DATA ON MANUFACTURE, IMPORT, EXPORT, USES AND RELEASES OF MUSK XYLENE (CAS NO 81-15-2) AS WELL AS INFORMATION ON POTENTIAL ALTERNATIVES TO ITS USE

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EXECUTIVE SUMMARY

Musk xylene belongs to the wider family of synthetic musks, which are a group of (chemically-unrelated) substances that emulate the aroma produced by natural musk. They are used in fragrance formulation, helping to 'fix' aromas and ensure persistence in a range of household products (such as detergents, fabric softeners, fabric conditioners, cleaning agents, air fresheners, etc) and cosmetic products (such as soaps, shampoos, perfumes, etc) (OSPAR 2004; RAR, 2005). OSPAR (2004), however, notes that musk xylene is primarily used in detergents and soaps (while musk ketone is used primarily in cosmetics).

There is currently no production of musk xylene in the European Union (EU). The Risk Assessment Report (RAR) also indicates that producers in China are now the most important source of musk xylene for the European market. It estimates the EU import volume for musk xylene at around 67 tonnes/year in 2000 (RAR, 2005).

Across the EU, a number of companies and retailers have specifically prohibited the use of musk xylene in their products as a result of the negative publicity of musks. AISE (the EU-wide industry association representing the detergents and cleaning products industry) also notes more generally that most of its member companies, if not all, have already phased out the use of musk xylene (starting a decade ago); for instance, in Germany, the detergents trade association has, since 1993, been advising its members not to use musk xylene (AISE, 2008). Considering that there has been noted reduction in the use of musk xylene (particularly in the last five years), a more reasonable import and use estimate of 25 tonnes/year has been derived in this study.

In terms of alternatives to musk xylene, polycyclic musks (such as HHCB and AHTN) were the initial replacements for musk xylene (and other nitromusks) in a number of consumer products; however, this trend has reduced significantly due to extensive coverage and criticism of these musks in consumer journals and NGOs campaigning actively for them to be banned (despite positive scientific assessments of the two main polycyclic musks under the Cosmetics Directive and the voluntary HERA programme). Recent trends seem to suggest that polycyclic musks are gradually being replaced by macrocyclic musks (such as civetone and ethylene brassylate), as well as other more novel musk compounds (such as cyclomusk).

Overall, it is the case that a reduction in the use of musk xylene has taken place and is currently on-going as an autonomous process without any regulatory pressure.

0 Background Information

0.1 *Background to the Study*

In the framework of the authorisation process, Member States Competent Authorities or the European Chemicals Agency (ECHA), on a request by the Commission, may prepare Annex XV dossiers for the identification of substances of very high concern (SVHC). Musk xylene is one of a number of substances for which an Annex XV dossier has been prepared by the Netherlands[1]. Therein, musk xylene is concluded to be very persistent and very bioaccumulative (vPvB) and, as such, has been put forward for consideration as a SVHC and potentially, subsequent inclusion on Annex XIV of the REACH Regulation[2].

ECHA has, therefore, commissioned this study on musk xylene in order to support the priority setting for this substance on the candidate list for inclusion in Annex XIV (Article 59 of the REACH Regulation), as well as define the conditions relating to the entries on Annex XIV (Article 58(1) of the REACH Regulation). The main objective of this study is to provide information on uses and releases of musk xylene, as well as identify and provide information on the properties and risk(s) of possible alternative substances and techniques.

0.2 *Methodology and Approach to the Study*

As noted in the Specific Terms of Reference, the main tasks to be performed include:

- collecting and analysing information on manufacture, import and export of musk xylene, as well as releases of the substance from manufacturing sites in the EU for assessing the contribution to the total mass balance and releases;

- collecting and analysing information on uses (identifying the most relevant), conditions of use and the lifecycle of the substance including the complexity of the supply chain for mapping its mass flow;

- developing an overview of releases from uses, identifying the uses causing the highest releases to the workplace and the environment while also considering releases from consumer use of preparations and articles; and

- identifying potential alternative substances and techniques and obtaining information on their intrinsic hazard properties, hazards and risks to human health and the environment allowing comparison with musk xylene.

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1 **Proposal for Identification of a Substance as a CMR Cat 1 or 2, PBT**, **vPvB or a Substance of an Equivalent Level of Concern**, Annex XV Report, submitted by The Netherlands, June 2008.

2 Annex XIV provides a list of substances subject to authorisation.

The approach to data collection for this study involved three elements:

- reviewing the Annex XV dossier for musk xylene and comments received as a result of its publication and circulation;
- reviewing the available data from other documents and the Internet; and
- consulting directly with trade associations through the use of e-mail questionnaires.

Three key industry associations were contacted during this study:

- the European Cosmetic, Toiletry and Perfumery Association (COLIPA) - representing the cosmetics industry;
- the International Association for Soaps, Detergents and Maintenance Products (AISE) - representing the detergents and cleaning products industry; and
- the European Flavour and Fragrance Association (EFFA) - representing the fragrances manufacturers.

We also contacted the European Chemical Industry Council (CEFIC).

The aim of contacting them was to ask them relevant questions on their use tonnages, releases, alternatives, etc. and to request their assistance in identifying companies which may be involved in the importation and use of musk xylene in the EU. AISE provided a detailed feedback to some of the questions; COLIPA also provided a response and CEFIC forwarded our questions to the relevant companies (as requested). We also undertook a review of information on uses, import tonnages and releases from other publicly available sources (e.g. the Internet and the risk assessment report by the Netherlands).

In general, there was very little quantitative data on tonnages (from the literature review) and due to the short timescale of the study, it was not possible to develop and implement a reliable survey of all the key stakeholders.

1 Information on Manufacture, Import and Export and Releases from Manufacture

1.1 *Manufacturing Sites and Manufacturing Processes*

There is currently no production of musk xylene in the European Union (EU) (RAR, 2005). The summary RAR (RAR, 2005) for musk xylene notes that several European companies stopped production of musk xylene in the last decade.

