SIDS Initial Assessment Report

For

SIAM 22

Paris, France, 18 – 21 April 2006

TOME 1: SIAR

Category Name **Long Chain Alcohols**

(C6-22 primary aliphatic alcohols)

1. and 2. Chemical Names and CAS numbers	**CAS no.**	**Chemical name**
	111-27-3	1-Hexanol
	111-87-5	1-Octanol
	112-30-1	1-Decanol
	112-42-5	1-Undecanol
	112-70-9	1-Tridecanol
	112-72-1	1-Tetradecanol
	629-76-5	1-Pentadecanol
	36653-82-4	1-Hexadecanol
	143-28-2	9-Octadecen-1-ol, (9Z)-
	629-96-9	1-Eicosanol
	661-19-8	1-Docosanol
	63393-82-8	Alcohols, C12-15
	66455-17-2	Alcohols, C9-11
	67762-25-8	Alcohols, C12-18
	67762-27-0	Alcohols, C16-18
	67762-30-5	Alcohols, C14-18
	67762-41-8	Alcohols, C10-16
	68551-07-5	Alcohols, C8-18
	68002-94-8	Alcohols, C16-18 and C18 Unsaturated
	68155-00-0	Alcohols, C14-18 and C16-18-unsatd.
	68333-80-2	Alcohols, C14-16
	68603-15-6	Alcohols, C6-12
	68855-56-1	Alcohols, C12-16
	75782-86-4	Alcohols, C12-13
	75782-87-5	Alcohols, C14-15
	80206-82-2	Alcohols, C12-14
	85566-12-7	Alcohols, C8-10
	85665-26-5	Alcohols, C10-12
	97552-91-5	Alcohols, C18-22
	90583-91-8	Tridecanol, branched and linear

3. Sponsor Country: United Kingdom

4. Shared Partnership with:	
5. Roles/Responsibilities of the Partners:	
- Name of industry sponsor /consortium	Global ICCA Aliphatic Alcohols Consortium
- Process used	The robust summaries were prepared by contractors to the Global ICCA Aliphatic Alcohols Consortium (GIAAC). The data matrix, SIAR and IUCLID dossiers were prepared by Shell Chemicals Ltd and a contractor, Peter Fisk Associates.
6. Sponsorship History	
- How was the chemical or category brought into the OECD HPV Chemicals Programme ?	
7. Review Process Prior to the SIAM:	All information was reviewed by the Global ICCA Aliphatic Alcohols Consortium. UK government (the Environment Agency of England and Wales, and MRC Institute for Environment and Health) peer-reviewed the SIDS documents, and audited selected key studies to check the robust study summaries.
8. Quality check process:	
9. Date of Submission:	
10. Date of last Update:	
11. Comments:	SIDS dossiers already existed for 1-Dodecanol (CAS 112-53-8) and 1-Octadecanol (CAS 112-92-5) (published in 1998 and 1995 respectively); the present document updates and extends the earlier ones; brings in new information, and therefore replaces it. No conclusions drawn in the earlier review are amended. Available data for these substances are compiled in SIDS dossiers related to each CAS number. The reliability of each data point has been considered during this period of review, in accordance with the guidance of the Fraunhofer Institut für Toxikologie und Aerosolforschung. The following standard reliability codes, defined by Klimisch *et al.* (1997)[1], apply, in accordance with the SIDS guidance: (1) Valid without restriction (2) Valid with restrictions (3) Invalid (4) Not assignable. Results considered to be Invalid are not used in the discussions or conclusions in this report. However, results which are of Non-assignable reliability may be fully valid, although

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[1] Klimisch, HJ, Andreae, E and Tillmann, U 1997. A systematic approach for evaluating the quality of experimental and ecotoxicological data. Reg.Tox. and Pharm. 25:1-5

insufficient details were available to be sure of this; therefore reliability (4) results are used in this report. The reliability code of each data point is given.

Key studies are flagged in the SIDS dossiers. These are studies with the highest reliability/adequacy. If several studies showed comparable reliability/ adequacy, the study with the lowest LC/LD/EC_{50} or NOEC/ NOAEL has been indicated as the key study. For some endpoints, fully reliable results are not available and it has been necessary to use a weight of evidence including results of studies of non-assignable reliability. In such cases the results are identified as key studies as they are of high importance to the data set.

