution is not available.

Conclusion

The major uses in Denmark of *n*-hexane as an extraction and reaction solvent occur in closed systems. Currently it seems that alternative technologies allowing substitution of *n*-hexane are not fully developed.

Most releases to the environment will be to air and should be minimised to the extent possible. Urban ambient air concentrations do not indicate any major health or environmental risk from *n*-hexane alone.

With regard to other professional uses information from the Product Register suggest that the consumption has been relatively stable since 2006. It is expected that industry in general has made an effort to substitute n-hexane containing products already before the turn of the millennium and n-hexane is often included in purchasing and substitution guidelines from major companies and sector organisation.

With regard to consumer products no overview of the uses and related exposure situation is available. However, available safety data sheets for known product types also intended for the consumer, suggest the *n*-hexane concentrations in most products is relatively low. As many of the products are not used frequently, there is on this basis no indication of a particular consumer risk.

No major data gaps have been identified.

Sammenfatning og konklusion

I perioden 2012-2015 skal alle 40 stoffer og stofgrupper på Miljøstyrelsens liste over uønskede stoffer (LOUS) kortlægges og vurderes. På baggrund af resultaterne vil den danske Miljøstyrelsen vurdere behovet for yderligere regulering, substitution/udfasning, klassificering og mærkning, forbedret affaldshåndtering eller yderligere informationsaktiviteter.

Denne undersøgelse vedrører n-hexan. Stoffet blev optaget på LOUS i 1999.

n-Hexan
n-Hexan er en flygtig kulbrinte, som medvirker til dannelse af ozon. *n*-Hexan forekommer i råolie i små koncentrationer og kan isoleres fra en række oliefraktioner i raffineringsprocessen (fx let og tung naphtha, let benzin eller BTX (benzen, toluen og xylen). For eksempel udgør n-hexan omkring 1-3% af blyfri benzin, hvorimod indholdet ifølge sikkerhedsdatablade er mindre end 0,5% i syntetisk alkylatbenzin til to- og fire takts motorer, undertiden kaldet "miljøbenzin".

Kommerciel hexan er en blanding, der indeholder ca. 52% n-hexan. Andre forbindelser i blandingen er fx varierende mængder af strukturisomere og relaterede kemikalier, såsom methylpentan og methylcyclopentan.

Lovgivning og anden regulering
n-Hexan er klassificeret som brandfarlig, reproduktionstoksisk, aspirationstoksisk, for specifik målorgantoksicitet efter enkelt og gentagen eksponering, samt for hudirritation. Derudover er stoffet farligt for vandmiljøet.

Hexan er forbudt til anvendelse i kosmetiske produkter i henhold til bilag II i kosmetikforordningen. *n*-Hexan er tilladt til brug som et ekstraktionsmiddel ved fremstilling af levnedsmidler og levnedsmiddelingredienser med visse begrænsninger med hensyn til restindhold og anvendelse i fremstillingen af forskellige fødevarer. n-Hexan er en anerkendt ozondanner, som anbefales at indgå i VOC måleprogrammer i henhold til bekendtgørelsen om styring og kontrol af luftkvaliteten. Danmark har adopteret EUs indikative 8-timers grænseværdi for eksponering i arbejdsmiljøet på 20 ppm eller 72 mg/m^3.

Ud over den lovgivning, der specifikt nævner n-hexan, er n-hexan også omfattet af anden lovgivning, der omfatter stoffer på baggrund af generiske klassifikationskriterier. Det samme er tilfældet i forhold til EUs og den Nordiske miljømærkeordning.

Stoffet er i øjeblikket under evaluering i CoRAP (eMSCA; Tyskland) grund af bekymringer for menneskers sundhed og udbredt åben anvendelse.

Fremstilling og anvendelse
Den samlede registrerede fremstilling og import af n-hexan i EU angives at være inden for mængdeintervallet 1.000-10.000 t/år.

I handelsstatistikken er n-hexan inkluderet i bredere varekoder og der er derfor ingen specifikke oplysninger om import/eksport af stoffet, eller af de tekniske blandinger af hexan, som er identificeret.

På grund af stoffets tekniske egenskaber anvendes n-hexan til en bred vifte af produkter og processer. Bortset fra forekomsten i brændstoffer til motorer er den væsentligste anvendelse i Danmark som ekstraktionsmiddel ved fremstilling af vegetabilske olier og som opløsningsmiddel ved fremstilling af pesticider. Hexan genindvindes og genbruges i begge produktionsprocesser. Fremstilling af fiskeolier er baseret på en blanding af hexaner. Ifølge oplysninger fra Produktregisteret anvendes mindre mængder i rengørings-og vaskemidler, lime, smøremidler og i korrosionsinhibitorer.

n-Hexan findes i en række forskellige forbrugerprodukter såsom lim, smøremidler, imprægneringssprays, sprøjtemaling, bilplejeprodukter og visse parfumerede produkter. Koncentrationen er typisk under 1 %, men højere koncentrationer på op til ca. 25% er set i produkter til eksempelvis vedligeholdelse og reparation af biler og maskiner. Disse produkter kan også anvendes af forbrugere.

n-Hexan har været fokus for substitution i mange årtier, men der er ikke ingen identificeret statistiske data til illustration af udviklingen.

Affaldshåndtering

n-Hexan er et letflygtigt kemikalie, som vil have en tendens til at fordampe under produktion og anvendelse. Det er derfor ikke sandsynligt, at stoffet ender i affaldsstrømmene i nogen betydelig mængde.

Miljømæssige effekter, skæbne og eksponering

n-Hexan er klassificeret som giftigt for vandlevende organismer, med langvarige virkninger (Kat. 2).

n-Hexan har lav opløselighed i vand (0,0098 g/l) og højt damptryk (10 kPa). Atmosfærisk fjernelse gennem reaktion med hydroxylradikaler er sandsynligvis den vigtigste abiotiske nedbrydningsvej for stoffet i miljøet. Baseret på "read-across" fra en undersøgelse om biologisk nedbrydning af nafta (hovedsageligt bestående af C4 - C11 alkaner), er hexan vurderet at være let bionedbrydelig.

Eksperimentelle data om bioakkumulering er ikke tilgængelige. Men baseret på logP (= log KOW = 3,3 - 4) , en estimeret log Koc på 2,9-3,6 og en anslået BCF på 453 , forventes n- hexan ikke at biokoncentrere eller bioakkumulere væsentligt i trofiske fødekæder.

Visse data for akut toksicitet i vandmiljøet er til rådighed, mens der er en generel mangel på kroniske data samt terrestriske data generelt. Den laveste koncentration med akut giftvirkning af n - hexan blev bestemt til 1,5 mg/L i en test med krebsdyret *Artemia salina*. Men for alle vandorganismer dækker de rapporterede effektkoncentrationer flere størrelsesordener, hvilket sandsynligvis skyldes metodologiske problemer ved de udførte test. Der er derfor behov for meget omhyggelig fortolkning af de rapporterede effektkoncentrationer.

Der er et betydeligt potentiale for udslip af n-hexan til luftmiljøet som resultat af anvendelse af brændstoffer til opvarmning eller transport. Atmosfæriske emissioner af n-hexan skyldes fordampning ved de industrielle anvendelser af stoffet eller på grund af ufuldstændig forbrænding af brændstoffer. Andre afgivelser omfatter industrielle udledninger, spildevand fra kommunale renseanlæg og diffus overfladeafstrømning, spild samt deponering af slam og andet affald. Der er ikke identificeret kvantitative data om emissioner til m i Danmark eller Europa. Forbrugerprodukter, der indeholder små mængder af n-hexan, forventes primært at give anledning til afgivelse til luft.

I Danmark er baggrundskoncentrationer af n-hexan i bymiljøer blevet målt i København siden 2009, på grund af, at stoffet er identificeret som en precursor for ozon. Niveauerne har ligget relativt stabilt i denne periode med en gennemsnitskoncentration på 0,15-0,19 µg/m^3.

Sundhedseffekter og eksponering

n-Hexan absorberes hurtigt gennem lungerne i forsøgsdyr og distribueres i kroppen med en affinitet for væv med højt fedtindhold. Særligt høje niveauer er blevet fundet i de perifere nerver. Dermal absorption er begrænset, men kan øges af andre opløsningsmidler. Hos mennesker optages n-hexan langsommere via lungerne end i dyr og meget langsomt gennem huden.

n-Hexan har lav akut toksicitet. De kritiske effekter af kronisk eksponering for n-hexan synes at være testikeltoksicitet og neurotoksicitet i forbindelse med både det centrale og perifere nervesystem. Perifer neuropati er velbeskrevet i forbindelse med industriel eksponering for n-hexan, især blandt arbejdere i skoindustrien. Effekterne som ses på testikler hos rotter er ikke vel-dokumenteret hos mennesker.

2,5-Hexandion er den vigtigste metabolit hos mennesker, der har været udsat for n-hexan, og stoffet mistænkes for at være årsagen til neurotoksicitet og toksiske effekter i testiklerne. De første symptomer på neurotoksicitet er normalt sensoriske og består af prikken, følelsesløshed, brændende eller prikkende fornemmelser i fødder eller tæer efterfulgt af progressiv muskelsvækkelse først i de nederste og derefter de øvre ekstremiteter. Distale nerver påvirkes normalt mere.

Der er et stort antal undersøgelser, der forbinder erhvervsmæssig eksponering for n-hexan med forekomsten af perifer neuropati hos mennesker især blandt skoarbejdere. Imidlertid rapporterer få af disse undersøgelser om luftkoncentrationen, og i de tilfælde, hvor eksponeringen er nævnt, er det ikke klart, om der henvises til n-hexan eller kommercielt hexan. Det rapporteres heller ikke om arbejdere blev udsat for blandinger af flygtige opløsningsmidler, og i givet fald hvad andelen af n-hexan var.

Der er ikke fundet oplysninger om eksponeringsniveauer relevante for danske anvendelser i industrien. De væsentligste anvendelser af stoffet som ekstraktions- eller reaktions-opløsningsmiddel finder sted i lukkede systemer og medfører næppe væsentlige eksponeringer i arbejdsmiljøet.

Der er begrænsede data tilgængelige vedrørende forbrugernes eksponering i Danmark. Da n-hexan er til stede i flere sprayprodukter og stoffet er flygtigt, kan forbrugerne potentielt udsættes for relativt høje koncentrationer i kort tid. Generelt forventes forbrugerne dog ikke at blive eksponeret hverken hyppigt eller i længerevarende perioder, og dermed forventes der ikke at være nogen væsentlig fare forhold til de langsigtede effekter af n-hexan.

Indirekte eksponering kan forekomme gennem luft, drikkevand og fødevarer. Koncentrationer på gennemsnitligt 0,16-0,19 $\mu g/m^3$ målt i byluften i København giver ikke anledning til væsentlige sundhedsmæssige betænkeligheder. Der er ikke fundet data om n-hexan i drikkevand eller fødevarer, som kan anvendes til at beskrive situationen I Danmark. Estimater fra Canada over det samlede bidrag af n-hexan med mad, især raffinerede vegetabilske olier, indikerer ikke nogen risiko for forbrugeren. Baseret på de begrænsede data, der er til rådighed, antages kombineret eksponering, ikke at ville udgøre et problem i forhold til de kritiske effekter af n-hexan.

Der er ikke meget information om danske forbrugeres udsættelse for n-hexan, og om hvorvidt visse produkttyper med højt indhold af *n*-hexan til fx bilreparation og vedligeholdelse kan resultere i uacceptable eksponeringer.

Alternativer til n-hexan

Det store forbrug af n-hexan i Danmark er baseret på n-hexan-rige blandinger af hexanisomerer, og det synes ikke sandsynligt, at n-hexan vil blive erstattet til disse anvendelser i den nærmeste fremtid. Til udvinding af spiseolier kan der kun anvendes opløsningsmidler, der er tilladt i henhold til lovgivningen.

Mange store virksomheder har udviklet retningslinjer for indkøb og substitution af opløsningsmidler, hvor n -hexan ofte er opført som et stof, der skal undgås eller begrænses, hvis tekniske krav gør det muligt.

Med hensyn til forbrugerprodukter, er n-hexan blevet erstattet i mange produkter før årtusindskiftet og n-hexan findes for det meste i mindre koncentrationer i produkterne. For de fleste typer af forbrugerprodukter vil der være tilgængelige alternativer uden hexan.

Hovedparten af de identificerede alternativer er også klassificerede som brandfarlige og er dermed ikke sikrere end n-hexan med hensyn til brandfarlighed. Heptan, der ofte foreslås som et alternative, har en strengere miljøfareklassificering og kan derfor være et problem i forhold til nogle anvendelser såsom rengøring. Fra et sundhedsmæssigt perspektiv deler flere af alternativerne nogle af de mindre kritiske sundhedsmæssige effekter med n-hexan. Ethanol, som er det mindst toksiske af de nævnte alternativer, er blevet testet som ekstraktionsmiddel, men en teknologisk løsning er ikke tilgængelig.

Konklusion

De vigtigste anvendelser af n-hexan i Danmark er som ekstraktions- og reaktionsopløsningsmiddel i lukkede systemer. I øjeblikket er lader det ikke til, at alternative teknologier er tilstrækkeligt udviklet med henblik på substitution af n-hexan.

De fleste udledninger til miljøet vil være til luft og bør minimeres i det omfang, det er muligt. Koncentrationer i byluften indikerer ikke umiddelbart nogen væsentlig sundheds-eller miljørisiko fra n-hexan alene.

Med hensyn til andre erhvervsmæssige anvendelser tyder oplysninger fra Produktregisteret på, at forbruget har været relativt stabilt siden 2006. Det antages, at industrien generelt har gjort en indsats for at erstatte produkter med indhold af n-hexan allerede før årtusindskiftet, og n- hexan indgår fortsat ofte i indkøbs-og substitutionsvejledninger fra store virksomheder og brancheorganisationer.