1.2 *Import and Export of the Substance on its own or in Preparations*

With regard to imports, the RAR (2005) indicates that producers in China are now the most important source for the European market. It estimates the EU import volume for musk xylene at around 67 tonnes/year (in year 2000). While there are no up-to-date data for current imports, a review of use patterns by companies in the EU (see Section 3) would suggest that this tonnage has decreased significantly. AISE (2008) highlights that the use volumes and scenarios considered in the RAR reflect the situation in the late 1990's and that there has been a clear reduction in usage since then. AISE also notes that, while they do not hold detailed information on the origin of raw materials used by their members, generally speaking, the detergents and cleaning products industry sources most of its raw materials from EU production sites (due to the transport and packaging costs), with only a small percentage of their raw materials being supplied by non-EU suppliers (as confirmed in AISE, 2007). Most companies also have procedures in place to ensure imported materials follow the same standards as EU manufactured products.

No exports of the substance on its own will be expected (as there is no EU production); however, it is possible that some exports of musk xylene in preparations (e.g. detergents) may occur. However, this is unlikely to be significant as the transport and packaging costs of producing in one country and supplying another national market where consumer tastes and branding may be different, mean that, in practice, trade of detergents and cleaning products outside of Europe is minimal (AISE, 2007). Furthermore, it is the case that the major multinational/large companies who are likely to be involved in global trade have largely phased out their use of musk xylene (due to the associated negative publicity, as can be seen on their websites and information brochures). Small and medium-sized enterprises (SMEs) are, therefore, more likely to be responsible for any on-going uses of musk xylene and their products are often sold within their own Member States. Exports of musk xylene as a substance or in preparations, is therefore, likely to be minimal.

1.3 *Import and Export of Articles Containing the Substance*

No detailed information is available on the amount of musk xylene which is imported or exported as substances in articles. Quantities are however, likely to be negligible, if any, as musk xylene is used in preparations, rather than articles.

1.4 *Releases from Manufacture*

There is no manufacture in the EU and, as such, no releases from manufacture.

2 Information on Uses and Releases from Uses

2.1 *Identification of Uses*

Musk xylene belongs to the wider family of synthetic musks, which are a group of (chemically unrelated) substances that emulate the aroma produced by natural musk. Musk ingredients are a very significant ingredient for fragrance formulation, helping to 'fix' aromas and ensure persistence in a range of consumer products. They are used (as fragrance and fragrance enhancers) in most fragrance mixtures for detergents[3], fabric softeners, fabric conditioners, cleaning agents, air fresheners and other household products and in cosmetic products[4] such as soaps, shampoos and perfumes (OSPAR 2004; RAR, 2005). OSPAR (2004) notes that musk xylene is primarily used in detergents and soaps (while musk ketone is primarily used in cosmetics).

2.2 *Quantification of Uses*

OSPAR (2004) sets out the available data on the consumption of musk xylene for a number of years prior to 2000 (as shown in Table 2.1 below).

Table 2.1: Estimated European Use Volumes for Musk Xylene

Year	Quantity (tonnes)	Percentage Drop
1992	174	-
1995	110	37%
1998	86	22%
2000	67	22%
2002	52	22%
2004	41	22%
2006	32	22%
2008	25	22%

Source: OSPAR (2004)

These data relate to the volumes used in fragrance compounding, (i.e. the preparation of mixtures that are used by the formulators of consumer products anywhere). The RAR notes that it was not possible to obtain the volumes in consumer products actually sold in Europe.

Shaded cells are calculated estimates for the purposes of this study.

As mentioned in Section 1, a review of use patterns by companies in the EU (see Section 1) would suggest that the use tonnage of 67 tonnes in 2000 has decreased significantly. AISE (2008) also highlights that the use volumes and scenarios considered in the RAR reflect the situation in the late 1990's and that there has been a clear reduction in usage since then. Hence, for the purposes of the mass balance, the figure of 67 tonnes per year is considered to be a *high estimate*.

[3] NACE code C20.4.1: Manufacture of soap and detergents, cleaning and polishing preparations.

[4] NACE code C20.4.2: Manufacture of perfumes and toiletries.

In the absence of recent quantitative information on use tonnages from industry, some estimates have to be made. Hence, assuming that the 22% drop observed between 1998 and 2000 is maintained up to 2008, the current use volume for musk xylene is calculated to be around 25 tonnes/year (which is considered to be a *reasonable estimate*).

2.3 *Quantification of Releases from Uses*

The RAR for musk xylene provides a starting point for collecting the required information for this task. It identified possible sources of musk xylene into the environment as occurring during its compounding into the fragrance (at six sites of unidentified location in the EU, at the time), the formulating of the fragrance into end products and the use of those end products (consumer use).

However, emissions from these point sources (formulation and compounding) have not been considered in this study due to lack of recent site-specific data and the overall decrease in use across Europe. OSPAR (2004) also indicates that point source releases from the formulation of products are negligible in relation to the overall diffuse releases to the marine environment due to the widespread dispersive use of consumer products containing musk substances.

In undertaking a mass balance of releases of musk xylene to the environment, a *high-case scenario* is derived, as follows:

- it is assumed that **67 tonnes/year** of musk xylene is still being imported into the EU and there is no EU production of musk xylene. The 67 tonnes is based on the information in the risk assessment report; however, a *reasonable-case scenario* of 25 tonnes is also included.

- it is further assumed (in line with the worst case scenario for the aquatic environment in the risk assessment) that 100% of the musk xylene used in compounding in Europe is used in consumer products in Europe (i.e. there are no exports of musk xylene as a pure substance). The RAR (2005) also assumes that there is no export of musk xylene in finished products from the EU. Taking into account the discussion in Section 1.2 which highlights the phase out of musk xylene (particularly by large companies likely to be involved in exports), this assumption is retained;

- it is assumed that around **54 tonnes** or 80% of this remaining tonnage is used in detergents, cleaning products and fabric softeners, while cosmetics (i.e. toiletries, colognes, shampoos, etc) and other uses account for **13 tonnes** or 20%.

  While this 80:20 split is a guess-estimate, it actually reflects the fact that musk xylene is primarily used in detergents and soaps while musk ketone is used in cosmetics (according to OSPAR, 2004). Also, while the cosmetics industry may argue that very little use is made of musk xylene, the final concentration of fragrances in detergents and soaps (0.2 - 1%) is much lower than that in cosmetic products where higher levels may be present;

- it is assumed (as a worst case) that 100% of the EU use volume of 67 tonnes is released into the waste water/sewerage and that no substance remains on the fabric, skin or surfaces or has evaporated. OSPAR (2004) notes that the fragrance ingredients used in washing and cleaning agents and in soaps and shower products are discharged after use via domestic waste water to the sewer and subsequently to a sewage treatment plant;

- it is further assumed that, for detergents, around 75% (**41 tonnes**) of the musk xylene ends up in domestic wastewater while 25% (**13 tonnes**) in industrial wastewater.