For transparency, some study summaries in the SIDS dossier have been transferred from the previously published version of IUCLID or from the previous SIDS submission. In some cases, it has not been possible to retrieve the original literature/study reports using the reported citation or as a result of literature searching. In some cases, change of business ownership meant that internal study reports cited in previous summaries could not be accessed. In some other cases, e.g. certain non-SIDS endpoints, and in areas where a very large amount of literature has been published, it was not considered necessary to pursue all individual published sources due to weight of evidence of more reliable results. In all cases, reliability (4) applies, because the original documentation has not been reviewed in the development of the dossier. Such results are clearly identified in the SIDS dossier and more details are given therein.

SIDS INITIAL ASSESSMENT PROFILE

<table>
<tr><td>**Chemical Category Name**</td><td>Long Chain Alcohols (C6-22 primary aliphatic alcohols)</td></tr>
<tr><td>**CAS Nos**</td><td>
<table>
<tr><th>Chemical name</th><th>CAS no.</th><th>Chemical name</th><th>CAS no.</th></tr>
<tr><td>1-Hexanol</td><td>111-27-3</td><td>Alcohols, C16-18</td><td>67762-27-0</td></tr>
<tr><td>1-Octanol</td><td>111-87-5</td><td>Alcohols, C14-18</td><td>67762-30-5</td></tr>
<tr><td>1-Decanol</td><td>112-30-1</td><td>Alcohols, C10-16</td><td>67762-41-8</td></tr>
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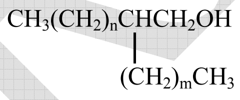
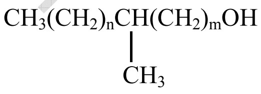
</table>
</td></tr>
<tr><td>**Structural Formula**</td><td>
<table>
<tr><td>$CH_3(CH_2)_nCH_2OH$</td><td>Linear
n = 4 to 20</td></tr>
<tr><td>$CH_3(CH_2)_nCH(CH_2OH)(CH_2)_mCH_3$</td><td>2-Alkyl branched
n + m = 3 to 18, and m is predominantly = 0.
Present in essentially-linear alcohols</td></tr>
<tr><td>$CH_3(CH_2)_nCH(CH_3)(CH_2)_mOH$</td><td>Other-methyl branching
n + m= 9 or 10
Present in essentially-linear Fischer-Tropsch derived alcohols</td></tr>
<tr><td>$CH_3(CH_2)_7CH=CH(CH_2)_7CH_2OH$</td><td>Unsaturated
9-Z unsaturated components are present in some commercial products.</td></tr>
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SUMMARY CONCLUSIONS OF THE SIAR

Category Rationale

This category covers a family of 30 primary aliphatic alcohols within a carbon chain length range of C6-C22. Commercial products generally include several aliphatic alcohol components, with a range of carbon chain lengths present. The family consists of alcohols with varying compositions and structures. Composition depends on the route to manufacture and the related feedstocks. Most of the alcohols have linear carbon chains but certain manufacturing processes create branched structures. Data are also available for eleven other similar substances, which support the category. Non-sponsored alcohols may not be HPV or may not be produced by members of the consortium, but have structures similar to sponsored linear alcohols.

Key points are that the members share:

- The same structural features
- Similar metabolic pathways
- Common mode of ecotoxicological action
- Common levels and mode of human health related effects.

This allows multi-component reaction products to be considered within the Category by the application of validated models of exposure and effects, on the basis of detailed knowledge of the composition. For the environmental end points, this has been done in two ways:

Read-across: this applies to biodegradability, for which sufficient data are available to allow read across from the pattern of degradation across the entire category to fill data gaps directly. For algae, read-across-based expert judgement was applied, taking into account measured and predicted effects in daphnids and fish for the substance of interest.

Modelling: a model of the ideal solubility of the components of the substances has been set up, which allows component and total solubility at any loading rate to be calculated. By use of knowledge of the properties of each component, ecotoxicological effects have been predicted.