Med hensyn til forbrugerprodukter er der på nuværende tidspunkt ikke noget overblik over anvendelser og eksponeringssituationer forbundet med brug af n-hexan. Sikkerhedsdatablade for kendte produkttyper, som også er beregnet til forbrugerne, tyder på, at koncentrationerne af n-hexan i de fleste produkter er forholdsvis lave. Da mange af disse produkter, ikke anvendes hyppigt, er der på det foreliggende grundlag ingen indikation af en væsentlig risiko for forbrugerne.

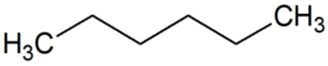
Der er ikke identificeret væsentlige datamangler.

1. Introduction to the substance

1.1 Definition of the substance

The name and other identifiers of *n*-hexane included in this study are listed in Table 1.

TABLE 1
NAME AND OTHER IDENTIFIERS OF *N*-HEXANE

Substance name	*n*-hexane
EC number	203-777-6
CAS number	110-54-3
Synonyms	hexane; normal hexane; hexyl hydride; skellysolve B; dipropyl; gettysolve-b; hex
Molecular formula	C_6H_{14}
Structure	
Molecular weight	86.18 g/mol

n-Hexane is a straight-chain, fully saturated hydrocarbon with six carbon atoms.

Pure *n*-hexane occurs in crude oil in small percentages and can be isolated from a number of oil fractions from the refinery process (e.g. light and heavy naphtha, light gasoline or BTX (benzene, toluene, and xylene). For example, *n*-hexane constitutes about 1 - 3% of unleaded gasoline (ASTDR, 1999) and less than 0.5 % in synthetic alkylate gasoline for two- and four stroke engines, sometimes named "environment petrol" according to safety data sheets on the Danish market. Special know-how and technology is required for the production of high-purity *n*-hexane.

Commercial hexane is a mixture that contains approximately 52% *n*-hexane (US EPA, 2005). Other compounds in the mixture are e.g. varying amounts of structural isomers and related chemicals, such as methylpentane and methylcyclopentane.

n-Hexane is a major component of some of fractions from distillation of crude oil. A large number of CAS numbers exist for these “Substances of Unknown or Variable composition” (UVCB). Until now, there has not been a coordinated use of the CAS numbers for mixtures containing a certain amount of *n*-hexane, a scan of Safety Data Sheets on the internet confirms this confusion. The Hydrocarbon Solvents REACH consortium undertaking the collective activities related to the registration of Hydrocarbon Solvents under REACH, has developed a naming convention for hydrocarbon solvents based on the chemical composition of the substance (HSPA, 2011). The new substance definitions and a category approach for the toxicological assessments are the basis for the classification and labelling of those substances. The hydrocarbon solvents described by a HSPA substance are a specific and narrower defined subset of one or more existing CAS numbers. However, this survey focuses on the substance *n*-hexane with the CAS no. 110-54-3. Further information on mixtures containing *n*-hexane is provided in chapter 3.

1.2 Physical and chemical properties

n-Hexane is a highly volatile hydrocarbon. The physical and chemical properties of *n*-hexane are shown in Table 2. The listed properties mainly refer to the registration dossiers available at ECHA's website. The registration dossiers may include different values for the same parameter; in this case, all values are indicated.

TABLE 2
PHYSICAL AND CHEMICAL PROPOERTIES OF THE SUBSTANCE (ECHA 2013).

Property	*n*-hexane
Physical state	Liquid
Melting point	-95.35 °C
Boiling point	68.73 °C
Relative density	0.6606 g/cm^3
Vapour pressure	10 kPa @ 9.8°C (16.2 kPa @ 20°C[1])
Surface tension	17.89 mN/m @ 25°C
Water solubility (mg/L)	0.0098 g/L @ 25°C
Log P (octanol/water)	4

1.3 Function of the substances for main application areas

Highly purified *n*-hexane is primarily used as a reagent or solvent for laboratory applications. Commercial hexane is an important solvent in many industries. In the food industry, mixtures containing *n*-hexane are used in processes for the extraction of edible fats and oils. *n*-Hexane is the solvent base for many commercial products, such as glues, inks, cements, paint thinners, cleaning agents and degreasers. It is also a component in fuels, and used as a blowing agent in polyurethane production.

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[1] http://Calculation of vapour pressure at 20°C: ddbonline.ddbst.com/AntoineCalculation/AntoineCalculationCGI.exe

2. Regulatory framework

This chapter gives an overview of how *n*-hexane is addressed in existing and upcoming EU and Danish legislation, international agreements and by EU and Nordic eco-label criteria. The chapter primarily focuses on legislation where *n*-hexane is addressed specifically by chemical name or CAS number. Legislation, where the substance is implicitly addressed, i.e. where *n*-hexane is included in the overall scope of a regulation/directive (e.g. due to the substance classification), is not listed. Examples of such legislation is the Statutory order on VOCs[2] implementing the EU Directive on Industrial emissions and the Statutory order on major accident hazards[3] implementing the Seveso Directive. These are of course equally important in relation to *n*-hexane.

In Appendix 1, a brief overview of legal instruments in the EU and DK is presented. The appendix gives a brief introduction to chemicals legislation, explains the lists referred to in section 2.1.3 on Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), and provides a brief introduction to international agreements and the EU and Nordic ecolabelling schemes.

2.1 Legislation

This section will first list existing legislation addressing *n*-hexane, and then give an overview of on-going activities, focusing on where *n*-hexane is mentioned in the pipeline in relation to various REACH provisions.

2.1.1 Existing legislation

Table 3 provides an overview of existing key legislation addressing *n*-hexane. For each area of legislation, the table first lists the EU legislation (if applicable) and then (as concerns directives) existing transposition into Danish law and/or other national rules. The latter will only be elaborated upon in case of Danish rules differ from EU rules.

By European legislation, hexane is prohibited in cosmetic products through the Cosmetics regulation. The Directive 2009/32/EC on extraction solvents used in the production of foodstuffs indicates application areas as well as maximum residues of hexane in certain foodstuffs where hexane extraction is used. The residue limit values are implemented in Denmark by the Statutory Order on Additives in Food.

The Commission directive on indicative occupational exposure values sets out an 8-hour limit value of 72 mg/m^3 (20 ppm) for hexane. The Danish occupational limit value is congruent with the EC indicative limit values. Short-term exposure limit values have not been defined for hexane in neither Danish nor European legislation. However, the exposure limits defined in the Executive Order no. 507 of 17th May 2011 indicate that the short-time exposure limit never must exceed the 2-times exposure limit value when exposed over 15 min.

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[2] Bekendtgørelse nr. 1452 af 20/12/2012 om anlæg og aktiviteter, hvor der bruges organiske opløsningsmidler

[3] Bekendtgørelse nr. 1666 af 14/12/2006 om kontrol med risikoen for større uheld med farlige stoffer

TABLE 3
LEGISLATION ADRESSING *N*-HEXANE

Legal instrument*1	EU/ DK	Substance as specified by the instrument	Requirements
Legislation addressing substances			
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, amending and repealing Directives 67/548/EEC and 1999/45/EC	EU	*n*-hexane, 203-777-6, 110-54-3	*n*-Hexane is included in the List of harmonised classifications of hazardous substances
Legislation addressing products			
Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products	EU	Hexane, 110-54-3	Listed in ANNEX II: LIST OF SUBSTANCES PROHIBITED IN COSMETIC PRODUCTS
Directive 2009/32/EC of the European Parliament and of the Council of 23 April 2009 on the approximation of the laws of the Member States on extraction solvents used in the production of foodstuffs and food ingredients	EU	Hexane[4]	Hexane is listed in ANNEX I including extraction solvents which are allowed in food or raw material processing. The following use conditions (with maximum residues in the extracted food stuff) have been defined for hexane: - Production or fractionation of fats and oils and production of cocoa butter (1 mg/kg) - Preparation of defatted protein products and defatted flours (10 mg/kg in the food containing the defatted protein products and the defatted flours, 30 mg/kg in the defatted soya products as sold to the final consumer) - Preparation of defatted cereal germs (5 mg/kg) The maximum residue limit in the foodstuff due to the use of hexane in the preparation of flavourings from natural fla-

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[4] Hexane means a commercial product consisting essentially of acyclic saturated hydrocarbons containing six carbon atoms and distilling between 64 °C and 70 °C

Legal instrument*1	EU/ DK	Substance as specified by the instrument	Requirements
			vouring materials is 1 mg/kg. The combined use of hexane and ethylmethylketone for extraction is forbidden.
Statutory Order No 542 of 27/05/2013 on additives, etc. to foods [Bekendtgørelse om tilsætninger mv. til fødevarer, BEK no. 542, 27/05/2013], Ministry of Food, Agriculture and Fisheries of Denmark	DK	Hexane	Included in part II and part III describing extraction agents' allowed application areas and maximum residues in foods The maximum residues for the specified application areas are congruent with Directive 2009/32/EC
Legislation addressing emissions to the environment (Ministry of Environment)			
Statutory Order No 1326 of 21/12/2011 on assessment and management of air quality [Bekendtgørelse om vurdering og styring af luftkvaliteten, BEK nr. 1326 af 21/12/2011] Ministry of Environment	DK	*n*-Hexane	The Danish EPA divides the country into zones and agglomerations, in which the air quality is to be assessed and managed in accordance with Directive 2008/50/EC and Directive 2004/107/EC. *n*-Hexane is listed in appendix X Measurements of ozone precursors: *n*-hexane is included in the list of recommended measured VOC.
Legislation addressing occupational exposures (Ministry of Employment)			
Commission Directive 2006/15/EC of 7 February 2006 establishing a second list of indicative occupational exposure limit values in implementation of Council Directive no 98/24/EC amending Directives 91/322/EEC and 2000/39/EC	EU	110-54-3, *n*-hexane	Listed in the Annex on INDICATIVE OCCUPATIONAL EXPOSURE LIMIT VALUES. Limit values are 8 hours: 72 mg/m³ (20 ppm). There are no short-term limit values or annotations for hexane.
Executive Order no. 507 of 17/05/2011 on Limit Values for Substances and Materials [Bekendtgørelse om grænseværdier for stoffer og materialer, BEK nr. 507 af 17/05/2011]	DK	*n*-Hexane	The order addresses any work with substances and materials, and any risk of exposure to workplace substances and materials. Hexane is listed in Section A on limit values for air pollution - List of limit values for gases, vapours and particulate

Legal instrument*1	EU/ DK	Substance as specified by the instrument	Requirements
			pollution. Limit values are congruent with the EF indicative limit values.
Executive Order No. 301 of 13/05/1993 on Determination of Code Numbers, [Bekendtgørelse om fastsættelse af kodenumre, BEK nr 301 af 13/05/1993] /Danish Ministry of Employment **Executive Order No. 302 of 13.05.1993 on Work with Code-Numbered Products** [Bekendtgørelse om arbejde med kodenummererede produkter, BEK nr. 301 af 13/05/1993] /Danish Ministry of Employment	DK	*n*-Hexane	The Metrological Occupational Air Requirements, called MAL [Danish: Måleteknisk Arbejdshygiejnisk Luftbehov] are defined for *n*-hexane as follows: ***n*-Hexane content > 0%** - MAL-factor (m³ air / 10 g substance): 78 - Content (limit weight %) / number after the hyphen: ≥ 0% / -1 Defines minimum safety measures which have to be applied when working with code-numbered products depending on working situations (outside, inside, large or small application areas) and processes (e.g. painting, grouting).
Executive Order on Working with Substances and Materials. [Arbejdstilsynets bekendtgørelse nr.292 af 26. April 2001 med senere ændringer.]			The executive order implements the EU Directive No 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work. According to the Statutory order the employer has the obligation to: - plan the work, in order to reduce any risk to the safety and health of workers rising from the presence of hazardous chemical agents, - replace hazardous substances, materials and work processes by less hazardous substances, materials and work processes, and - develop workplace guidelines for the use of hazardous substances and materials.
Bekendtgørelse om arbejdets udførelse nr. 559 af 17. juni 2004.			Section 16. Any unnecessary exposure of substances and materials must be avoided.

*1 Unofficial translation of name of Danish legal instruments.

2.1.2 Classification and labelling

Harmonised classification in the EU

Table 4 lists the harmonised classification and labelling for *n*-hexane according to Annex VI of the CLP Regulation. *n*-Hexane is classified in the following hazard classes: flammable liquids, reproductive toxicity, aspiration toxicity, specific target organ toxicity after single and repeated exposure, and skin irritation, and furthermore as hazardous to the aquatic environment.

TABLE 4
HARMONISED CLASSIFICATION ACOORDING TO ANNEX VI OF REGULATION (EC) NO 1272/2008 (CLP REGULATION)

Index No	International chemical identification	CAS No	Classification		Labelling
			Hazard Class and Category Code(s)[1]	Hazard statement Code(s)[2]	Pictogram
601-037-00-0	*n*-hexane	110-54-3	Flam. Liq 2	H225	
			Skin Irrit. 2	H315	
			Asp. Tox. 1	H304	
			STOT SE 3	H336	
			STOT RE 2 [3]	H373 [4]	
			Repr. 2	H361f [5]	
			Aquatic Chronic 2	H411	

[1] Hazard Class - Flam. Liq.: Flammable liquid; Skin Irrit.: Skin irritation; STOT SE: Asp. Tox.: Aspiration toxicity; Specific target organ toxicity — single exposure; STOT RE: Specific target organ toxicity — repeated exposure; Repr.: Reproductive toxicity; Aquatic Chronic: Hazardous to the aquatic environment.

[2] Hazard statement codes - H225: Highly flammable liquid and vapour; H315: Causes skin irritation; H304: May be fatal if swallowed and enters airways; H336: May cause drowsiness or dizziness; H373: May cause damage to organs through prolonged or repeated exposure; H361f: Suspected of damaging fertility; H411: Toxic to aquatic life with long lasting effects.

[3] Minimum classification, applies when classification according to the criteria in Directive 67/548/EEC does not correspond directly to the classification in a hazard class and category under the CLP Regulation.