  This 75%:25% split is based on expected purchase and use patterns for detergents and cleaning products between the domestic sector and industrial and institutional sector[5]. In the absence of better information, it is assumed that 100% (**13 tonnes**) of cosmetics will end up in domestic wastewater;

- in the RAR (2005), for private use and the regional scale, a split up of 30% discharge directly to surface water and 70% to an STP was assumed. According to the Technical Guidance Document (TGD) on Risk Assessment (EC, 2003), a default split up of 20% directly to surface water and 80% to an STP is recommended. The latter might be more representative for the current situation within the EU. For domestic wastewater, therefore, it is assumed that **11 tonnes** goes directly to surface water and **43 tonnes** to an STP. It is assumed that 100% of industrial wastewater ends up in an STP such that the total amount of musk xylene in STP is **56 tonnes** (43 + 13);

- according to the 2005 RAR, the local STP model (SimpleTreat) within EUSES 2.0.3 (EC, 2004) estimates the following default distribution for musk xylene in a sewage treatment plant (STP): air: 0%, water: 43% and sludge: 57%. However, some studies (cited in the 2005 RAR) indicated that the musk xylene removal within a STP can be very high i.e. 95-98%. As these data do not allow making a clear, quantitative distinction between sorption to sludge and (bio)degradation, the default STP distribution will be used, as follows:
  - 43% (**24 tonnes**) will be discharged with the effluent into the freshwater environment;
  - 57% (**32 tonnes**) will be removed by adsorption to sludge; and
  - 0% (**0 tonnes**) to air.

  These are based on the default guidelines in the TGD (EC, 2003) for a chemical (such as musk xylene) that is not easily degradable ($kbio_{stp} = 0\ hr^{-1}$) having a Henry's law constant of 0.0595 $Pa.m^3/mol$ and log K_{ow} of 4.9; and

5 According to information produced by AISE, the household products sector was valued at around €24 billion and €29 billion in 2006 and 2007 respectively while the Industrial and institutional products was valued at around €6 billion and €6.5 billion in 2006 and 2007 respectively.

- the musk xylene which ends up in sludge is then sent to incineration, landfill or spread on agricultural soil (which may be washed off into the aquatic environment). No experimental data are available on the partitioning of musk xylene between water and soil, sediment or sludge.

Figures 2.1 and 2.2 provide a mass balance based on tonnages of 67 tonnes and 25 tonnes respectively and on the assumptions outlined above.

Figure 2.1: Estimated Mass Balance for Musk Xylene – High-case Scenario

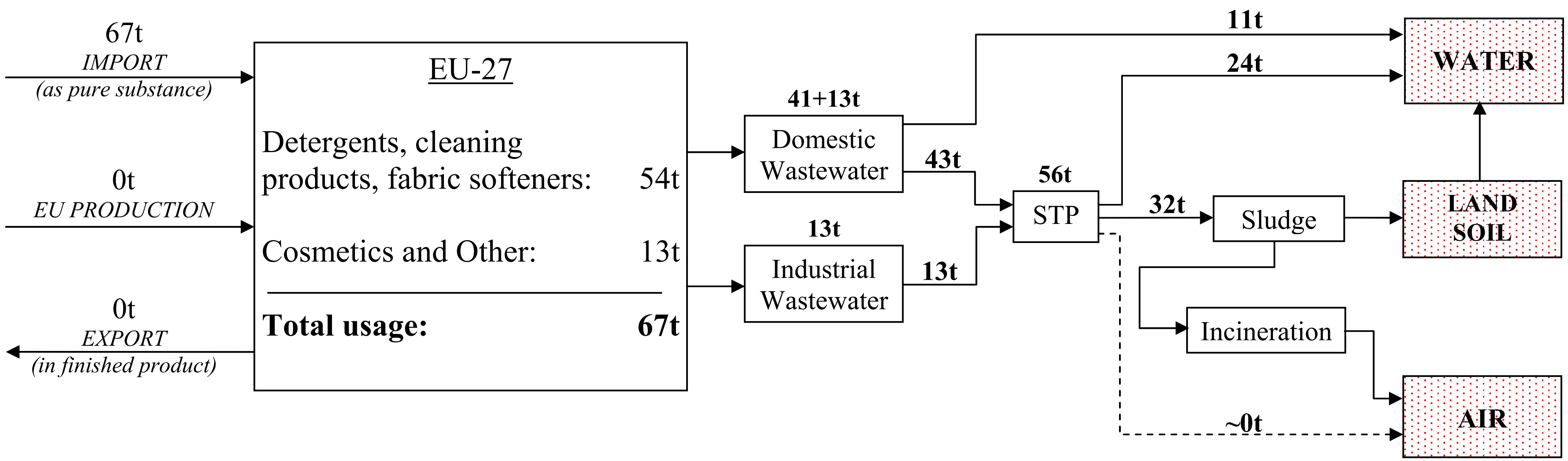
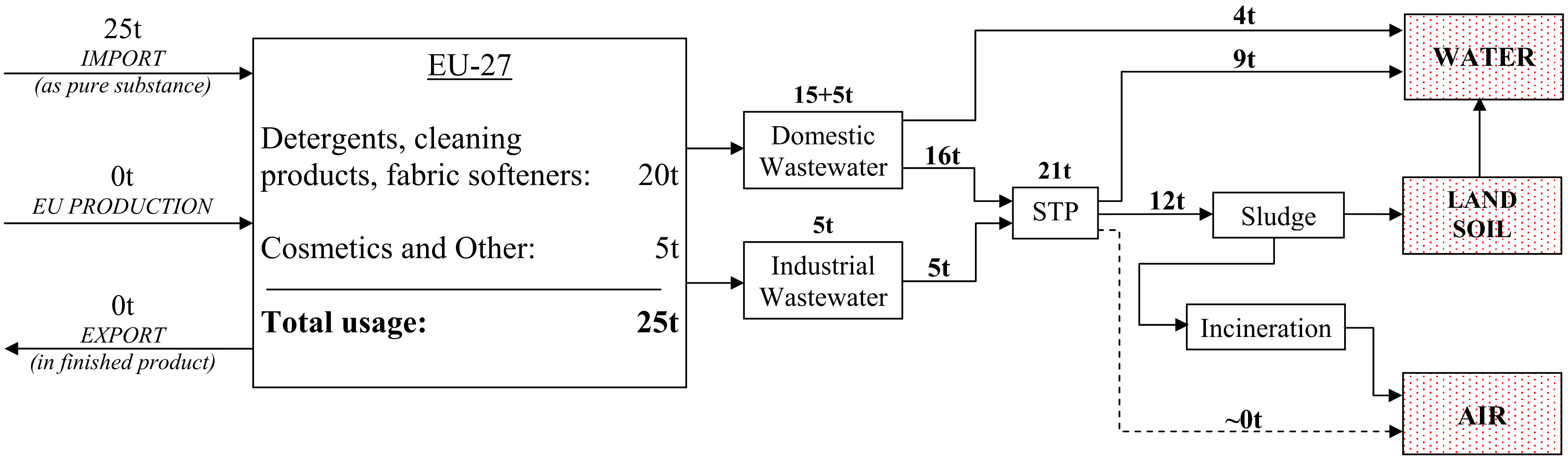