Human Health

Considering the manufacturing processes two sub-categories of aliphatic alcohols can be distinguished:

- Linear alcohols: Saturated or unsaturated primary -non-branched- aliphatic alcohols containing an even number of carbon atoms.
- Essentially linear alcohols: Saturated, primary linear aliphatic alcohols and their saturated, mono branched primary alcohol isomers of corresponding carbon chain length

A detailed assessment of the toxicological database of both sub-categories shows that the linear and the essentially linear alcohols are of a low order of toxicity following acute and repeated exposures. The endpoints of skin and eye irritation show a trend within each of the sub-categories with the lower members of the category displaying a more pronounced response than the longer-chained-alcohols. The overall toxicological profile of the sub-categories of linear and essentially linear alcohols is qualitatively and quantitatively similar for all end points assessed. The observed relationship between chain length and toxicological properties is equally present for both sub-categories. Moreover, the mammalian metabolism of the aliphatic alcohols is highly efficient and proceeds similarly for each of the sub-categories. The first step of the biotransformation the alcohols are oxidised to the corresponding carboxylic acids, followed by a stepwise elimination of C2 units in the mitochondrial β-oxidation process. The metabolic breakdown of mono-branched alcohol isomers is also highly efficient and involves processes that are identical to that of the linear aliphatic alcohols. The presence of a side chain does not terminate the β-oxidation process, however in some cases a single Carbon unit is removed before the C2 elimination can proceed.

Surrogate and supporting substances have been assessed for this category in order to address potential concerns associated with differing degrees of branching and to justify the read-across within the sub-category of the essentially linear alcohols.

Aliphatic alcohols are absorbed by all common routes of exposure, widely distributed within the body and efficiently eliminated. There is a limited potential for retention or bioaccumulation for the parent alcohols and their biotransformation products.

The category of the long-chain aliphatic alcohols as a whole is of a low order of acute toxicity upon inhalational, oral or dermal exposure. The members of this category are generally of a low volatility and the acute lethal concentration exceeds the saturated vapour pressure. In most cases the acute oral and dermal LD50 values exceed the highest dose tested and, depending on the test protocol, range from >2000 to >10,000 mg/kg.

Overall, the toxicology database shows an inverse relationship between chain length and toxicity. The shorter chain alcohols tend to induce more pronounced effects when compared to materials with a longer chain length.

This is illustrated most clearly by the degree of irritation in skin and eye irritation studies in laboratory animal studies. For the aliphatic alcohols in the range C6 – C11 a potential for skin and eye irritation exists, without concerns for tissue destruction or irreversible changes. Aliphatic alcohols in the range C12 – C16 have a low degree of skin irritation potential; alcohols with chain lengths of C18 and above are non-irritant to skin. The eye irritation potential for alcohols with a chain length of C12 and above has been show to be minimal.

Aliphatic alcohols have no skin sensitisation potential.

Repeated exposure to aliphatic alcohols is generally without significant systemic toxicological findings and this category is therefore regarded to be of a low order of toxicity upon repeated exposure At the lower end, members of this category induce local irritation at the site of first contact. Other notable findings observed for several members within this group suggest mild changes consistent with low-grade liver effects with the changes in essentially linear alcohols being slightly more pronounced than in linear alcohols. Typical findings include: slightly increased liver weight, in some cases accompanied by clinical chemical changes but generally without concurrent histopathological effects. Special studies demonstrated that this category does not have a potential for peroxisome proliferation. CNS effects were absent upon inhalation or dietary administration, however 1-hexanol and 1-octanol showed a potential for CNS depression upon repeated administration of a bolus dose. Similarly, 1-hexanol and 1-octanol induced respiratory distress upon repeated administration of a bolus dose. Aliphatic alcohols do not have a potential for peripheral neuropathy. Typical NOAEL's recorded for this category range between *ca*. 200 mg/kg/day to 1000 mg/kg/day in the rat upon sub-chronic administration via the diet.

Several members of the long chain aliphatic alcohol category were used as a vehicle or solvent in chronic skin painting studies. Although the validity of such experiments is limited, there was no evidence of a carcinogenic potential for this category. Long chain aliphatic alcohols do not contain structural elements of concern for potential interaction with DNA and have been shown to be without mutagenic activity, primarily on the basis of Ames assays and mouse micronucleus assays.