[4] Hazard statement not specifying the route of exposure as the necessary information is not available.

[5] 'Suspected of damaging fertility or the unborn child'. According to the criteria, the general hazard statement can be replaced by the hazard statement indicating only the property of concern, where either fertility or developmental effects are proven to be not relevant.

Self-classification in the EU

The notified classifications are almost all completely congruent with the harmonised classification. A few notifiers do report acute toxicity H331 (3 notifiers out of ca. 2000) and STOT RE 1; H372 instead of H373 (17 notifiers out of ca. 2000).

2.1.3 REACH

n-Hexane is not restricted in the 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).

n-Hexane is registered with a full registration under REACH in the 10,000 - 100,000 t/y band.

Candidate list / Authorisation List / REACH Annex XIV

n-Hexane is not on the Candidate list of Substances of Very High Concern for Authorisation, or on the Authorisation list. The substance is not included in REACH Annex XIV (List of substances subject to authorisation).

Registry of Intentions

n-Hexane is listed in the registry of withdrawn Harmonised Classification and Labelling intentions and submissions. The intention was originally submitted by Norway who has earlier had a different classification of *n*-hexane than the EU.

Substance evaluation

n-Hexane is included in the first Community Rolling Action Plan (CoRAP 2012-2014) for evaluation in the year 2012 by Germany due to concerns about human health. N-hexane was selected for substance evaluation due to the CMR-properties and neurotoxic effects. There are several registrations of different registrants leading to a higher tonnage and exposure level than concluded in the single dossiers. The intention of the substance evaluation is to evaluate the risks arising from the aggregated exposure. The current status is marked as "ongoing" (May 2014).

TABLE 5
SUBSTANCES IN THE DRAFT COMMUNITY ROLLING ACTION PLAN, 2012-2014 (ECHA, 2014).

CAS No	EC No	Substance Name	Year	Member State	Initial grounds for concern
110-54-3	203-777-6	*n*-hexane	2012	Germany	Human health/CMR and neurotoxicity; Exposure/Wide dispersive use, high aggregated tonnage

2.1.4 Other legislation/initiatives

No other legislation or initiatives have been identified.

2.2 International agreements

n-Hexane is not mentioned in the international conventions and agreements that are relevant for this survey (OSPAR, HELCOM, ROTTERDAM, STOCKHOLM, Basel, CLRTAP). These conventions are concerned with environmental effects of chemical substances and/or persistent substances, properties which are not the main concerns relating to *n*-hexane.
For further information on the conventions, consult Appendix 1:

2.3 Eco-labels

The EU and Nordic eco-labelling have been searched for criteria excluding or restricting the use of *n*-hexane in eco-labelled products. *n*-Hexane is not mentioned specifically in any of the relevant criteria. It should however be stressed that *n*-hexane may be restricted due to general restrictions based on classification of substances as e.g. STOT RE or Repr. or according to criteria related to VOC content. For example, ingredients classified as dangerous substances, such as substances with risk phrases R62 (Possible risk of impaired fertility) are not allowed in eco-labelled indoor paints and varnishes (Nordic Ecolabelling, 2014a; *n*-hexane is classified as R62 according to the DSD Classification). (The criteria document for indoor paints and varnishes is currently under revision).

The same applies to e.g. product groups of car and boat care products (Nordic Ecolabelling, 2014b), chemical building products (Nordic Ecolabelling, 2014c), and office and hobby supplies (Nordic Ecolabelling, 2014d), in which hexane could be present as a constituent (solvent) or as a residue from use as a process chemical.

2.4 Summary and conclusions

n-Hexane is classified in the following hazard classes: flammable liquids, reproductive toxicity, aspiration toxicity, specific target organ toxicity after single and repeated exposure, and skin irritation, and furthermore as hazardous to the aquatic environment.

Hexane is addressed in several Danish and European legislative instruments. Hexane is prohibited for use in cosmetic products according to Annex II of the Cosmetic Regulation. Residue content and application in preparations of different food items is defined by Danish legislation.

With respect to the environment, hexane is recommended to be measured in assessing and managing air quality, since it is recognized as an ozone precursor VOC.

A community indicative occupational exposure limit value is established for *n*-hexane. The Danish occupational exposure limit is identical with the European indicative 8-hour limit at 20 ppm.

The substance is currently evaluated under CoRAP due to concerns about human health and wide dispersive use.

3. Manufacture and uses

3.1 Manufacturing

3.1.1 Manufacturing processes

Light naphtha is refined to obtain pure *n*-hexane (REACH registration number 01-211-948-0412-44-xxxx).

Pure *n*-hexane occurs in crude oil in small percentages and can be isolated from a number of oil fractions from the refinery process (e.g. light and heavy naphtha, light gasoline or BTX (benzene, toluene, and xylene). It is difficult to achieve high purity of *n*-hexane and special know-how and technology is required. The processes involve molecular sieve adsorption (where the straight *n*-paraffin is held in the cavities of the sieve and branched hydrocarbons go straight through), batch azeotropic distillation, superfractionation and extractive distillation (Environment Canada, 2009). The energy consumption for *n*-hexane purification using the mentioned traditional purification technologies is high.

In addition to pure *n*-hexane, a number of C6 rich aliphatic naphthas with a content of *n*-hexane have been registered under REACH and are sold under different names and CAS numbers. The following table from the Hydrocarbon Solvents Producers Association, HSPA, shows the different C6 products that have been defined by HSPA for REACH registration (Table 6). These broader range distillation point substances are manufactured via distillation of a suitable hydrocarbon feedstock, which may be straight-run gasoline distilled from crude oil. Note that the CAS numbers provided in the table are used to define C6 aliphatics as well as other aliphatics.

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TABLE 6

DIFFERENT C6 PRODUCTS ACCORDING TO THE HYDROCARBON SOLVENTS PRODUCERS ASSOCIATION (HSPA, 2011)

HSPA Category	HSPA substance name	REACH registration provisional EC No.	Related CAS No.(s)	Related CAS No.(s) Substance name
C6 Aliphatics	Normal-Hexane	203-777-6	92112-69-1	Hexane,-branched-and-linear
			110-54-3	Hexane
C6 Aliphatics	Hydrocarbons, C6, isoalkanes, <5% *n*-hexane	931-254-9	64742-49-0	Naphtha (petroleum), hydrotreated light
C6 Aliphatics	Hydrocarbons, C6, *n*-alkanes, isoalkanes, cyclics, *n*-hexane rich	925-292-5	64742-49-0	Naphtha (petroleum), hydrotreated light
			93165-19-6	Distillates (petroleum), C6-rich
			92112-69-1	Hexane,-branched-and-linear

HSPA Category	HSPA substance name	REACH registration provisional EC No.	Related CAS No.(s)	Related CAS No.(s) Substance name
C6 Aliphatics	C6 Aliphatics	930-397-4	92062-15-2	Solvent naphtha (petroleum), hydrotreated light naphthenic
			64742-49-0	Naphtha (petroleum), hydrotreated light
C6 Aliphatics	Hydrocarbons, C7, *n*-alkanes, isoalkanes, cyclics	927-510-4	64771-72-8	Paraffins (petroleum), normal C5-20

3.1.2 Manufacturing sites and volumes

Based on information in the REACH registration and Internet search, no manufacturing site of *n*-hexane has been identified in Denmark.

Compared with the number of European manufacturers of commercial hexane, there are few manufacturers of pure *n*-hexane. The following companies and sites in Europe have registered *n*-hexane under REACH and are manufacturing in Europe:

- Bitolea S.p.A, Italy: *n*-hexane 95 and *n*-hexane 99;
- DHC Solvent Chemie GmBH, Germany: *n*-hexane 95 and *n*-hexane 99;
- Haltermann GmbH: *n*-hexane 95 and *n*-hexane 99;
- Neste Oil Oyj, Finland. It has been confirmed by Neste Oil that *n*-hexane is an isolated intermediate in the petroleum refinery, not a product.

There are no statistical data to support an estimate of the volume manufactured by company or the total volume manufactured in Europe. The REACH registration is in the 10,000 – 100,000 tonnes per annum range (aggregated tonnage) but includes also volumes from importers that have registered.

3.2 Import and export *n*-hexane in Denmark and EU

In the recent nomenclature, *n*-hexane is not included (Commission Regulation (EU) No 927/2012) as a special entry, but covered by the generic CN code 2901 10 00 (Acyclic hydrocarbons – saturated). It has therefore not been possible to identify import and export data for *n*-hexane for neither Denmark nor the EU. Likewise, there is no PRODCOM code available for *n*-hexane.

Some companies have registered *n*-hexane under REACH but do not seem to be manufacturing in Europe (registration as only representatives):
- Chevron Philips Chemicals International NV, Belgium. High purity hydrocarbons and solvents are produced by Chevron Philips Chemicals only in Texas (information from their web site)

The following only representative companies have registered *n*-hexane under REACH for import by their clients:
- BiPRO GmbH Grauertstrasse 12, 81545, Munich, Germany
- REACHLaw Ltd. Keilaranta 15, 02150, Espoo, Finland

3.3 Use

3.3.1 General use

n-Hexane's high solubility for oil combined with its low boiling point makes it suitable for the use in a wide variety of applications. The major global uses of *n*-hexane as reported in the literature are listed below (Environment Canada, 2009; US EPA, 2005):

- a component in fuels and other petroleum products
- solvent extraction of vegetable oils and defatting of fish meal (extraction of fish oil)as blowing agent
- as an inert solvent for carrying out other chemical reactions ("reaction solvent" "reaction medium" or "diluent")
- special purpose solvent and cleaning agent (degreaser)
- in laboratories

Detailed information about the global or EU consumption of *n*-hexane for different uses has not been possible to obtain.

Component in fuels and other petroleum products:

Motor fuel contains small amounts (1-3%) of *n*-hexane. End-use fuels formulated with *n*-hexane containing products is a major global use of *n*-hexane. This use is not represented in the data on *n*-hexane use but is reported in other categories in the statistics, with the statistical data for fuel.

Solvent extraction of vegetable oils and defatting of fishmeal

n-Hexane or hexane mixtures rich in *n*-hexane are used for the extraction of vegetable oils from various seeds and crops to obtain a higher yield of oil from the seeds than a mechanical screw press allows. In the 1970s, it was estimated that soybean oil extraction accounted for approximately 30% of all uses of *n*-hexane in the US. The oil is used for nutrition but also for production of bio diesel. In the extraction process, vegetable oil is mixed with cooled hexane in a fractionation plant. Part of the oil will crystallize as a solid that can be filtered from the liquid part. After the solid part has been melted, hexane is removed by evaporation. Hexane is circulated in a closed system and reused.

Solvent extraction with hexane is also used in the fish industry to reduce the fat content in the meal from certain fish. According to FAO (1986), reduction of the oil content from 10% to 1% in menhaden, pilchard or anchovy meal would require about 4 litres of hexane per kilogramme of meal.

Hexane is listed in part II of Annex 1 to the EU Directive 2009/32/EC on extraction solvents used in the production of foodstuffs and food ingredients. The Directive provides maximum limits for residual hexane in the products (see chapter 2). Hexane is defined in the Directive as follows: "Hexane means a commercial product consisting essentially of acyclic saturated hydrocarbons containing six carbon atoms and distilling between 64 °C and 70 °C. The combined use of Hexane and Ethylmethylketone is forbidden". This definition excludes 3 of the 4 hexane blends that have been registered under REACH because of their boiling range and only leaves the pure *n*-hexane and one of the *n*-hexane rich blends registered under list number 930-397-4 as possible hexanes for extraction of food materials.

Some of the use of *n*-hexane in this industry might have been reported to the Danish Product Register under a different CAS number as a broader mix of hexanes.

In laboratories

n-Hexane is used as an extractant for no*n*-polar compounds and in calibration of instruments for analysis of volatile organic compounds (VOCs) and total petroleum hydrocarbons (TPHs). To obtain a high grade of purified *n*-hexane laboratories sometimes carry out their own fractionated distillation but many products are available from the traditional suppliers to laboratories.

Blowing agent
n-Hexane is used as a physical blowing agent in a number of plastic foams like PU (polyurethane) foam for thermal insulation, PET (polyethylene terephthalate) foam and acrylic plastic. Other substances that are used for the same purpose are HCFC 142b, HFC 134 A, iso-pentane, *n*-heptane, CO_2, N_2. It should be noted that HCFC 142 is covered by the phaseout schedule according to the terms of the Montreal Protocol and its amendment calling for a 90% reduction in consumption in 2015, 99.5 % in 2020 and 100 % in 2030 (US EPA, HCFC Phaseout Schedule).

Reaction Medium
n-Hexane is used in the production of polyethylene as reaction solvent or slurry liquid phase for several commercial polyethylene processes. *n*-Hexane is similarly used as a reaction solvent in several commercial polypropylene processes. In these processes, *n*-hexane is enclosed in a reaction system and continually recycled, with minimal loss.

A technical grade of hexane, containing 47% *n*-hexane and 53% mix of 4 other C6 aliphatics is used as the reaction solvent in the production of diethyl- and dimethylthiophosphorylchloride, both intermediates for the production of some organophosphate insecticides.

Special purpose solvent and cleaning agent (degreaser)
n-Hexane is used in adhesives, sealants, binders, fillers, lubricants, paints and coatings, brake cleaners, degreasers and in cleaners used in the printing industry (rotogravure and flexo) as further described in section 3.3.3. As solvent in rubber (adjustment of the viscosity of the rubber used for tire production), rubber cement and in adhesives like those used for shoe making and repair, adhesives for holding the ends of tin cans, adhesives used in the production of balls used in several sports, and in adhesives used for production of tapes, bandages and dressings (Environment Canada, 2009; ECHA Dissemination Database: Registration Dossier for *n*-hexane).

The US Household Products Database from the National Library of Medicine lists 85 consumer products containing *n*-hexane with typical concentrations between 5 and 20 %. The products are mainly adhesives (spray or liquid), cleaners and miscellaneous car maintenance products.

n-Hexane is listed on the list of propellants and solvents that are permitted in aerosols up to 1 litre in Denmark.