Figure 2.2: Estimated Mass Balance for Musk Xylene – Reasonable-case Scenario



3 Information on Alternatives

3.1 *Identification of Alternative Substances and Techniques*

Fragrances/perfumes are usually made up of top, middle and base notes. The base notes are usually the strongest scent and last longer than the top and middle notes (which are perceived shortly after application of the perfume). Base notes are, therefore, chosen because of their fixative properties, strength and/or scent. Musk xylene is one of a number of base notes which may be employed to 'fix' aromas in a range of consumer products.

There are four main groups of synthetic musks which may, in theory, be considered to be alternatives to musk xylene (taking into account existing restrictions on their use in certain products, e.g. cosmetics). These are: nitromusks, polycyclic musks, macrocyclic musks and alicyclic musks.

- *Nitromusks*, the common name for a group of (artificial) nitrogen-containing musks (produced by nitration of organic compounds), includes a number of compounds, such as: musk ketone, musk ambrette, musk tibetene, musk *alpha* and musk moskene (in addition to musk xylene) (Huber the Nose, nd; Rowe, 2004).

- *Polycyclic musks*, the common name for synthetic musks with rings in their chemical structure, are the most commonly produced and used musks. They include substances such as traseolide (ATII), celestolide (ADBI), fixolide/tonalide (AHTN), versalide (ATTN), galaxolide (HHCB), etc. These polycyclic musks are applied in consumer products such as perfumes, cosmetics, soaps, shampoo, detergents, fabric conditioners, cleaning products, air fresheners, etc (HERA, 2004).

- *Macrocyclic musks*, refer to macrocyclic ketones or lactones having 10 - 15 carbons in their ring structures (OSPAR, 2004) and include compounds such as ethylene brassilate, globalide (habanolide), ambrettolide, muscone, cyclopentadecanolide (exaltolide), velvione, civettone, etc (TNO, 2005; Rowe, 2004; Huber the Nose, nd).

- *Alicyclic musks*, otherwise known as cycloakyl ester or linear musks, are a relatively novel class of musk compounds, which have only recently (in the 1990s) been produced at a commercial scale and include compounds such as cyclomusk, helvetolide and romandolide (Kraft, 2004; Marcus, 2004).

Table 3.1 overleaf provides details of each of the musk compounds by group.

In discussing these alternatives, it is important to bear in mind that while, in theory, all the above synthetic musks possess what is often referred to as a "*typical musky odour*", in practice, the odour profile for each compound is different and the resulting fragrance is a function of the manufacturing process as much as the type and quantity of musk compound used.

Table 3.1: Names of Alternative Musk Compounds (with CAS No)		
Trade Names	**Official Name**	**CAS Number**
Nitromusks		
Musk Ambrette	2,6-dinitro-3-methoxy-4-t-butyl-toluene:	83-66-9
Musk Ketone	4,6-dinitro-3-acetyl-5-t-butyl-toluene	81-14-1
Musk Moskene	4,6-dinitro- l , l ,3,3,5-pentalmethyl-indane	l16-66-5
Musk Tibetene	2,6-dinitro-3,4,5-trimethyl-l-t-butyl-benzene	145-39-1
Polycyclic musks		
DPMI, Indanone, Cashmeron	6,7-dihydro-l , l 2,3,3-pentalmethyl-4(5H)	l 922-67-4
ADBI, Celestolide, Clysolide	4-acetyl- l , l -dimethyl-6-t-butyldihydro-indene	l3l7l-00-1
HHCB, Galaxolide, Musk GX, Abbalide	l ,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexa1methylcyclopenta-2benzopyran	1222-05-5
AHMI, Phantolide	5-acetyl-l , l ,2,3,3,6-hexamethyl-indane	l5323-35-0
AHTN, Tonalide, Fixolide, Tetralide	7-acetyl-l , l,3,4,4,6-hexamethyl-l ,2,3,4-tetrahydronaphthalene	1506-02-1
ATTI, Traseolide	5-acetyl-l , l ,2,6-tetramethyl-3-isopropyl-indane	68140-48-7
Macrocyclic musks		
Muscone	3-methyl-cyclopentadecanone	541-91-3
Exaltolide, Thibetolide, Cyclopentadecanolide	oxacyclohexadecan-2-one	106-02-5
Ambrettolide	Z-oxacyclo-heptadec-8-en-2-one	123-69-3
Ethylene brassylate, Astratone, Musk T	l,4-dioxacycloheptadecane-5, 17-dione	105-95-3
Civetone	Z-9-cycloheptadecen-l-one	542-46-1
Musconate	l,4-dioxacyclo-hexadecane-5, 16-dione	54982-83-1
Habanolide		111879-80-2
Alicyclic musks		
Cyclomusk	5-isopropenyl-β-β-2-trimethyl cyclopent-1-ene-1--propyl propionate	84012-64-6
Helvetolide	1-propanol,2(1(3,3methylcyclohex)ethoxy]2-methyl, propanoate	141773-73-1*
Romandolide	1-[3,3-dimethyl-1-cyclohexyl)-ethoxycarbonyl]methyl propanoate	**
** EINECS No 415-490-5* *** EINECS No 431-700-8*		

The actual manufacture of a fragrance formulation is a simple, batch process involving the mixing of a range of ingredients (including natural aroma ingredients, bases (proprietary blends of fragrance ingredients), solvents and synthetic ingredients, etc) to a specific 'recipe'. The number of ingredients per fragrance can be very high. For a medium-sized formulator, the average formulation could contain around 50 ingredients, but some of these may be bases consisting of up to 100 (potentially secret) substances (Defra & DTI, 2005).