On the basis of the lack of adverse findings in the reproductive organs in repeated dose toxicity studies and in screening studies for reproductive effects this category is considered without a potential for adverse effects on fertility and reproductive toxicity. Similarly, developmental toxicity studies in substances belonging to this category and aliphatic alcohols supporting this category studies have confirmed the lack of potential adverse effects on the developing foetus.

Environment

The general trends in the data show properties that vary with carbon chain length in accordance with normal expectations. As carbon chain length increases melting point increases, boiling point increases and vapour pressure decreases; one consequence of this is that flash point temperatures increase at higher molecular weight. Water solubility decreases and the octanol-water partition coefficient increases with increasing carbon chain length.

Physicochemical properties vary, as described, across members of the Category. Ranges of key property values are:

- Melting point: from ca. –50°C *(measured; Hexanol)* to +72.5°C *(measured; Docosanol)*
- Boiling point: from 158°C *(measured; Hexanol)* to ca. 400°C *(upper limit of measured boiling range for C18-22 alcohols, supported by estimated value for Docosanol)*
- Density: from ca. 0.80 g/cm^3 to ca. 0.85 g/cm^3 *(measured; range across category)*
- Vapour pressure: from 8.2E-08 hPa *(estimated; Docosanol)* to 1.22 hPa *(measured; Hexanol)*
- Water solubility: from ca. 0.001 mg/l *(measured; Octadecanol)* to 5900 mg/l *(measured; Hexanol)*
- Partition coefficient: from 2.03 *(measured; Hexanol)* to >7 *(measured, Eicosanol)*

Environmental Fate

Reliable measured data show that alcohols with chain lengths up to C18 are readily biodegradable *(measured; hexanol, octanol, decanol, dodecanol, tetradecanol, hexadecanol and octadecanol)*. At carbon chain lengths up to C16, most tests showed that pass levels for ready biodegradation were reached within the 10-day window, with removal levels up to 100% over the timescale of the test. Chain lengths of C16-18 achieved ready test pass levels (62% to 76% in tests on single chain lengths) but not within the 10 day window. The one test on a single carbon chain length greater than C18 (docosanol) showed degradation of 37%. In additional studies conducted at environmentally realistic concentrations with radiolabelled substances (C12-16), very high rates of degradation have been measured (very rapid rate constants, with ca. 75-85% removed as CO_2 and metabolites).

These rates accord with field data for measured concentrations in waste-water treatment plant influent and effluent showing greater than 99% removal for carbon numbers 12 to 18. This summary of degradation is applicable to both linear and branched components of substances in the category. Therefore, the whole category is considered to show very high levels of biodegradability. Rapid degradation is also indicated by the removal rates in the chronic aquatic toxicity tests for the lower solubility substances (C10 to C15), where rapid removal of the substance from the test medium was observed, most likely due to biodegradation by micro-organisms.

All of the alcohols in this group would be expected to be stable in respect of abiotic degradation in water. Photo-oxidation in aqueous systems will not be significant. Alcohols have no hydrolysable groups and are therefore not susceptible to hydrolysis. Oxidation would not be expected under normal environmental conditions.

The substances are susceptible to atmospheric degradation by hydroxyl radicals, with half-lives ranging between ca. 10-30 hours (based on measured and estimated rate constants, for a hydroxyl radical concentration of 5E+05 molecules/cm^3). Longer chain lengths have shorter estimated half-lives within this range.

No reliable guideline-standard measured bioconcentration data are available. Bioconcentration factors (BCF) calculated on the basis of log Kow range from 7.0 for C6 to a maximum of 46000 for C16, reducing to 1100 for C22. For hexadecanol, the BCF (Q)SAR estimates a value of 45300 (recalculated from the parabolic Connell and Hawker equation), but a measured value of 56 and a range of values from 507-1550 from two unreliable studies exist; BCF data for alcohols similar to those in this family but with 2.1-2.9 branches per molecule also indicate that BCF (Q)SAR overestimate BCF. Log Kow-based BCF (Q)SAR predictions also take no account of biotransformation/metabolism of alcohols in living organisms, the natural mechanism for their removal. For these reasons it is expected that category members will have a low potential for bioaccumulation.