The use of *n*-hexane as degreaser was in the global news in 2011 because a large number of Chinese workers at a supplier to Apple were poisoned from the use of the substance to degrease the touch screen panels that are produced for tablets (New York Times, 22 February 2011). A total of 137 cases of *n*-hexane poisoning were also mentioned in the 2011 report on Supplier Responsibility from Apple Inc. (2011).

Other uses
A number of additional uses are reported including:

- carrier or propellant in perfumes (*n*-hexane may not be used in cosmetic products in Europe. But as listed below, *n*-hexane has been registered under REACH with the use in perfumes and fragrances as well as for personal care products for private use)
- in the manufacture of veterinary medicinal ingredients
- in no*n*-mercury low temperature thermometers
- denaturing agent
- to help shape pills and tablets in the pharmaceutical industry.

The uses of hexane as registered under REACH are summarized in Table 7. As described earlier, there exists a long range of consumer uses comprising, amongst other, use in adhesives, sealants, anti-freeze and de-icing products, coatings and paints, thinners, and paint removers.

TABLE 7
USES IN EUROPE REPORTED IN THE REACH REGISTRATIONS (ECHA DISSEMINATION DATABASE, REGISTRATION DOSSIER FOR *N*-HEXANE)

	Manufacture	Formulation	Uses at industri-al sites	Professional use	Consumer use
Manufacture of substance	✔		✔		
Distribution of substance	✔	✔			
Formulation & (re)packing of substances and mixtures		✔			
Polymer processing		✔	✔	✔	
Use in a laboratory		✔	✔	✔	
Use in coatings			✔	✔	
Use in cleaning agents			✔	✔	
Blowing agents			✔	✔	
Functional fluids			✔	✔	
Mining Chemicals			✔		
Used as a fuel			✔		
Adhesives, sealants					✔
Anti-freeze and de-icing products					✔
Biocidal products (e.g. disinfectants, pest control)					✔
Coatings and paints, thinners, paint removers					✔
Fillers, putties, plasters, modelling clay					✔
Finger paints					✔
Non-metal-surface treatment products					✔
Ink and toners					✔
Leather tanning, dye, finishing, impregnation and care products					✔
Lubricants, greases, release products					✔
Perfumes, fragrances					✔
Polishes and wax blends					✔
Textile dyes, finishing and impregnating products					✔
Cosmetics, personal care products					✔

According to the ECHA web site, the classification of *n*-hexane has been notified to ECHA by a total of 2630 companies. This indicates the number of European companies that are using the substance in products that they place on the market. (The seven companies that have registered *n*-hexane are included in this number). This number does not give any information as to how many products that are on the market containing *n*-hexane.

3.3.2 Consumption of *n*-hexane in EU

As mentioned in section 2.1.3, *n*-hexane is registered under REACH in the tonnage band 10,000 to 100,000 t/year.

No further information on *n*-hexane manufacturing or consumption volumes in the EU has been identified.

3.3.3 Consumption of *n*-hexane in Denmark

Data on *n*-hexane registered in the Danish Product Register were retrieved in March 2014.

The Danish Product Register includes hazardous chemical substances and mixtures which are produced or imported for professional use in quantities of 100 kg or more per year. Hazardous substances and mixtures include:

- Substances and materials that are classified as hazardous under the Danish Ministry of the Environment's regulations, or contain 1% or more of a substance classified as hazardous to health or environment.
- Substances and mixtures assigned an occupational exposure limit in the WEA list of Limit Values for Substances and Materials.
- Mixtures that contain 1% or more of a substance that has been assigned an occupational exposure limit in the WEA list of Limit Values for Substances and Materials

The data from the publicly available part of the Danish Product Register (SPIN database) show that the main no*n*-confidential uses of *n*-hexane are as solvent, in degreasers and, in minor amounts in miscellaneous products like cleaning and washing agents, paints and varnishes, adhesives, lubricants, anti-corrosion materials, casting slips for plastic, process regulators.

The no*n*-confidential uses add up to 11.9 tonnes in 2011, while the total consumption is reported to be approximately 246 tonnes. The total has been relatively stable since 2000 except in 2002 and 2003 where the consumption increased to 942.6 and 955.8 tonnes respectively. The data in general indicate that the majority of the consumption is by a few users and the actual use of the substance is confidential.

Data from 2012 from the Product Register show a total of approximately 243 tonnes.

Solvent

In Denmark, the solvent extraction with hexane is used by at least one company, Aarhus Karlshamn (AAK), which is one of the world's leading producers of high value-added speciality vegetable fats. The company confirms that they are using hexane for extraction in the production of rapeseed and other vegetable oils. In the case of rapeseed oil, the clean seeds are steamed and crushed into thin flakes in a rolling mill. The flakes are heated up before the fat is pressed out. Any remaining oil in the cake is extracted with the help of hexane, which is recycled in a condensation process. The rapeseed oil gained by this extraction is cleaned of any residual hexane. The amount of hexane used is about 1 kg hexane per ton of seeds (raw material) (AAK, 2014). Another Danish producer of rapeseed oil has informed that they do not use solvent extraction. One of the Danish manufacturers of edible oil informs in their environmental permit that they use 70 tonnes of hexane per year (mass balance).

Hexane, primarily in the form of iso-hexane, is also used in Denmark in small amounts for solvent extraction in the production of fishmeal and fish oil. Denmark is the seventh biggest fishmeal producing country in the world and the fourth biggest producer of fish oil. There are currently three remaining fishmeal production sites along the West coast of Denmark and one on the Faroe Islands. The average Danish production of fishmeal over a 5-year period (2008-2012) was 160,000 t/year and the average production of fish oil from 2008-2012 was 60,000 t/year. The production in 2012 was unusually low (less than 80.000 t fishmeal and ca. 30.000 t fish oil) due to very low fishing quotas (Marine Ingredients Denmark, 2014). However, the solvent extraction method which is only carried out by one company in Denmark, specialised in production of marine phospholipids, is only applied when the levels of dioxin in fish is above a certain level. Only 2,000 t/y have been treated in the period 2008 – 2012 and facility has only been running for 14 days/y. The volume of hexane in the extraction facility is 60 m^3. The used hexane is condensed and recycled. Residues in the products constitute 5 – 10 ppm in fish meal and 1 ppm in fish oil. It is planned to change the production to health food products which will at the same time mean that solvent extraction must be carried out with pure *n*-hexane (Polar Omega a/s, 2014).

A technical grade of hexane is used as the reaction solvent in the production of two intermediate products for organophosphate insecticides. The production process is applied large scale at Cheminova in Denmark where most of the hexane is regenerated. During the purification process, *n*-hexane is distilled from the reaction mixture and condensed, and the remaining *n*-hexane in the process air is recovered using active carbon pellets. 60 % of the remaining *n*-hexane in the process air bind to the carbon pellets and are afterwards released, collected and re-utilised in the production; 40% is incinerated. In 2012, the amount regenerated was 720 tons of hexane saving the company more than half a million Danish kroner (Krogh and Jensen, 2014).

The amounts of *n*-hexane used for no*n*-confidential uses as solvent reported to the Danish Product Register for the period 2000 to 2011 are shown in Figure 1 (SPIN, 2013). Recycling of *n*-hexane used as an extraction solvent is most likely part of the explanation for the variation in consumption.

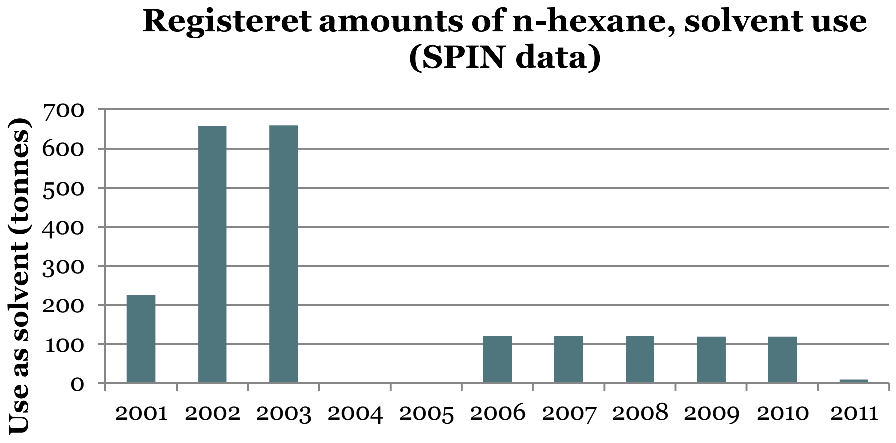

FIGURE 1

USE OF *N*-HEXANE AS SOLVENT IN DENMARK. AMOUNTS REGISTERED IN 2005 AND 2005 ARE 1 TONNE AND 0.6 TONNES, RESPECTIVELY. (DATA FROM SPIN DATABASE).

Fuels for engines

The amounts of gasoline ('motorbenzin' in Danish) with the CAS no. 86290-81-5 registered in the Danish Product Register for the period 2000 to 2011 are shown in the following figure.

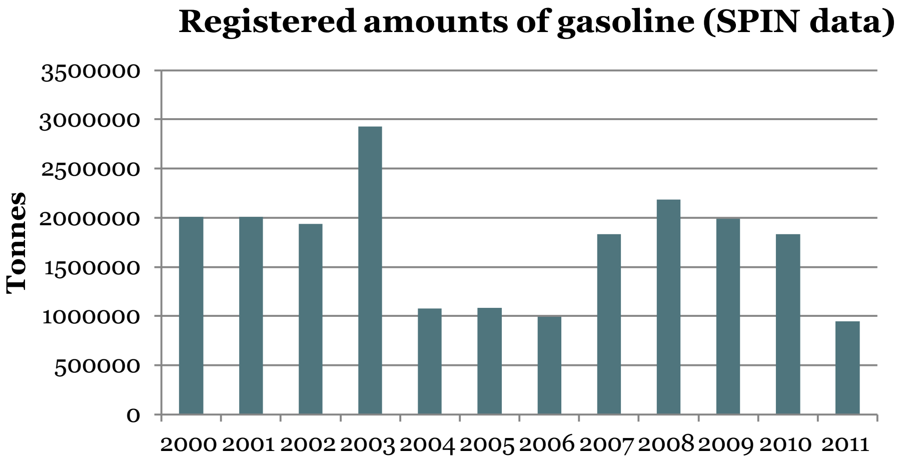

FIGURE 2
REGISTERED AMOUNTS OF GASOLINE ("MOTORBENZIN" IN DANISH), CAS NO. 86290-81-5, CONTAINING < 5 % *N*-HEXANE. (DATA FROM SPIN DATABASE)

Safety data sheets for gasoline as registered in the SPIN database typically report that the content of *n*-hexane is <5 % which corresponds to the concentration of 1–3 % as reported for unleaded gasoline.

According to information from EOF (the industry association for oil companies in Denmark – in Danish: Energi- og Olieforum), the consumption of gasoline in 2012 was a little less than 2 million m^3 (EOF, 2014). This corresponds to 2 million litres which would theoretically contain approximately 45,000 tonnes of *n*-hexane assuming a density of 0.75 and a maximum content of 3 % *n*-hexane. The gasoline consumption in 2012 is comparable to the gasoline consumption in 1986. Through the 1980's and 1990's the consumption has increased and then gradually decreased again through the 2000's.

As mentioned in the ATSDR profile (ATSDR, 1999), the dual role of *n*-hexane as a component of refined petroleum fuels and as a highly refined, specialized product for other end-uses lead to complications in making estimates of actual production levels. No formal production statistics were identified associated with the *n*-hexane contained in heating or motor fuels from companies documented as producing appreciable amounts of *n*-hexane for commercial use.

Other uses
Other uses are shown in Figure 3 and comprise applications in adhesives, paints and varnishes, as well as cleaning agents.

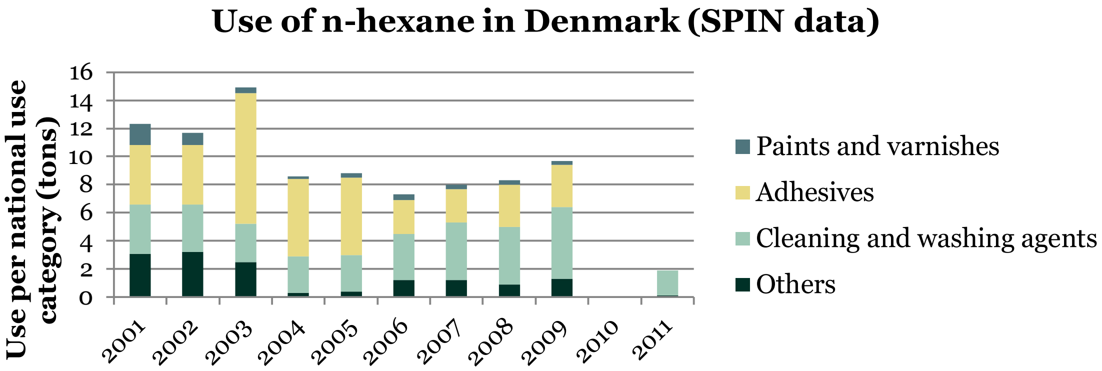

FIGURE 3
USE OF *N*-HEXANE IN DENMARK ACCORDING TO USE CATEGORY (DATA FROM SPIN DATABASE)

Consumer products
Consumer products that contain small amounts of *n*-hexane include gasoline, rubber cement, type-over correction fluids, non-mercury (low temperature) thermometers, alcohol preparations, and aerosols, and perfumes. *n*-Hexane is also a component of preparations such as paint thinners, general-purpose solvents, degreasing agents, and cleaners. (NPI, 2014).

Internet search for Danish safety data sheets for products also available for the consumer, show that e.g. glues, lubricants, water proofing sprays and spray paints, and also different car care products contain small amounts of *n*-hexane, typically below 1%, but in some cases up to 5 % and even higher. Concentrations of up to 25% are seen in different products likely to be used by both consumers and professionals such as certain multipurpose grease products used for car and machinery maintenance and repair work.