The skill of the fragrance formulator is to identify the combination of natural and synthetic ingredients to achieve the aroma required by the customer, at the right price and to the right specification. The specification of the fragrance is based on the nature of its use in downstream applications. This will dictate properties such as (Defra & DTI, 2005):

- the level of persistence required (for example, for the fragrance to remain detectable on fabrics through laundering, drying and storage in the case of household fabric conditioners);
- the environment in which the fragrance must operate (e.g. high temperature, wet and dry conditions); and
- the chemistry of the product within which it will be included (e.g. the other ingredients within the fabric conditioner).

Following from the fact that any given fragrance is actually a collection of ingredients, the individual musk compounds being discussed should be considered within the context of contributing a given fragrance. While the typical musky odour will be present across the musks, the exact "note" may differ for each musk compound. For instance, nitromusks are described in general as possessing a warm, powdery scent with an amber overlay; musk ketone is specifically described as possessing a sensual warmth and musk ambrette as having a floral tone. Polycyclic musks such as Galaoxide are described as having a sweet powdery smell while macrocyclic musks such as Habanolide and helvetolide are described as having a metallic nuance and a fruity undertone respectively (Boisdejasmin, 2005). Overall the synthetic musks range dramatically in terms of their odour profiles.

In summary, it is the case that alternative fragrances to those based on musk xylene do exist; however, replicating the exact musk xylene fragrance in a consumer product is not straightforward as it is a function of the formulation process, the formulator's skill and the type and concentration of specific musk compound(s) used.

The information on alternatives below is based mainly on a review of published and publicly available documents. Information has not been sought from individual companies (apart from that available on their websites) as fragrance ingredients are generally considered to be trade secrets and industry associations contacted indicate that they do not discuss these issues for anti-trust law reasons. The Detergents Regulation does not also require companies to publish details of every single ingredient in their fragrances.

3.2 *Information on Alternatives*

3.2.1 Human Health and Environmental Effects

3.2.1.1 Nitromusks

In the family of nitromusks, musk xylene and musk ketone are the two substances of commercial importance; the assessment of alternatives will, therefore, focus primarily on musk ketone (which is on a priority list under the EC Existing Substances Regulation (ESR)).

The summary risk assessment report for musk ketone (RAR, 2004) concludes that for both human health and environmental end-points, *there is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already* (conclusion ii).

Musk ketone is also considered not to be a PBT candidate substance. Although the Persistence (P) criterion seems to be fulfilled, the Bioaccumulation (B) criterion is not met as the experimental BCF is below 2000. The Toxicity (T) criterion would be a borderline case for ecotoxicity with the tentative NOECs of 10µg/l for two species. For human health toxicity, the situation around musk ketone fulfilling the T-criterion was not clear as more information should be provided about its potential carcinogenicity (RAR, 2004).

3.2.1.2 Polycyclic Musks

In the family of polycyclic musks, AHTN and HHCB are the two substances of commercial importance; the assessment of alternatives will, therefore, focus primarily on AHTN and HHCB which are also on priority lists under the ESR.

The environmental risk assessment for AHTN and HHCB (HERA, 2004) (which is based on monitoring data rather than a modelling approach) shows that (1) sufficient data are available to assess the environmental risks; (2) the assessment can be based on measured concentrations in the Northern region of the EU; (3) risk ratios are generally below 1; (4) however, for sediment organisms living in areas contaminated with a high effluent load, the risk ratios may be above 1. However, it is noted that the uncertainty around the toxicity to sediment organisms is high which is incorporated as an additional factor in the risk ratios (HERA, 2004).

The human health risk assessment for HHCB (HERA, 2004a) shows that HHCB has a low acute toxicity either by the oral or dermal route. Inhalation exposure has been estimated to be negligible relative to dermal exposure and it is not a skin or eye irritant. HHCB shows no phototoxicity potential on humans at concentrations significantly higher than would be encountered from the use of fragranced consumer products. There is also no significant evidence either from animal or human studies of potential for dermal sensitisation. HHCB is a non-genotoxic substance. The mutagenicity data and the repeated dose studies with HHCB do not indicate a concern with regard to carcinogenicity nor does HHCB possess any structural features that would raise a concern. In the unlikely event of maximum exposures from direct and indirect skin contact as well as from the oral route via dishware residues, the estimated exposure to HHCB from its use in household cleaning products is around 0.07 µg/kg bw/day. Comparison of this exposure to the NOAEL indicates a margin of safety of at least 350,000 and supports the conclusion that there is no significant risk to human health from exposure to HHCB as used in household cleaning products (HERA, 2004).

In summary, HHCB does not pose a risk of adverse health effects to consumers from use in household cleaning products. The uses of HHCB in cosmetics have been reviewed by the SCCNFP (SCCNFP, 2002 in HERA, 2004a), which concluded "*that HHCB can be safely used as a fragrance ingredient in cosmetic* *products without any restriction for its use*" (HERA, 2004a). SCHER, in its opinion, also indicated that it agreed with the conclusion (ii)[6] (*there is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already*) proposed by the RAR for all the assessments (SCHER, 2008).

HHCB does also not meet the criteria for PBT chemicals (as confirmed by SCHER, 2008). TNO (2005) notes that although polycyclic musks have been tested in the past and shown no toxicological or dermatological effects, their high levels of use, chemical stability and low biodegradability make them potential environmental contaminants due to their bioaccumulation. Because of this potential to bioaccumulate, polycyclic musks are being replaced by macrocyclic musks (whose structure suggests a more ready degradation). OSPAR (2004) notes that a request was addressed to the European manufacturers of consumer products to reduce the amount of nitromusks and polycyclic musks in all consumer products that are discharged with wastewater to the lowest level needed for technical reasons.