Fugacity modelling shows that the predicted fate of all of the Category members varies depending on the route of release into the environment. For chain lengths C10 and above, alcohol released to water is predicted to partition into sediment. When alcohols are released to air, for chain lengths C14 and above, less than half of alcohol ultimately present in the environment can be found in air.

The situation for modelling exposure of multi-component substances is complicated by the fact that, given a particular route of exposure, each component will behave independently on release to the environment.

Effects on aquatic organisms

Alcohols in this Category act by non-polar narcosis and demonstrate a similar order of magnitude of toxicity in fish, invertebrates and algae. For pure substances, as chain length increases, lipophilicity increases and aqueous solubility decreases. There is an associated increase in aquatic toxicity up to a limiting chain length, at which very low aqueous solubility limits the bioavailable concentration of the alcohol in the water, resulting in a concentration at which no effects are exerted (the cut-off). Consequently, longer chain lengths show no toxicity. For aquatic organisms the chain length cut-off for acute effects lies at C13 to C14 (depending on the test species). For chronic effects, the cut-off for effects in invertebrates is in the region of C15. [The cut-off for chronic effects is probably not a limitation due solely to solubility, but is due to a limitation of the concentration at the site of action. This is not an artefact of the protocol used for the studies].

Effect concentrations vary, as described, across members of the Category. Ranges of key property values, including lowest and highest measured data as well as lowest estimated values as appropriate, are:

- Acute effects in fish (96h LC_{50}): from 0.48 mg/l *(estimated, C12-14 alcohols)* and 0.7-0.8 mg/l *(nominal, C6-12 alcohols)* to 97 mg/l *(measured, Hexanol)*. No effects up to limit of water solubility for single chain lengths >C13-14 and for some multi-component substances.
- Acute effects in invertebrates (EC_{50}): from 0.13 mg/l *(48h estimated, C14-16 alcohols)* and 0.8-1.1 mg/l *(96 h nominal, 1-undecanol)* to 200 mg/l *(24h nominal, Hexanol)*. No effects likely up to the limit of water solubility for single chain lengths >C13 and for some multi-component substances.
- Acute growth rate effects in algae (72 h E_rC_{50}): from ca. 0.1 mg/l *(nominal, C10-16 and C12-16 alcohols, and estimated for various substances)* to 80 mg/l *(measured, Hexanol)*. No effects likely up to the limit of water solubility for single chain lengths >C14 and for some multi-component substances.
- Chronic effects in invertebrates: 21-day $NOEC_{repro}$ from 0.0098 mg/l *(measured, tetradecanol, based on mean measured initial concentration)* to 1 mg/l *(measured, octanol)*. No effects are expected for single chain lengths >C15 up to limit of aqueous solubility.

In this assessment, trends between aquatic toxicity and carbon chain length are based on normal (linear) alcohols, since data do not exist on single carbon chain length, essentially-linear, alcohols. However, the comparability of the toxicity of straight chain and essentially linear alcohols is shown by a comparison of commercial products. The data sets for essentially pure substances have been interpreted in terms of conventional (quantitative) structure-activity relationships ((Q)SARs), by correlation of the effect concentrations with octanol-water partition coefficients.

In summary, the ranges of expected environmental behaviours of these substances could be characterised as follows.

- For short chain category members (≤C11): high solubility; acute toxicity to aquatic organisms in the range 1-100 mg/l, chronic toxicity to aquatic organisms in the range 0.1-1.0 mg/l; readily biodegradable;
- For mid-range chain length category members (C11-C13): low solubility; acute toxicity in the range 0.1-1.0 mg/l, well-characterised chronic toxicity to aquatic organisms in the range 0.1-<1.0 mg/l; very high biodegradability (readily biodegradable with extremely high removal in environmentally relevant concentrations);
- For longer chain length category members (C14-15): low solubility limits bioavailability and hence acute effects are unlikely to be expressed, well-characterised chronic toxicity to aquatic organisms in the range 0.01 mg/l – limit of solubility; very high biodegradability (readily biodegradable with extremely high removal in environmentally relevant concentrations);
- For the longest chain category members (≥C16): low solubility limits the dissolved (and hence bioavailable) concentration of the alcohol to the extent that neither acute nor chronic toxicity are likely to be exhibited; also significantly biodegradable (considered equivalent to inherent biodegradation; very extensive removal seen under environmentally relevant conditions) but more adsorbing than the lower homologues.