N-hexane is used also as a carrier and extraction solvent in manufacture of fragrances for other purposes than cosmetics and may therefore be found in small amounts in scented products.

3.4 Historical trends in use

3.4.1 EU

N-hexane has been extensively used in the industry for decades, alone or mixed with other solvents, and has also been utilised in many consumer products. However, observations of *n*-hexane neuropathy in workers with repeated exposure in the shoe manufacturing industry already in the 1950's followed by many case stories from both industrial settings with poor ventilation and e.g. among glue sniffers, along with the high volatility of the substance have made *n*-hexane a subject for substitution.

Many companies have over the years voluntarily, or supported by regulatory requirements or customer demands, taken initiative to substitute *n*-hexane with other less hazardous substances in both industrial settings and in consumer products.

No statistical data have been identified to illustrate the development.

3.4.2 Denmark

The total consumption of *n*-hexane in Denmark is given in Figure 4. According to the data available from the SPIN database, the yearly consumption did not change significantly, varying between 250 and 360 t/y during the period from 2005 – 2011. Available data from the Danish Product Register (SPIN) indicates that the total use of *n*-hexane in Denmark (reported as the pure *n*-hexane) has stayed almost constant the last 3 years. There was a peak of use in 2002 and 2003 which, based on the data seems to be from the use as solvent.

The data further demonstrate that the total number of products containing *n*-hexane and placed on the Danish market or imported has decreased steadily since 2001 with a peak in 2002, 2003 and 2004. Only 250 products containing *n*-hexane were registered in 2011 (data not shown).

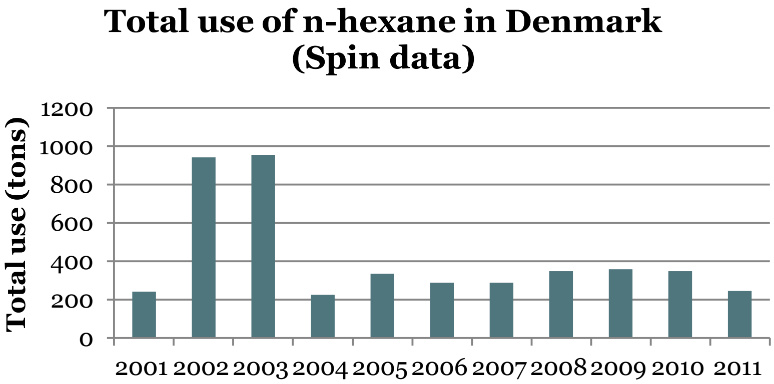

FIGURE 4
TOTAL USE OF *N*-HEXANE IN DENMARK (DATA FROM SPIN DATABASE)

3.5 Summary and conclusions

Pure *n*-hexane occurs in crude oil in small percentages and can be isolated from a number of oil fractions from the refinery process. The total registered manufacture and import of *n*-hexane in the EU are indicated to be within the tonnage band 10,000-100,000 t/y.

In the trade statistics *n*-hexane is included in broader commodity codes and therefor no specific data on import/export for *n*-hexane or for the technical blends of hexanes have been identified.

Due to its technical properties *n*-hexane is used for a wide variety of products and processes. Except for its presence in fuels for engines, the major use in Denmark is as an extraction solvent used in manufacture of vegetable oils, and as a reaction solvent in manufacture of pesticides. Hexane is recovered and recycled in both production processes.

According to information from the Product Register considerably smaller amounts are used in cleaning and washing agents, adhesives, lubricants, and corrosion inhibitors.

N-hexane is also present in a number of different consumer products such as glues, lubricants, water proofing sprays, spray paints, car care products, and certain scented products. Concentrations are typically below 1 % but higher concentrations up to ca. 25 % are seen in products for maintenance and repair of cars and machinery which may also be used by consumers.

N-Hexane has been the focus for substitution for many decades, but no statistical data have been identified to illustrate the development.

4. Waste management

4.1 Waste from manufacture and industrial use of *n*-hexane

n-Hexane is not manufactured in Denmark and therefore no waste from manufacturing of the substance is generated.

The major use of *n*-hexane in Denmark is as a solvent in the production of vegetable oil, fish oil, fishmeal and organophosphate insecticides. In these production processes *n*-hexane is recovered or incinerated with process air if not possible to recover. Some *n*-hexane is released to air, e.g. from the production of vegetable oil, according to the environmental approval for a new facility for fractionation of oil using cooled down hexane (Miljøcenter Århus, 2008) and some n-hexane mixed with other substances is also disposed of as waste.

Hexane is highly flammable; therefore *n*-hexane or mixtures with significant amounts of *n*-hexane are classified as hazardous waste.

In Denmark, waste containing hexane from manufacturing processes will typically be collected and treated as organic chemical waste which is incinerated (either o*n*-site or by Nord) and the substance is completely destroyed. However, it is expected that hexane will evaporate during production or use of the product and therefore only small amounts will end up in the waste stream.

4.2 Waste products from the use of *n*-hexane in mixtures and articles

Due to its classification (section 2.1.2) and in accordance with the Danish Statutory order on waste (BEK no. 1309 of 18/12/2012) Annex 4, products and mixtures containing *n*-hexane must be disposed of as hazardous waste if they contain more than 0.5% *n*-hexane.

In Denmark, waste containing hexane will typically be collected and treated as organic chemical waste, in which case the waste is incinerated and the substance is completely destroyed.

Due to the volatile properties of the substance, *n*-hexane will most likely have evaporated from any articles containing residues of the substance.

4.3 Release of *n*-hexane from waste disposal

No studies regarding release of the substance from disposal of waste containing the substance have been identified. Release from incineration is not relevant.

4.4 Summary and conclusions

N-Hexane is a highly volatile chemical which will tend to evaporate during production and use. It is therefore not likely to end up in the waste streams in any considerable amounts.

5. Environmental effects and exposure

5.1 Environmental fate

5.1.1 Degradation

Abiotic degradation
Photodegradation is not considered a relevant degradation pathway, since *n*-hexane does not absorb ultraviolet light. The dominant atmospheric removal mechanism for *n*-hexane is generally regarded to be decomposition by hydroxyl radicals. Calculations assuming typical hydroxyl radical concentrations have suggested a half-life of approximately 2.9 days (ATSDR 1999).

n-Hexane can react with nitrogen oxides to produce ozone precursors under controlled laboratory conditions, however, the smog-producing potential of *n*-hexane is evaluated to be very low compared to that of other alkanes or chlorinated VOCs.

Hydrolysis is not a relevant degradation mechanism as *n*-hexane, similar to other alkanes, is resistant to hydrolysis (ATSDR 1999).

ECHA's registration data for *n*-hexane do not comprise data on abiotic degradation.

Biodegradation
With respect to biodegradation, the attention is generally on complex mixtures of hydrocarbons, which will be present at, e.g., oil spills. In such situations the heavier fractions or less volatile (usually C10 or longer chain alkanes, aromatics, and/or polycyclic aromatics) are of greater concern than the lighter constituents.

A read-across study on biodegradation of naphtha (mainly consisting of C4 - C11 alkanes) is available from ECHAs registration data on *n*-hexane. 98 % of the test substance was degraded at the end of 28 days, and 83% was degraded at the end of the 10 -day window. Therefore, *n*-hexane is evaluated to be readily biodegradable and does not inhibit biodegradation. The conclusion is supported by a QSAR study on hexane.

Generally, unless *n*-hexane is buried in deeper layers of a soil or sediment, volatilization is assumed to occur at a much higher rate than any biotic or abiotic degradation processes.
In deeper soil layers or sediments, *n*-hexane may be fairly persistent. This is due to slow chemical hydrolysis and limited potential for biodegradation under anoxic and/or nutrient-poor (N, P) conditions.

5.1.2 Distribution

The physical properties of *n*-hexane determine its transport and partitioning in the environment.

The dominant transport process from water is volatilization. The US EPA estimated half-lives for *n*-hexane in water with any degree of turbulent mixing (e.g. rivers) at 3 hours, and no longer than 6.8 days for standing bodies of water (e.g. small ponds) (ATSDR 1999).

In soil, the dominant transport mechanism for *n*-hexane close to the surface can likewise be expected to be volatilization considering the low water solubility (0.0098 g/L) and high vapour pressure (10 kPa), even though binding to the soil organic matter might be significant in organic soils. No experimental information focusing directly on *n*-hexane transport in soil is available (ATSDR 1999).
The low density of the substance (0.66 g/mL) suggests a low potential for leaching into deeper soil layers, since *n*-hexane would tend to float on top of the water-saturated zone (also called light non-aqueous phase liquid, LNAPL).

Experimental data on bioaccumulation are not available. Based on the log octanol/water partition coefficient (log P = 3.3 - 4) and the estimated log sorption coefficient (log K_{OC} = 2.9 – 3.6, ATSDR 1999), *n*-hexane is not concentrated to a large extent in biota. A calculated bioconcentration factor (BCF) of 453 for a fathead minnow suggests a relatively low potential for *n*-hexane to bioconcentrate or bioaccumulate in trophic food chains (ATSDR 1999). The calculated BCF is also far below the REACH PBT bioaccumulation criterion of 2000 for aquatic species.

5.2 Environmental hazard

5.2.1 Classification

n-Hexane is classified as toxic to aquatic life with long lasting effects (cat. 2).

TABLE 8
ENVIRONMENTAL CLASSIFICATION OF *N*-HEXANE ACOORDING TO ANNEX VI OF REGULATION (EC) NO 1272/2008 (CLP REGULATION).

Index No	International chemical identification	CAS No	Classification	
			Hazard Class and Category Code(s)	Hazard statement Code(s)
601-037-00-0	hexane	110-54-3	Aquatic Chronic 2	H411

5.2.2 Environmental effects

Aquatic toxicity
A number of ecotoxicity tests are available from the US EPA ECOTOX database (2014).
The lowest effect concentrations for each organism group are presented in Table 9.

14 acute fish studies are listed in the ECOTOX database covering the freshwater species *Oryzias latipes, Pimephales promelas, Pleuronectes ferrugineus, Oreochromis mossambicus,* and *Leuciscus idus,* as well as a single saltwater species, *Oncorhynchus kisutch*. The most and least sensitive of the tested species appear to be *Pimephales promelas* with an LC50 of 2.5 mg/L, and *Oryzias latipes* with an LC50 of > 10,000 mg/L, respectively.

For aquatic invertebrates, studies on both fresh- and saltwater are presented, covering 7 species (*Artemia salina, Cyclops viridis, Homarus americanus, Daphnia magna, Tetrahymena pyriformis, Brachionus calyciflorus, Brachionus plicatilis*). The effect concentration range for the saltwater species was 1.5 to 154 mg/L, while the EC50 for freshwater species ranged from 3.8 to > 1000 mg/L.

EC50 values are available for six species/genera of alga (*Anabaena* sp., *Chlamydomonas angulosa, Chlorella* sp., *Nostoc* sp., *Macrocystis pyrifera, Skeletonema costatum*). Two marine organism studies (from 1964 and 1977) reported photosynthesis effects on *Macrocystis pyrifera* (large brown algae) and *Skeletonema costatum* (a diatom) at 10 mg/L and 0.3 mg/L, respectively. The latter study was a field study and is therefore not comparable with the other studies. The six remaining studies report growth inhibition or physiological effects at EC50 ranging from 8.1 – 52,800 mg/L.

Further, aquatic tests were made with snails; *Melanoides tuberculata,* LC50 = 1,900 mg/L, and *Crassostrea giga,* which showed abnormal development effects in the concentration range 10 – 10,000 mg/L.

With respect to sediment dwelling organisms, tests with a worm (*Branchiura sowerbyi*) and an insect species (*Chironomidae*) indicate that these animals are less susceptible (effect concentration ≥ 595 mg/L).

Thus, the lowest effect concentration of 1.5 mg/L has been determined in a test with the small crustacean *Artemia salina*. However, for all organism groups the effect concentrations range over several orders of magnitude, which is supposedly related to methodological issues and not to toxicity mechanism of *n*-hexane.

In most cases, the effect concentrations listed in the database exceed the water solubility of *n*-hexane, which is about 10 mg/L. It is usually not reported, if a solvent is used to achieve the stated test concentrations. Likewise, set-up of the system (static system or flow-through) influences the study results. All studies on aquatic toxicity listed in the ECOTOX database were static studies apart from the freshwater fish study on *Pimephales promelas*. In static test systems, part of the test material is likely to evaporate before the end of the exposure period, rendering the actual exposure lower than the nominal concentration.

Actual exposure concentrations are therefore unknown. Also possible toxicity interactions of *n*-hexane and a possible solvent are not known. In conclusion, the reported effect concentrations should be interpreted very cautiously.

TABLE 9
OVERVIEW OF DATA ON TOXICITY OF *N*-HEXANE TO AQUATIC ORGANISMS IN LABORATORY STUDIES (DATA FROM THE US EPA ECOTOX DATABASE)

Group	Species	Study type*	Endpoint*	Value (mg/L)
Fish, freshwater	*Pimephales promelas*	96 h, flow-through	LC 50	2.5
Fish, marine	*Oncorhynchus kisutch*	96 h, static	NR	100
Invertebrates, freshwater	*Daphnia magna*	48 h, static	EC50	3.8
Invertebrates, marine	*Artemia salina*	24 h, solvent; 2-Propanone, static	EC50	1,5
Algae, freshwater	*Chlamydomonas angulosa*	3 h, static	EC50 on photo-synthesis	8.1
Algae, marine	*Macrocystis pyrifera*	48 - 96 h, NR	EC50 on photo-synthesis	10

* NR – not reported.

Terrestrial toxicity

No laboratory toxicity tests for terrestrial organisms were available.

5.3 Environmental exposure

5.3.1 Sources of release

n-Hexane is a component of refined petroleum products, therefore there is considerable potential for releases to environmental media through the use of fuels for heating or transportation.
Its physical properties as a light alkane make it most suitable for use in gasoline, while it can also be a minor constituent (less than 1% by weight) of other petroleum products. For modern gasoline mixtures, the total percentage by weight of the *n*-hexane component is approximately 3% (ATSDR 1999).