3.2.1.3 Macrocyclic Musks

There appears to be little information on the health and environmental risks from macrocyclic musks. The physicochemical data (and chemical structure) of the macrocyclic musks indicate that they seem to have a more favourable environmental profile (e.g. better microbial decomposition) compared with polycyclic musks and nitromusks (OSPAR, 2004; TNO, 2005). This is, however, yet to be confirmed.

3.2.1.4 Alicyclic Musks

There is no information available at this time.

3.2.1.5 Summary of Health and Environmental Effects

In summary, it can be seen that current 'self-regulation' and trend of the market with regard to musk xylene has resulted in a shift to less hazardous substitutes (compared with musk xylene); however, there are still important data gaps which still exist before a conclusive answer can be provided on the hazardous properties for both the macrocyclic and alicyclic musks.

Tables 3.2 and 3.3 provide a summary of the health and environmental (PBT) properties of the various musk compounds.

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6 For the aquatic environment, including sediments and STP, all PEC/PNEC values are below 1. For the soil compartment and marine environment, all PEC/PNEC values are below 1. For the secondary poisoning all PEC/PNEC values are below 1, both for aquatic (fish) and terrestrial (earthworm) environment.

Table 3.2: PBT Properties of Musks			
Substance	**Persistence (P)**	**Bioaccumulation (B)**	**Toxicity (T)**
Musk xylene	P or vP	B or vB	Uncertain
Musk ketone	P or vP	Not B	Uncertain
AHTN	Potentially P	Not B	Not T
HHCB	Potentially P	Not B	Not T
Macrocyclic musks	Not P	No data	No data
Alicyclic musks	No data		

Table 3.3: Summary Comparison of Health Endpoints for Musk Ketone and HHCB		
Endpoint	**Musk Ketone**	**HHCB**
Skin Irritation	Not irritating	Not irritating
Eye Irritation	Not irritating	Not irritating
Skin Sensitisation	Weak sensitising properties in guinea pig. Up to a concentration of 5%, it is not skin sensitising in humans	No significant evidence of dermal sensitisation
Acute Toxicity	No risk of concern concluded with regard to acute dermal effects or by inhalation exposure	Low acute toxicity either by the oral or dermal route (LD_{50} values >3000 mg/kg) Inhalation exposure is estimated to be negligible relative to dermal
Mutagencity	Non-genotoxic	Non-genotoxic
Reproductive Toxicity	Taking into account intra- and interspecies differences, the margin of safety indicates no concern for developmental effects to the progeny of consumers	In a 90-day study in rats, there were no adverse effects at the highest dose tested, 150 mg/kg bw/day. There were no indications of effects on fertility or the developing foetus at levels as high as 50 mg/kg bw/day
Source: RAR, 2004; HERA, 2004a		

3.2.2 Technical and Economic Feasibility and Availability

3.2.2.1 Nitromusks

In the family of nitromusks, musk tibetene and moskene are of little commercial importance while musk ambrette is not produced or used anymore due to its sensitivity and neurotoxic effects (TNO, 2005; Huber the Nose, nd)[7]. Musk xylene and musk ketone are, therefore, the nitromusks of major commercial significance and have been produced and sold in the largest quantities (historically). Musk ketone is not produced in the EU, and the import in 2000 is estimated at 35 tonnes per year (RAR, 2004).

[7] In July 1995, the use of musk ambrette was included in the '*list of products cosmetics must not contain*' (Annex 2 of the Cosmetic Directive 76/768/EEC). The same action was taken in 1998 for musk tibetene and moskene (Directive 98/62/EC of 3 September 1998). Limit concentrations were also introduced for other nitromusks in several cosmetic products.

However, over the last decade, musk xylene and musk ketone have been detected in the environment, human fat tissue and breast milk, and a number of risk assessments have been undertaken (HERA, 2004). As a result of these findings (and regardless of the risk assessment findings), a number of perfume and consumer product companies took steps to voluntarily phase out the use of these nitromusks (including the low volume nitromusks) in their products. It is worth noting that, in addition to the environmental and health concerns, the dangerous production process for these nitromusks (which means that over the years explosions occurred in a number of factories) and the increasing availability and commercialisation of the polycyclic musks also contributed to the decreasing demand for and use of nitromusks (Huber the Nose, nd).

Across the EU, a number of companies and retailers have specifically prohibited the use of musk xylene in their products as a result of the negative publicity of musks (EuroCommerce, 2004; Defra & DTI, 2005). For instance, one global detergents and cleaning products company indicates that it has removed musk ketone from its laundry products, while also limiting (and replacing) any new uses whenever perfumes are being discontinued or reformulated. Overall, a reduction in the use of nitromusks of around 95% has been achieved in this company[8]. Another company (which set a voluntary deadline for complete substitution of these musks by July 2008) indicates that alternatives to musks are available and a lot of work is still being carried out by fragrance houses to increase the number of alternatives[9]. AISE (2008) notes more generally that most of its member companies, if not all, have already phased out the use of musk xylene (starting a decade ago); for instance, in Germany, the detergents trade association has, since 1993, been advising its members not to use musk xylene.

3.2.2.2 Polycyclic Musks

AHTN and HHCB are by far the polycyclic musks of economic importance, representing about 95% of the EU market for all polycyclic musks[10] (HERA, 2004). The production of these two substances takes place at one site for each substance in the EU and the production volume for HHCB is reported to be between 1,000 and 5,000 tonnes per year (HERA, 2004a). Industry estimates that 20 to 30% of the total production is exported as finished fragrance mixture or in consumer products (cosmetics, detergents, cleaning agents, etc.), whereas import volumes are expected to be far below the export volumes. A significant part of the production of AHTN and HHCB is also exported as the ‘pure substance’ outside the EU (HERA, 2004).

Table 3.4 provides estimated use volume for musk xylene, musk ketone, HHCB and AHTN in 2000. In terms of their technical suitability, polycyclic musks (as well as nitromusks) are considered to be low-cost fragrance ingredients which

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8 www.pgperspectives.com/en_UK/productingredient/nitormusks_en.html

9 www.boots-csr.com/library/6%20Artificial%20musks%206.pdf

10 The total use volume for 2000 of AHMI, AITI and ADBI together was 30 tonnes (HERA, 2004).

not only determine the odour of a product, but also have a positive effect on the quality of a fragrance.