Gasoline use can result in a variety of atmospheric emissions of *n*-hexane due to evaporation during refuelling and storage, and exhaust releases in case of incomplete combustion. In its review, ATDSR (1999) evaluates the largest release of hexane to be to air due to the volatility of the substance.

Releases to water may happen from a number of sources including industrial discharges, effluents from municipal waste-treatment plants, and nonpoint-source runoff from roads and other surfaces. *n*-Hexane can be released to soil or sediments from spills, during the landfilling of sludge and other wastes generated from industrial processes, as well as municipal sewage treatment (ATSDR 1999).

Industrial releases of *n*-hexane in Europe have been assigned to the following environmental release categories according to ECHA registration data (January 2014):

ERC 1: Manufacture of substances
ERC 2: Formulation of preparations
ERC 3: Formulation in materials
ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles
ERC 5: Industrial use resulting in inclusion into or onto a matrix
ERC 6d: Industrial use of process regulators for polymerisation processes in production of resins, rubbers, polymers

Consumer products that contain small amounts of *n*-hexane are expected primarily to result in releases to air.

5.3.2 Monitoring data

n-Hexane is not included in the Danish environmental surveillance programme, NOVANA. However, urban background concentrations of the some ozone precursors have been measured in Copenhagen since 2009. The annual average concentration of *n*-hexane was 0.16 µg/m³ and the 90% percentile was 0.27 µg/m³ in 2012. Figures from previous years are given in Table 10.

TABLE 10
ANNUAL CONCENTRATIONS BASED ON DAILY AVERAGES IN URBAN BACKGROUND MEASURED ON H.C. ØRSTEDS INSTITUTE IN COPENHAGEN.

Number of samples	Concentration in air (µg/m³)	90% percentile	Year	Reference
200	0.15	0.31	2009	Ellermann et al. 2010
216	0.19	0.36	2010	Ellermann et al. 2011
307	0.19	0.33	2011	Ellermann et al. 2012
246	0.16	0.27	2012	Ellermann et al. 2013

5.4 Environmental impact

Reviews containing environmental impact assessments are currently not available and it is beyond the scope of this survey to provide an environmental risk assessment of hexane. The environmental properties of hexane are summarised in section 5.5.

The Danish soil quality criterion for volatile hydrocarbons (C_6 –C_{10}) from oil or gasoline products is 25 mg/kg. The groundwater quality criterion is 9 µg/litre for the sum of hydrocarbons (C_6 – C_{35}). (Danish EPA, 2014). The guideline value (B-value) for industrial air pollution is 0.4 mg/m^3 (Danish EPA, 2002). National emission ceilings for certain atmospheric pollutants and certain processes are also relevant in relation to *n*-hexane.

5.5 Summary and conclusions

n-Hexane is classified as toxic to aquatic life with long lasting effects (cat. 2).

n-Hexane has a low water solubility (0.0098 g/L) and high vapour pressure (10 kPa). Atmospheric removal through reaction hydroxyl radicals might therefore be the most important abiotic degradation process. By means of a read-across study on biodegradation of naphtha (mainly consisting of C4 - C11 alkanes), hexane was evaluated to be readily biodegradable.

Experimental data on bioaccumulation are not available. However, based on the log P (= log K_{OW} = 3.3 - 4), an estimated log K_{OC} of 2.9 – 3.6, and an estimated BCF of 453, *n*-hexane is not expected to bioconcentrate or bioaccumulate significantly in trophic food chains.

Acute aquatic toxicity data are available from the US EPA ECOTOX database, while there is a general lack of chronic and terrestrial data. The lowest acute toxic effect concentration of *n*-hexane was determined at 1.5 mg/L in a test with the small crustacean *Artemia salina*. However, for all aquatic organisms the reported effect concentrations cover several orders of magnitude, which is most likely related to methodological problems and requires very careful interpretation of the listed effect concentrations.

There is considerable potential for releases of *n*-hexane to environmental media through the use of fuels for heating or transportation. Atmospheric emissions of *n*-hexane are due to evaporation during processing of the substance or due to incomplete combustion of fuels. Other releases include industrial discharges, effluents from municipal waste-treatment plants, and nonpoint-source runoff, spills, sludge and other waste deposition.

Quantitative data on emissions to environmental compartments in Denmark or Europe could not be identified. Consumer products that contain small amounts of *n*-hexane are expected primarily to result in releases to air.

In Denmark, urban background concentrations of *n*-hexane have been measured since 2009 in Copenhagen, because of the substance's identification as an ozone precursor. The measurements have been relatively stable with an average of 0.15 to 0.19 µg/m^3.

6. Human health effects and exposure

6.1 Human health hazard

6.1.1 Classification

n-Hexane is subject to harmonised classification as a toxic to reproduction (cat. 2), harmful if swallowed (cat. 1), toxic to organs through repeated or single exposure (cat. 2 and cat. 3, respectively), and as a skin irritant (cat. 2) (Table 11).

TABLE 11
HARMONISED CLASSIFICATION ACOORDING TO ANNEX VI OF REGULATION (EC) NO 1272/2008 (CLP REGULATION)

Index No	International chemical identification	CAS No	Classification	
			Hazard Class and Category Code(s)	Hazard statement Code(s)
601-037-00-0	hexane	110-54-3	Repr. 2 Asp. Tox. 1 STOT RE 2 * Skin Irrit. 2 STOT SE 3	H361f ***: H304 H373 ** H315 H336

* Minimum classification for a category.

** Hazard statement not specifying the route of exposure as the necessary information is not available.

*** ‘Suspected of damaging fertility or the unborn child’. According to the criteria, the general hazard statement can be replaced by the hazard statement indicating only the property of concern, where either fertility or developmental effects are proven to be not relevant.

6.1.2 Toxicokinetics

Toxicokinetic data are based on the toxicological review on hexane from the US EPA (2005).

Oral exposure studies evaluating absorption of *n*-hexane in humans or laboratory animals are not available. However, absorption following oral exposure can be determined by identification of *n*-hexane and its metabolites in expired air, serum, and urine. Several studies indicating oral absorption are available.

Evidence of absorption upon inhalation exposure in humans is also limited, but has been investigated in studies with exposed workers. Absorption rates were estimated at 17 – 24 %.

Several inhalation studies in humans and animals demonstrate the distribution of *n*-hexane. The following partition coefficient values were calculated: olive oil: air, 146; blood: air, 0.80; and 1.0, 2.8, 5.0, 5.0, 3.0, 5.2, and 104 for lung, heart, muscle, brain, kidney, liver, and fat: air, respectively.

These values correspond to those values reported in other studies and clearly present *n*-hexane affinity for fatty tissues. Blood levels of *n*-hexane have shown to decrease rapidly to approximately half the steady state exposure values within the first 10 minutes and reached steady state levels by 100 minutes. The average half-life for *n*-hexane in blood was 1.5–2 hours.

No studies investigating the distribution of *n*-hexane following oral exposure in humans or laboratory animals are available.

In the liver, *n*-hexane is metabolized to various metabolites, which are then distributed in the blood to various organs and tissues, including the liver, kidney, and brain. The primary metabolite, 2,5-hexanedione, is believed to be the major toxic metabolite produced in humans. In rats, the primary metabolite following inhalation exposure was 2-hexanol, followed by 4,5-dihydroxy-2-hexanone.

Several human inhalation studies have provided evidence for the elimination of *n*-hexane and metabolites following occupational and voluntary exposures to *n*-hexane. The main route is via urine, while alveolar excretion of *n*-hexane has been shown to account for 10% of the total uptake following inhalation exposure. Occupational exposure studies have also shown that urinary concentrations of 2,5-hexanedione may build up during the course of a workweek. Therefore, urinary levels may not consistently reflect the ambient *n*-hexane exposure concentrations.

6.1.3 Acute and chronic effects

The US EPA (2005) has compiled a large number of epidemiological studies investigating the health effects of *n*-hexane in occupational environments.

In many studies, inhalation exposure to hexane has been associated with incidences of headache, hearing deficit, dysesthesia in limbs, reduced sensation, dizziness and sleepiness, and muscle weakness. These symptoms are consistent with neurophysiological findings in exposed individuals, hereunder increased numbers of polyneuropathy cases and decreased nerve conduction velocity.

The relationship between the occurrence of intracranial tumours among employees at a petrochemical plant and inhalation exposure to *n*-hexane and a number of other chemical compounds was studied. No relationship was found between exposure to *n*-hexane and the occurrence of intracranial tumours (US EPA, 2005).

Neurophysiological effects could also be determined in an occupational study with shoe workers several months after exposure was stopped/reduced to trace amounts. Still, the previously exposed workers showed increased signs of polyneuropathy compared to unexposed workers. Another study with cases of polyneuropathy at a ball-manufacturing plant in Taiwan observed recovery of neurological symptoms in a follow-up at the factory 2 years after the ventilation system had been changed and solvent operations including hexane handling were enclosed. Vision changes in relation to *n*-hexane exposure have also been reported in several studies, amongst other impaired colour vision and maculopathy.

A few studies investigated the effects of *n*-hexane on the immune system with contradicting conclusions. A significant inverse correlation also was found between the immunoglobulin levels and the 2,5-hexanedione concentrations in the exposed group, while no differences were detected in white blood cell counts, natural killer cytotoxic activity and serum levels of interleuki*n*-2 between exposed and unexposed subjects (US EPA, 2005).

Consumers

Consumer exposure to *n*-hexane is not expected to give rise to major concern. Most consumer products contain relatively low levels of *n*-hexane and are not used frequently. Some product types such as adhesives, sealants and grease or special products used for car or machinery repair may contain higher concentrations. These may result in high short-term exposures, but are expected to be used infrequently.

Scented toys may release *n*-hexane as demonstrated by a Danish consumer survey. Although the specific product is no longer on the market there is a possibility that children may be exposed to small amounts of *n*-hexane over a shorter period of time from scented products like this. As *n*-hexane has low acute toxicity, no significant effects are expected this exposure.

6.1.4 Reproductive toxicity

A number of animal studies investigated reproductive and developmental effects of hexane exposure. Various stages of atrophy of the testicular tissue (incidence and severity of effect not reported by the study authors) following oral administration of hexane metabolites and a high dose of *n*-hexane (3980 mg/kg-day) was reported in rats. An inhalation study with rats also observed testicular lesion as an effect of repeated hexane exposure, however, the lesions were partly reversible. Sperm morphology and reproductive index were not affected in male mice following exposure to hexane vapour. Several inhalation studies concluded that *n*-hexane has little or no effect on reproduction and development of rats or mice (US EPA, 2005).

An oral exposure study with mice dams reported no reproductive, developmental, or teratological effects of *n*-hexane in mice dosed with *n*-hexane by injections up to 2200 mg/kg/day. First at significantly increased concentrations (7920 and 9900 mg/kg/day), detrimental effects were observed. Therefore the authors suggested that *n*-hexane is not teratogenic at concentrations associated with overt maternal toxicity. Spermatoxic tests showed no change in parameters in rats orally exposed to *n*-hexane (US EPA, 2005). A selection of study results on reproductive and developmental effects is presented in Table 12.

TABLE 12
EFFECT CONCENTRATONS FOR EFFECTS ON REPRODUCTION (DATA FROM US EPA, 2005).

Organism	Exposure conditions	Effect	Effect level	Concentration
Mice	Oral, daily dose, gestation day 6-15	Reproductive, developmental, or teratological effects	NOAEL	2200 mg/kg bw
Mice	Oral, daily dose, gestation day 6-15	Dam mortality	LOAEL	9900 mg/kg bw
Mice	Oral, daily dose, gestation day 6-15	Decreased fetal birth weight	LOAEL	7920 mg/kg bw
Rats	Oral, daily dose, 5 consecutive days	Spermatoxic effects (head counts, sperm velocity, sperm morphology, and the histopathology)	NOAEL	10.000 mg/kg bw
Rats	Inhalation, 20 h/day, gestation day 6-19	Developmental effects	NOAEL	200 ppm
Rats	Inhalation, 6 h/day, gestation day 8-16	Decreased birth weight of pups	NOAEL	1000 ppm

Organism	Exposure conditions	Effect	Effect level	Concentration
Mice	Inhalation, 20 h/day, gestation day 6-17	Decreased birth weight of female pups	LOAEL	5000 ppm
Mice	Oral, 20h/day, 5 consecutive days	Effects on sperm morphology	NOAEL	5000 ppm

6.1.5 Mode of action

Ultrastructural studies indicate that nervous system toxicity induced by *n*-hexane may be the result of a sequence of events leading to degeneration of the axons. This sequence has been investigated in after after repeated dose exposure and is described as follows (US EPA, 2005): "Sciatic, tibial, and plantar nerves were investigated by light microscopy. The authors described focal condensation of neurofilaments, mitochondria, and smooth endoplasmic reticulum with increase in the number of neurofilaments. The earliest pathological indicator of peripheral nerve axonal degeneration was axonal swelling in the distal nonterminal region of the large myelinated fibers. These axonal swellings appeared first proximal to the nodes of Ranvier and ascended the nerve with further exposure. Paranodal swelling was accompanied by shrinkage and corrugation of the adjacent distal internode. Paranodal myelin sheaths split and retracted leaving giant axonal swellings near the nodes of Ranvier. The study authors suggested that Schwann cells may become associated with these denuded regions and remyelinate short segments. Remyelinated segments then mark the position of the axonal swellings that were resolved without fibre breakdown or total internodal demyelination."

Several studies suggest that the metabolite, 2,5-hexanedione, is the primary toxic agent by which *n*-hexane brings about neurotoxicological effects. 2,5-Hexanedione has been shown to have approximately 38 times the neurotoxic potency of *n*-hexane (on an equimolar basis). The onset of distal axonal degeneration following 2,5-hexanedione administration has been observed in rats, mice, cats, and birds (US EPA, 2005). The mode of action is suggested to imply the binding of 2,5-hexanedione to proteins, forming pyrrole adducts then undergoing oxidation, leading to protein cross-linking. For example, 2,5-hexanedione was shown to cross-link neurofilaments proteins of spinal cord when administered to male rats for 180 days in drinking at a concentration of 5000 mg/L.

A substantial body of physiological and biochemical studies *in vitro* and *in vivo* indicate that cross-linking of neurofilamentous proteins takes place as a result of exposure to 2,5-hexanedione. A consistent observation made between species, between adult and immature members of the same species, and within individual humans and animals, was that longer axons in the peripheral nervous system and central nervous system were more vulnerable to the toxic effects of *n*-hexane and its metabolites than shorter axons. The axonal swellings that initially occurred proximal to nodes of Ranvier in the most distal internodes of the longest axons were filled with disorganized masses of neurofilaments (US EPA, 2005).

6.1.6 No effect-levels

Occupational exposure limit values

Occupational exposure limit values for *n*-hexane for selected European countries are presented in Table 13.

TABLE 13
OCCUPATIONAL EXPOSURE LIMIT VALUES FOR *N*-HEXANE FOR SELECTED COUNTRIES (GESTIS DATABASE)

	Limit value 8-hours		Limit value short term	
	ppm	mg/m³	ppm	mg/m³
Belgium	20	72	-	-
Denmark	20	72	2 x limit value (15 min)	2 x limit value (15 min)
European Union[1]	20	72	-	-
France	20	72	-	-
Germany	50	180	400	720
Sweden	25	90	50	180
The Netherlands	20	72	-	144
United Kingdom	20	72	-	-

[1] Indicative OEL (see Chapter 2)

Denmark has adopted the EU indicative occupational exposure limit values. However, as demonstrated in Table 13, not all EU countries have chosen to adopt the EU indicative (non-binding) occupational exposure limit for N-hexane.

Derived no-effect levels and limit values

Derived no-effect levels for *n*-hexane registered under REACH are shown in Table 14. The DNELs are from a joint submission and are established by the registrant for systemic effects from long term exposure in the different exposed populations by inhalation or the dermal route, and for the general population also from the dermal route. ECHAs dissemination website does not include the full justification behind the values. DNELs are used for risk assessment of specific exposure situations.

TABLE 14
DERIVED NO-EFFECT LEVELS (DNELS) FOR MTBE (ECHA, 2013A)

Population / - route	Exposure	Value	Dose descriptor / Assessment factor	Sensitive end-point
Workers - inhalation	Long term exposure - systemic	75 mg/m³	LOAEC / 3	Neurotoxicity
Workers - dermal	Long term exposure - systemic	11 mg/kg bw/day	NOAEL / 3	Neurotoxicity
General population - inhalation	Long term exposure - systemic	16 mg/m3	NOAEL / 5	Neurotoxicity
General population - dermal	Long term exposure - systemic	5.3 mg/kg bw/day	NOAEL / 5	Neurotoxicity
General population - oral	Long term exposure - systemic	4 mg/kg bw/day	NOAEL / 5	Neurotoxicity

6.2 Human exposure

6.2.1 Direct exposure

Consumers

Consumers are exposed primarily by inhalation but also dermal contact with different consumer products containing *n*-hexane. Examples are adhesives, sealants, spray paints, silicon removers, and water proofing sprays.

Maximum concentrations of *n*-hexane for different types of products according and publically available information as summarised by Environment Canada are shown in Table 15 together with use conditions based on consumer product exposure model parameters (frequency of use and exposure duration) from ConsExpo (Environment Canada, 2009).

TABLE 15
CONSUMER PRODUCTS CONTAINING *N*-HEXANE AND USE CONDITIONS BASED ON EXPOSURE MODEL PARAMETERS (ENVIRONMENT CANADA, 2009)

Consumer product	Maximum conc. of *n*-hexane in %	Frequency of use (events/year)	Exposure duration (min)
Construction Adhesive	30	2	240
Gasket Sealant	25	3	45
Spray Paint	20	2	20
Weatherstrip Adhesive	15	N/A	N/A
Spray Adhesive	30	12	240
Weatherstrip Cement	8.9	7	16

The products listed in the table are primarily for professional use but may be used by consumers. Most products specifically targeting the consumer market have typically lower concentrations of *n*-hexane.

As part of the Danish EPA surveys on chemicals in consumer products, *n*-hexane has been found in very low concentrations in cuddly toys for children in a consumer survey investigating the content of sensitising substances as well as releases of certain volatile substances including *n*-hexane in scented toys intended for children at the age of 0 to 10 years. Measurements of the emission from a vanilla scented cuddly toy showed a release of *n*-hexane of 16 µg/m^3 (Glensvig and Pors, 2006).

In another consumer survey from the Danish EPA investigating the release of chemical substances from electric and electronic products, *n*-hexane was emitted from an electrical panel at concentrations of 7.2 µg/unit/hour after 7 hours and <2 µg/unit/hour after 9 days (Mortensen, 2005).

No further data describing direct exposure to Danish consumers have been identified.

Occupational exposure

Occupational exposure to *n*-hexane and mixtures containing *n*-hexane include groups such as refinery workers, shoe and footwear assembly workers, laboratory technicians, workers involved in extraction of fish meal, fish oil and vegetable oils, workers involved in manufacture of pharmaceuticals and pesticides, laboratory technicians, workers in textile and furniture manufacturing, workers operating or repairing typesetting and printing machinery, workers in the electronics industry, construction workers, carpet layers, carpenters, auto mechanics and gas station employees, workers in plants manufacturing tires or inner tubes, and workers in air transport and air freight operations.

Due to the high volatility and flammability of *n*-hexane containment of the substance in industrial settings is important. The odour threshold is reported to be approximately 60 ppm / 210 mg/m^3 (IPCS, 1991) which is higher than the Danish occupational exposure limit of 20 ppm / 72 mg m^3.

In Denmark, the major industrial uses involve recovering of the *n*-hexane and occupational exposure is expected to be limited.

As *n*-hexane is a component in jet fuel, measurements of this substance among other VOCs were made in Copenhagen Airport at Gate B4 in 2010 in order to monitor the occupational exposures of workers in this area. The average concentration measured in the period 20.10.2010 to 17.11.2010 was 0.21 µg/m3 compared to the average urban background of ca. 0.20 at H.C. Ørstedsvej in Copenhagen (Ellermann *et al.*, 2011).

No specific information on more recent occupational *n*-hexane exposures in Denmark have been identified based on literature search and contact with the Danish Working Environment Authority.

6.2.2 Indirect exposure

Air

As mentioned in section 5.3.2, the average annual urban background concentrations of *n*-hexane in 2012 measured in Copenhagen was 0.16 µg/m^3 and between 0.16 and 0.19 µg/m^3 in the period 2009 to 2012.

No other individual measurements of *n*-hexane in Denmark have been identified. *n*-Hexane may, however also be included in measurements of total concentrations of volatile organic compounds.

Soil

n-Hexane has relatively low absorptivity to soil or sediment and releases to the environment are expected primarily to end up in the air and water compartments. If spilled on the ground, the substance will evaporate or leach into the groundwater. Exposure via soil is therefore not considered relevant.

Drinking water

No measurements of *n*-hexane in drinking water in Denmark have been identified. Drinking water is not expected to be a relevant source of *n*-hexane exposure.

Food

Residues of *n*-hexane used from solvent extraction may be found in vegetable oils and fish oils for consumption, typically at levels of approximately 1 ppm.

Environment Canada (2009) has estimated upper-bounding daily intake of –*n*-hexane from foods based on the level of residual *n*-hexane typically found in refined vegetable oils (0.8 ppm). The estimates are shown in Table 16.

TABLE 16
UPPER-BOUNDING DAILY INTAKE OF –*N*-HEXANE FROM FOODS BASED ON THE LEVEL OF RESIDUAL *N*-HEXANE TYPICALLY FOUND IN REFINED VEGETABLE OILS (ENVIRONMENT CANADA, 2009)

Age group	**Percentile**	**Intakes of vegetable fats and oils from all food sources (g/kg-bw/day) 1**	Daily intake of *n*-hexane **(mg/kg-bw/day)**
6-8 years	50%	0.73	0.58
	90%	1.58	1.26
	95%	1.81	1.45
19-30 years	50%	0.28	0.22
	90%	0.71	0.57
	95%	0.87	0.70

No measurements of *n*-hexane in Danish food have been identified.

Indoor climate

n-Hexane is often measured as part of the total concentration of VOCs in the indoor climate. No measurements of *n*-hexane

Review of Canadian studies by Environment Canada (2009) showed that the highest concentration of *n*-hexane in indoor air in a critical data set (Canadian studies in the 1990s-2000s) was 138 µg/m3 from a study conducted in Windsor, Ontario in 2006. This study was performed over a two year period in 2005 and 2006, and the mean concentration of *n*-hexane ranged from 2.3 to 8.0 µg/m3. In other studies, the mean concentration of *n*-hexane ranged from 1.2 to 8.0 mg/m3.

No Danish indoor climate measurements of *n*-hexane have been identified.

6.3 Bio-monitoring data

Industrial hygiene surveys of occupationally exposed workers have shown good correlations between the extent of occupational exposure to *n*-hexane and the concentration of the metabolite, 2,5-hexanedione in the urine. 2,5-Hexanedione is also the substance responsible for the effects on the peripheral nervous system. To protect against the onset of subclinical and clinical neuropathological symptoms of *n*-hexane exposure, ACGIH has proposed a BEI (Biological exposure index) of 0.4 mg/L as an acceptable concentration of 2,5-hexanedione in urine at the end of shift on the last day of a workweek (EPA, 2005).

n-Hexane can also be measured in exhaled air. However, the short half-life of the substance means that the concentration in exhaled air will only reflect the exposure situation immediately before the measurement.

No results from biomonitoring of *n*-hexane in Denmark have been identified.

6.4 Human health impact

Workers

No information on exposure levels in the Danish work environment was available. A search in the statistical data on industrial injuries available from the homepage of the National Board of Industrial Injuries[5] did not provide any hits for neither '*n*-hexane' nor 'peripheral neuropathy'.

There is no indication that the existing risk reduction measures are not sufficient.

Humans exposed via the environment

The principal source of exposure to *n*-hexane is expected to be through inhalation of ambient and indoor air. The DNEL for systemic effects from long term inhalation exposure for the general public was 16 mg/m^3 in the REACH registration dossier. When this DNEL is compared with the sum of the average levels in ambient air in Copenhagen (1.6 – 1.9 µg/m^3) and the average concentration levels for indoor climate measured in Canadian studies (1.2 to 8.0 mg/m^3) no major concern is identified.

6.5 Summary and conclusions

n-Hexane is absorbed rapidly through the lungs in experimental animals and is widely distributed in the body with an affinity for tissues high in lipid content. Particularly high levels have been found in peripheral nerves. Dermal absorption is limited, but may be enhanced by other solvents. In humans, *n*-hexane is absorbed more slowly via the lung and very slowly through the skin.

n-Hexane has low acute toxicity. The critical effects of chronic exposure to *n*-hexane appear to be testicular toxicity and neurotoxicity both to the central and peripheral nervous systems. Peripheral neuropathy is well described after industrial exposure to *n*-hexane, particularly in shoemakers. The testicular effects observed in rats have not been well documented in humans. Hexane is also irritating to skin.

2,5-Hexanedione is the main metabolite found in humans exposed to *n*-hexane and the substance suspected of being responsible for the neurotoxicity of the substance and toxic effects in the testes. The first symptoms of neurotoxicity are usually sensory and consist of tingling, numbness, burning, or prickling sensations in the feet or toes followed by progressive muscle weakness first in the lower and then upper extremities. Distal nerves are more commonly affected.

There is a large number of studies linking occupational exposure to *n*-hexane to the incidence of peripheral neuropathy in humans particularly among shoemakers. However, few of these report air concentrations, and where exposures are quoted, it is not clear whether they refer to *n*-hexane or to commercial hexane. Also workers were exposed to mixtures of volatile solvents and the proportions of *n*-hexane are not reported.

Denmark has adopted the EU indicative occupational exposure limit value of 20 ppm or 72 mg/m^3. No information on exposure levels relevant for Danish industrial uses is available. However, the major applications of the substance as an extraction or reaction solvent take place in closed systems and are less likely to result in significant workplace exposures.

Very limited data are available regarding consumer exposure in Denmark. As *n*-hexane is present in several spray products and taking the volatility of the substance into account, consumers may be exposed to relatively high concentrations on a short term basis. However, in general the consumers are not expected to be exposed on frequent basis or for long periods of time, and are thereby not expected to be at risk in relation to the long-term effects of *n*-hexane.

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[5] http://www.ask.dk/da/Statistik/Erhvervssygdomme-fordelt-pAa-diagnoser/2011.aspx

Indirect exposure can occur through air, drinking water and food. Urban air concentrations measured in Copenhagen of on average 0.16-0.19 µg/m^3 do not give grounds for major health concerns. No data on *n*-hexane in drinking water or food has been identified for the Danish situation. Data from Canada estimating the total contribution from *n*-hexane containing food, in particular refined vegetable oils, do not indicate any risk for the consumer. Based on the limited database, combined exposures illustrating the Danish situation do not seem to be a concern in relation to the critical effects of *n*-hexane.

Data gaps

There is little information on how Danish consumers are exposed to *n*-hexane and if certain product types, e.g. for car repair and maintenance, may result in unacceptable exposures.

7. Information on alternatives

7.1 Identification of possible alternatives

The following sections discuss possible alternatives of *n*-hexane in its main uses.

7.1.1 Alternatives to *n*-hexane in solvent extraction

The first industrial operations in Europe of solvent extraction of editable oils were established in 1870. Carbon disulphide was the first patented solvent but other used solvents were petroleum naphthas, trichloroethylene, and ethanol. The use of trichloroethylene stayed in the US at least until the 1950s but there were problems with cattle dying of a “bloody nose disease” when fed with the product. At that time the purer solvents, distilled with a narrow distillation range, became available, and *n*-hexane rich solvents became the solvent of choice. Although alternatives to hexane for solvent extraction of oil seeds have been investigated for decades it is still the major solvent in use.