Table 3.4: European Use Volume (in tonnes)				
	1992	**1995**	**1998**	**2000**
Musk xylene	174	110	86	67
Musk ketone	124	61	40	35
HHCB	2,400	1,482	1,473	1,427
AHTN	885	585	385	358
Source: OSPAR, 2004				

OSPAR (2004) reports that substitution of these four musk fragrances is already taking place and confirms that a number of European companies have stopped including polycyclic musks (and nitromusks) in their detergents and cosmetics. OSPAR (2004) also highlights the presence of polycyclic musks-free consumer products being marketed as evidence that substitution has already taken place somehow. This information is in line with that provided in a number of reports and also provided on company websites.

In a study by RPA for UK Defra & DTI (2005), a number of fragrance formulators contacted indicated that they already had to undertake a significant amount of reformulation, in response to requests from customers to exclude particular ingredients from products supplied to them. This affected in particular the use of artificial musks. One of the companies indicated that despite positive scientific assessments of the two polycyclic musks under the Cosmetics Directive and the voluntary HERA programme, downstream users were still asking for a ban on these musks. This was because NGOs and consumer organisations continued to criticise the use of these substances. There had been extensive coverage of musks in consumer journals and NGOs were campaigning actively for their banning[11]. This led to significant pressure on retailers, and on manufacturers of branded cosmetics and household products, to prohibit the use of all artificial musks. As a result of this pressure, one cosmetics manufacturer participating in the study banned the use of nitromusks and the three polycyclic mucks of concern in new fragrances, with a view to phasing out their use by 2008. Similar policies have been adopted by other manufacturers and by retailers across Europe (Defra & DTI, 2005).

As at 2005, a study by TNO examining the presence of artificial musks in various brands of perfume found that out of 36 perfumes tested, nitromusks were found in a limited number of products (20% of the samples) with musk ketone found in only a single product (an older type of perfume)[12]. The polycyclic musks were found in all samples. Interestingly, a newer set of musks (known as macrocyclic musks) were found in 21 samples and were the major musks in 11 of the samples. TNO (2005) noted that this seemed to suggest that polycyclic musks were gradually being replaced by macrocyclic musks.

[11] For instance, WWF believes that the use of musk xylene, musk ketone, AHTN and HHCB should be banned as soon as possible (WWF, nd).

[12] For context, a survey in 1997 of 114 cosmetic products showed that musk ketone was the most prominent musk and was found in around 50% of samples (Rooselaar & Weijland, 1997 in TNO, 2005).

3.2.2.3 Macrocyclic Musks

Amongst the macrocyclic musks, thibetolide (exaltolide), together with ethylene brassilate, was indicated to be the most used macrocyclic musk (TNO, 2005) although this may have changed. There are a number of other modern macrocyclic musks such as muscenone and nirvanolide, which are considered to be the perfumery materials of choice (in terms of power, diffusivity and character) when it comes to replacing polycyclic musks and nitromusks in older formulations (Rowe, 2004).

In terms of technical suitability, the odour profiles (i.e. intensity, tonality, odour threshold, tenacity, etc) for macrocyclic musks are completely different from those for nitromusks and polycyclic musks. Kraft & Swift (2005) indicate that they differ technically from the other musks possessing superior odour characteristics; Huber the Nose (nd), however, indicates that this difference in odour profiles is the reason some products still rely on fragrances containing nitromusks and polycyclic musks, even newly introduced ones.

Macrocyclic musks are also less economic compared to the other musks. In fact, they were not commercially produced and commonly utilised until the late 1990s due to difficulties in their synthesis, relatively high cost of production and consequently higher price (and were consequently treated as trade secrets). Rowe (2004) notes that to replace or even outperform polycyclic musks and nitromusks in diverse applications, one can either lower the production price of macrocyclic musks or increase their odour intensity, which means lowering their odour threshold. The latter option allows for more complex synthetic approaches and accordingly higher production costs (Rowe, 2004).

In cost terms, although 1:1 substitution of nitromusks and polycyclic musks by macrocyclic musks would be ideal, the price of macrocyclic musks is two to four times higher than polycyclic musks (Defra & DTI, 2005). Defra & DTI (2005) note that although it is the customers who require nitromusks and polycyclic musks to be replaced, they have not been willing to accept an increase in the price of fragrances. Formulators have, therefore, used only the amount of macrocyclic musks that can be obtained at the same price (using larger volumes of the cheaper macrocyclic musks), adjusting other ingredients to retain the properties of the fragrance as far as possible. This finding is in line with those in the TNO (2005) study which suggests that the reason for the higher additions of macrocyclic musks (compared with nitromusks and polycyclic musks) was that greater quantities may be required to achieve a similar profile.

The exact impact of this price differential on the cost of the final end-product is currently unclear. However, it is the case that the cost of producing a fragrance is dependent upon the number (quantity) and nature of ingredients used, with the cost of ingredients accounting for up to 50% of the fragrance price. The quantity of fragrance in the final product also varies, depending on the nature of the product. For a cosmetics manufacturer, fragrances could account for around 1% by volume on average, varying by product (for example perfumes contain a high proportion of fragrance by volume, whilst the fragrance content of a skin cream could be around 0.2% and soap around 1%). However, they are more expensive than other ingredients, contributing around 3% of raw materials cost. The average fragrance content of a household product is around 0.5% for laundry products and 0.2% for surface cleaners, but can be up to 1% for certain products. Again, the costs of fragrances are much higher than the costs of other ingredients and can account for 10% of the total ingredient costs. Overall, it is the case that the higher the number of ingredients, the greater the complexity and potentially the quality of the fragrance, so that there is a trade-off between quality and cost. The production process itself is relatively low-cost, due to its simplicity; however, the level of expenditure on R&D is relatively high, as product innovation is a continuous process (Defra & DTI, 2005).

Although no data are available for the use of macrocyclic musks in Europe, it is indicated that less than 25% of the musks produced worldwide in 1998 were macrocyclic musks; this number has been projected to grow to 60-65% by 2008 (mainly because of (perceived) risks associated with nitromusks and polycyclic musks) (Moore, 2005).

3.2.2.4 Alicyclic Musks

Alicyclic musks, otherwise known as cycloakyl ester or linear musks, are a relatively novel class of musk compounds, which have only recently (in the 1990s) been produced at a commercial scale. They are different in structure to the musks already discussed in that they are modified akyl esters. Common musks of this class include: cyclomusk, helvetolide and romandolide (Kraft, 2004; Marcus, 2004). No further information is currently available on these types of musks.