Catastrophic explosions have occurred during time due to the high flammability of hexane and since the 1970's more focus has been on the health and environmental effects of *n*-hexane. In December 2007 there was a large explosion in Aarhus from hexane used for solvent extraction. Such incidents and the hazards to human health and the environment have pushed for substitution consideration.

Important properties of the solvent to be used include vaporization temperature, boiling point, oil solubility, viscosity, specific gravity, polarity, reactivity, purity and stability to heat, light and water. As the solvent is recycled, it must withstand repeated cycles of heating, vaporisation and cooling. Stability is also required to prevent contamination of meal and oil with potentially hazardous decomposition products (Johnson & Lusas, 1983). *n*-Hexane is characterised by low vaporization temperature, high stability, low corrosiveness and low greasy residual effects and has therefore from a technical point of view been an excellent choice (Anderson G.E., 2011).

Research on alternative solvents has suggested ethanol, isopropanol, methylene chloride, aqueous acetone, and hexane/acetone/water mixtures but it seems that it is difficult to find a replacement that has the same ability to produce a high-quality edible oil (colour, taste and other food properties).

Various alcohols, e.g. isopropyl alcohol or a 3:2 mixture of hexane and isopropyl alcohol are alternatives that have been tested.

Solvents that are allowed to be used for extraction in relation to food and food ingredients according to the current legislation in EU are shown in Table 17.

TABLE 17
EXTRACTION SOLVENTS ALLOWED IN FOOD OR RAW MATERIAL PROCESSING (2009/32/EC)

Solvents with no restrictions	Solvents for which conditions of use are specified
Propane Butane Ethyl acetate Ethanol Carbon dioxide Acetone Nitrous oxide	Hexane Methyl acetate Ethylmethylketone Dichloromethane Methanol Propan-1-ol Propan-2-ol Diethyl ether Cyclohexane Methyl acetate Butan-1-ol Butan-2-o 1,1,1,2-tetrafluoroethane

Other, more recent studies suggest Soft Aqueous Processing which is a low temperature extraction method with the use of enzymes and fractionation using membranes. Such methods make the use of organic solvents for extraction superfluous or reduce the amounts to be used (Parmentier, 2006 a).

Multi-enzyme hydrolysis as a pre-treatment option to improve solvent extraction and its eventual adaptation to conventional processes has been tested in relation to extraction of soybean oil (Grasso et al., 2012). I was concluded that that enzymatic hydrolysis is a pre-treatment option that could be incorporated into the current processes of soybean oil solvent extraction. The improvements obtained could be applied at industrial level and result in faster extraction processes, higher oil yield and/or decreased amount of solvent used. Many other studies investigating the application of enzymatic hydrolysis of oilseeds can be found in the literature.

It appears that research and development efforts are still being carried out to find the proper methodology and optimum processing parameters (for example, solvent, pH, temperature, enzymatic concentration, hydrolysis period) that will enhance both the oil availability and extractability. Also aqueous enzymatic extraction is studied as another promising technique where hydrothermal pretreatment is given prior to oil extraction to activate the native enzymes present in the oilseeds and to loosen their structure for the extraction of extra oil with better quality (Ghosh et al., 2007).

It is mentioned in one of the Danish environmental permits for a solvent extraction plant that for the sake of the quality of the final edible oils there is no good alternative to hexane for the oil seed extraction performed.

For the production of bio diesel from vegetable oils, i*n*-situ transesterification eliminates the hexane extraction process. In that kind of process, alcohol serves both as an extracting agent for the oils from the seeds and as a reagent for alkyl esters production. *In situ* transesterification offers the advantages of substituting hexane and minimizing oil losses.

7.1.2 Alternatives to *n*-hexane in laboratories

Ethoxynonafluorobutane is a substitute for *n*-hexane in normal-phase high-performance liquid chromatographic separations. One difficulty with substitution is that *n*-hexane is specified in many laboratory standards (Kagan, 2001).

7.1.3 Alternatives to *n*-hexane as a blowing agent

Substitution among physical blowing agents will depend upon equipment design for liquid vs gas blowing agent, explosion-proof status, solubility of the blowing agent in molten and cooled polymer foam, and the rate and consequences of diffusion of the agent from the finished foam (Acton (Ed), 2013).

Depending upon the specific equipment and conditions, iso-pentane or iso-hexane might be the closest substitutes for *n*-hexane in this application. It is expected that this use of *n*-hexane is limited to very specialized foam products.

7.1.4 Alternatives to *n*-hexane as a reaction medium

The polyethylene and polypropylene processes which use *n*-hexane as either the reaction solvent or the liquid phase for slurry reactions are highly specific to *n*-hexane due to the specific combination of solubility, boiling range and chemical stability. One of the polypropylene processes may be able to use heptane in combination with or to replace hexane. However, there are no polyethylene or polypropylene plants in Denmark.

7.1.5 Alternatives to *n*-hexane as special purpose solvent and cleaning agent (degreaser)

Water-based cleaners, both for industrial, professional and domestic use, will most often be available, but require a different technique and sometimes also new equipment.

Many large companies have developed solvent selection and replacement guides to be used in relation to purchasing of products and production planning. In such guides *n*-hexane is often is listed as a substance to avoid or restrict and substitute with e.g. heptane[6] if possible.

In the printing industry, vegetable oil-based cleaners can sometimes be used instead of hexane (IRTA, 2006).

Adhesives for the shoe manufacturing industry typically contained large amounts of *n*-hexane. The *n*-hexane has been partly substituted during the past 30 years with substances like ethyl acetate, cyclohexane, hexane isomers, methyl ethyl ketone, heptane and acetone (US NIH, 2014).

7.1.6 Hazard classification of suggested alternatives

The hazard classifications of the substances suggested as alternatives to *n*-hexane in the different application areas are shown in Table 18. Alternatives that are not identified by CAS number or chemical name are not included, e.g. vegetable oils and enzymes suggested for pre-treatment to improve solvent extraction. Suggested mixtures of the listed substances are also not included in the table.

All suggested substances except methylene chloride are classified as highly flammable. Although their flash points are not identical, they are not directly safer alternatives with regard to flammability.

Methylene chloride is not flammable but is classified for carcinogenicity with Carc.2 (Suspected of causing cancer) and thereby not an attractive alternative with regard to health hazard and the requirements that follow according to occupational health and safety legislation. Only ethanol is not classified for any health or environmental hazards.

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[6] Example of solvent substitution guide: http://safety.dept.shef.ac.uk/chemical/Solvent%20Substitution.pdf

TABLE 18
CLASSIFICATION OF SUGGESTED ALTERNATIVES TO *N*-HEXANE

Substance name	CAS no.	Suggested application area	Hazard Class and Category Code(s) and Hazard Statement Codes	Pictograms
Harmonised classifications				
Acetone	67-64-1	Solvent extraction Special purpose solvent Cleaning agent	Flam - Liq. 2; H225 Eye Irrit. 2; H319 STOT SE 3;H336	
Cyclohexane	110-82-7	Special purpose solvent Cleaning agent	Flam. Liq. 2; H225 Asp. Tox- 1; H304 Skin Irrit. 2; H315 STOT SE 3;H336 Aquatic Acute 1; H400 Aquatic Chronic 1; H410	
Ethanol	64-17-5	Solvent extraction	Flam. Liq. 2; H225	
Ethyl acetate	141-78-6	Special purpose solvent Cleaning agent	Flam. Liq. 2; H225 Eye Irrit. 2; H319 STOT SE 3;H336	
Heptane	142-82-5	Reaction medium Special purpose solvent Cleaning agent	Flam. Liq. 2; H225 Asp. Tox- 1; H304 Skin Irrit. 2; H315 STOT SE 3;H336 Aquatic Acute 1; H400 Aquatic Chronic 1; H410	
Isopropyl alcohol	67-63-0	Solvent extraction	Flam. Liq. 2; H225 Eye Irrit. 2; H319 STOT SE 3;H336	
Iso-hexane	107-83-5	Solvent extraction Blowing agent Special purpose solvent Cleaning agent	Flam. Liq. 2; H225 Asp. Tox- 1; H304 STOT SE 3;H336 Aquatic Chronic 2; H411	
Iso-pentane	78-78-4	Blowing agent	Flam.- Liq. 1; H224 Asp- Tox- 1; H304 Skin Irrit. 2; H315 STOT SE 3;H336 Aquatic Chronic 2; H411	
Methylene chloride	75-09-2	Solvent extraction	Carc. 2;H351	
Methyl ethyl ketone	78-93-3	Special purpose solvent Cleaning agent	Flam. Liq. 2; H225 Eye Irrit. 2; H319 STOT SE 3;H336	
Industry classifications				

Substance name	CAS no.	Suggested application area	Hazard Class and Category Code(s) and Hazard Statement Codes	Pictograms
Ethoxynonafluoro-butane	163702-05-4	Laboratory	Flam - Liq. 2; H225 (22)[*] Skin Irrit. 2; H315 (23)[*] Eye Irrit. 2; H319 (23)[*] STOT SE 3;H335 (23)[*]	🔥 ❗

[*]: Number of notifiers of the hazard class shown in brackets.

7.2 Historical Trends and Future Trends

Other solvents have substituted the use of *n*-hexane in many consumer products or the *n*-hexane containing products have been replaced with other chemical-type products that are water-based.

The large-scale uses of *n*-hexane in Denmark for solvent extraction and as reaction solvent in the production of insecticides do not seem to decrease as these processes depend on the technical properties of the solvent. These uses are in closed systems.

7.3 Summary and Conclusions

The high volume uses in Denmark are based on *n*-hexane rich blends of hexane isomers and it does not seem likely that the *n*-hexane will be replaced for these applications in the near future. For solvent extraction of edible oils, only solvents that are allowed according to the legislation in this area can be used.

Many large companies have developed solvent selection and replacement guides where *n*-hexane often is listed as a substance to avoid or restrict where technical requirements makes it possible.

With regard to consumer products, *n*-hexane has been substituted in many products before the turn of the millennium and *n*-hexane is mostly found in smaller concentrations in the majority of the products. For most of the consumer product type alternatives will be available without hexane.

As indicated in Table 18, most of the identified alternatives are also highly flammable and are not safer alternatives with respect to flammability. Heptane, which is often suggested as an alternative has a stronger environmental classification and may therefore be a concern in relation to uses such as cleaning and washing. From a health perspective several of the alternatives share some of the less critical health effects of *n*-hexane. Ethanol, which is the least toxic of the alternatives, has been tested as an extraction solvent, but a technological solution is not available.

8. Abbreviations and acronyms

ASTDR	Agency for Toxic Substances and Disease Registry
BCF	Bioconcentration factor
BTX	Benzene, toluene, and xylene
CLP	Classification, Labelling and Packaging Regulation
DT	Degradation time
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
EPA	Environmental Protection Agency
EU	European Union
HELCOM	The Baltic Marine Environment Protection Commission (Helsinki Commission)
HSPA	Hydrocarbon Solvents Producers Association
Kow	Octanol/water partitioning coefficient
Koc	Organic carbon/water partitioning coefficient
Kp	Partial pressure equilibrium constant
LC	Lethal effect concentration
LNAPL	Light no*n*-aqueous phase liquid
LOUS	List of Undesirable Substances (of the Danish EPA)
NIH	National Institute of Health
NPI	National Pollutant Inventory
NOAEL	No observable adverse effect level
NOEC	No observable effect concentration
NOVANA	Danish national monitoring and assessment programme
OECD	Organisation for Economic Co-operation and Development
OSPAR	Convention for the Protection of the Marine Environment of the North-East Atlantic
PEC	Predicted environmental concentration
PNEC	Predicted no effect concentration
QSAR	Quantitative Structure and Activity Relationship
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
STP	Sewage treatment plant
SVHC	Substance of Very High Concern
UVCB	Substances of Unknown or Variable composition, Complex reaction products or Biological materials

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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).
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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 no*n*-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[7] and the CLP Regulation[8] are the overarching pieces of EU chemicals legislation regulating industrial chemicals. The below will briefly summarise the REACH and CLP provi-

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

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

sions 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 risks 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 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 list[9]
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.

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.

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[9] 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).

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 recommendationsset 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.

CLRTAP - Convention on Long-range Transboundary Air Pollution

Since 1979 the Convention on Long-range Transboundary Air Pollution (CLRTAP) has addressed some of the major environmental problems of the UNECE (United Nations Economic Commission for Europe) region through scientific collaboration and policy negotiation.

The aim of the Convention is that Parties shall endeavour to limit and, as far as possible, gradually reduce and prevent air pollution including long-range transboundary air pollution. Parties develop policies and strategies to combat the discharge of air pollutants through exchanges of information, consultation, research and monitoring.

The Convention has been extended by eight protocols that identify specific measures to be taken by Parties to cut their emissions of air pollutants. Three of the protocols specifically address the emission of hazardous substances of which some are included in LOUS:

- The 1998 Protocol on Persistent Organic Pollutants (POPs); 33 Parties. Entered into force on 23 October 2003.
- The 1998 Protocol on Heavy Metals; 33 Parties. Entered into force on 29 December 2003.
- The 1991 Protocol concerning the Control of Emissions of Volatile Organic Compounds or their Transboundary Fluxes; 24 Parties. Entered into force 29 September 1997.

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 decisio*n*-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.

Survey of n-hexan
This survey is part of the Danish EPA's review of the substances on the List of Undesirable Substances (LOUS). The survey concerns the aliphatic organic substance n-hexan. This substance was included in the LOUS list in 1999. The report defines the substance and present information on the use and occurrence of n-hexan 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 det alifatiske organiske stof n-hexan. Rapporten definerer stoffet og indeholder blandt andet en beskrivelse af brugen og forekomsten af styren 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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