3.2.2.5 Other

In terms of alternative approaches to substitution, OSPAR (2004) notes that since fragrance compounds are such complex mixtures, replacement of nitromusks or polycyclic musks may be achieved by a variety of ways, including a change of brand-specific odours.

3.2.2.6 Summary of Technical and Economic Aspects

In summary, the available alternatives appear to be technically suitable for the various end-products in which they are used, however, it is important to keep in mind the complexity of replacing an odour simply by replacing a single substance. In practice, the odour profile for each compound is different and the resulting fragrance is a function of the manufacturing process as much as the type and quantity of musk compound used.

Regarding the economic feasibility of substitutes, it is clear that although macrocyclic musks appear to be more costly compared to musk xylene (and other musks), there is no indication that disproportionate impacts of substitution have been encountered and some companies have already incurred these costs in any case.

3.3 *Summary on Alternatives*

Table 3.5 below provides a summary of the picture across the various types of musks.

Table 3.5: Summary Comparison of Alternative Musks				
	Nitromusks	**Polycyclic**	**Macrocyclic**	**Alicyclic**
Availability and Future Trend	Decreasing use	Significant current use	Increasing use foreseen	Novel
Health/Environmental Risks	Have largely been phased out due to health and environmental concerns	Considered to be more acceptable compared with nitromusks	Appear to be more acceptable compared with other musks, but data gaps remain	Large data gaps at present
Technical Feasibility	Been used in the past but largely phased out	Been used for many years successfully	Been used more recently, but equally successfully	Still novel and, as far as aware, not widely tested
Economic Costs	Decreasing use which has been largely phased out	Account for a huge portion of the current market; costs are, therefore, not an issue	More expensive than the other musks. Market is, however, expected to increase significantly in future	Unknown

Across all the substances, it is considered that with regard to the:

- *availability of substitutes*: there are suitable alternatives to musk xylene on the European market (where these include other musk substances and/or alternative odours) and further research is still being carried out;

- *technical suitability of substitutes*: the available alternatives appear to be technically suitable for the various end-products in which they are used;

- *economic feasibility of substitutes*: although macrocyclic musks appear to be more costly compared to musk xylene (and other musks), there is no indication that disproportionate impacts of substitution have been encountered and some companies have already incurred these costs in any case; and

- *environmental and health impacts of substitutes*: there are some data gaps which may need to be addressed (for instance, for alicyclic and macrocyclic musks).

Overall, it is the case that the reduction of the use of musk xylene is currently on-going as an autonomous process without any regulatory pressure.

With the context of authorisation, it should also be noted that the use of musk xylene may be exempt from authorisation *when present in preparations below a concentration limit of 0.1% by weight*[13] (which applies only to substances listed in Annex XIV on the basis of being persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB), amongst others).

[13] OSPAR (2004) notes that the final concentration of fragrances (where this could include musk xylene and up to 50 other ingredients) in detergents and soaps ranges from 0.2 to 1%, although higher levels may be present in cosmetic products. It is, therefore, possible that the actual concentration of musk xylene only is below 0.1% in some consumer products or can be reduced below this threshold.

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Annex 1: List(s) of information requirements for priority setting and specification of conditions for authorisation

Table 1: Overview on tasks related to work package 1 (grey shaded fields not relevant)

Manufacture, trade and formation	**Process** (narrative description)	**Locations** (number of M sites; spatial distribution) [2]	**Tonnage manufactured, imported, exported or formed**	**Releases to working environment** [3]	**Releases to environment** (t/y released to air, wastewater or to waste)
Manufacture EU Process A					
Manufacture EU Process B					
Total Manufacture			**0 t/yr**		
Import subst. on its own			25 t/yr		
Import subst. in preparations			n/a		
Import subst. in articles[2]			n/a		
Import into EU (total)			**25 t/yr (downward trend)**		
Export subst. on its own			0		
Export subst. in preparations			n/a		
Export subst. in articles[1]			n/a		
Export from EU (total)			**0 t/yr**		
Global manufacture			**n/a**		
Unintentional formation during incineration (EU)	n/a				
Unintentional formation in processes (EU)	n/a				
Unintentional formation by transformation/degradation (EU)	n/a				
Total unintentional formation (EU)				**0 t/yr**	**0 t/yr**

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

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

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

Table 2: Overview on tasks related to work package 2 (grey shaded fields not relevant)

Uses	Use Process (description: narrative and by use descriptor system)	Amount used (t/y)	Number of sites of use [1] (#)	Spatial distribution of emission sites [1]	Releases to working environment [3]	Releases to environment (t/y released to air, wastewater or to waste)
Formulation						
Formulation 1	Detergents and Cleaning Products	~20 t/yr				
Formulation 2	Cosmetics and Toiletries	~5 t/yr				
∑ Formulation		**25 t/yr (downward trend)**	**<10**	**n/a**	**minimal**	
End uses						
End Use 1	Detergents and Cleaning Products	~20 t/yr		wide dispersive use		~20 t/yr
End Use 2	Cosmetics and Toiletries	~5 t/yr		wide dispersive use		~5 t/yr
∑ End Uses		**25 t/yr (downward trend)**		**wide dispersive use**		**25 t/yr**
Consumer use						
Substance in articles [2]		25 t/yr				n/a – articles do not contain musk xylene
Substance in preparations		**25 t/yr (downward trend)**	wide dispersive use	wide dispersive use		**13 tonnes/yr to water; 12 tonnes/yr to sludge**
∑ consumer use of subst. in articles and preparations						

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

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

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

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

YEAR n	**Manufacturing** (t/y)	**Manufacturing** # sites	**Formulation** (t/y)	**Formulation** # sites	**Use 1** (t/y)	**Use 1** # sites	**Use n** (t/y)	**Use n** # sites
Member state								
Austria								
Belgium								
…								
Total	**0**	**n/a**	**25t/yr**	**<10**	**25 t/yr**	**wide dispersive use**		

YEAR n+1	**Manufacturing** (t/y)	**Manufacturing** # sites	**Formulation** (t/y)	**Formulation** # sites	**Use 1** (t/y)	**Use 1** # sites	**Use n** (t/y)	**Use n** # sites
Member state								
Austria								
Belgium								
…								
Total	**0**	**n/a**	**25t/yr**	**<10**	**25 t/yr**	**wide dispersive use**		