Exposure

Total global production of these long chain aliphatic alcohols by consortium members in 2002 was estimated as approximately 1580 thousand metric tonnes annually. Approximately 50% of the total production volume is used directly in final products (industrial/commercial products and various consumer/personal care products). The remainder is processed as an intermediate (with approximately 65% of the intermediate volume being site limited).

Exposure could arise in association with production, formulation and industrial use of these substances. Within commercial use, the substances are used principally as synthetic intermediates with low expected release levels. For the 50% of Category members intentionally used directly in industrial/commercial and consumer products, release to the environment can be anticipated (especially via waste water treatment plant effluent after disposal to drain). Monitoring data are available from wastewater treatment plant effluents in USA, Canada, UK, Netherlands, Spain, Italy and Germany. The 90th percentile for individual monitored effluent measurements worldwide, not accounting for treatment type and flow, is 2.121 µg/L and the global average is 1.057 µg/L. Modelled (SIMPLETREAT) mixing zone concentration is estimated at ~ 0.02 µg/L from a manufacturing plant.

These substances are also produced naturally, in all living organisms, from bacteria to man, and thus are widely present throughout the natural world. It is clear that measurements of long chain alcohol in environmental matrices will reflect the combination of both natural and anthropogenic sources. An environmental exposure assessment is available in the Annex and: (http://www.bangor.ac.uk/~oss034/Fatty_Alcohol_Natural_and_Anthropogneic_Sources.doc).

Occupational Exposure: As a rule aliphatic alcohols are manufactured and processed in established chemical complexes in closed installations; these are usually operated at high temperature and pressure. At these sites standard personal protective equipment is routinely applied to prevent direct skin and eye contact. Generally, aliphatic alcohols are of a low volatility and as a rule engineering controls are available preventing the need for respiratory protection. For non-routine operations involving a break in enclosed systems a higher level of protection is applied. Operations with a potential for significant exposure require a permit to work system and a case-by-case assessment is made for appropriate protective measures. Exposure through the use of products in industry and commerce is mitigated by applying measures aimed to prevent direct skin and eye contact by following the recommendations in the material safety data sheet (MSDS).

Consumer Exposure: Aliphatic alcohols are formulated in consumer laundry, cleaning and personal care products. Product labels reflect the hazard potential of the chemical ingredients in these products and include first aid instructions in case of non-intentional exposure.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemicals of the category of the long chain aliphatic alcohols are of low priority for further work. The members of this category are of a low order of toxicity by all common routes of exposure upon acute or repeated exposure. Overall, the toxicology database for this category shows an inverse relationship between chain length and toxicity. The key human health hazards identified for this category are the irritative properties for skin and eye of aliphatic alcohols with chain lengths of C11 or below. These hazards are well characterized and do not lead to tissue destruction or irreversible changes. They should nevertheless be noted by chemical safety professionals and users.

Environment: The category comprises a homologous series of linear and essentially linear C6 - 22 alcohols. Increasing carbon chain length leads to a predictable pattern in physico-chemical properties; this drives a distinct range of fate behaviours in the environment. Category members all have the same mode of ecotoxicological action. In addition, all of the category members are rapidly biodegradable especially at environmentally relevant concentrations. Alcohols are metabolised/biotransformed in living organisms; this biotransformation suggests that bioaccumulation potentials based on octanol-water partition coefficients may be overestimates. Measured BCF data on a related alcohols Category supports the concept that the bioaccumulation potential of these substances will be lower than estimated from log Kow.

Many of the substances in the category do not present a hazard for the environment (acute aquatic toxicity >100 mg/l, or above water solubility with no effects exhibited) and are of low priority for further work. These category members are CAS Numbers: 36653-82-4, 629-96-9, 661-19-8, 143-28-2, 67762-27-0, 67762-30-5, 97552-91-5, 68155-00-0.

Some of the substances in this category present a hazard for the environment (acute toxicity to fish, daphnids and algae in the range 1 - 100 mg/l). However all of these substances are readily biodegradable. Therefore these subgroup members are of low priority for further work. These subgroup members are CAS Numbers: 111-27-3, 111-87-5, 85566-12-7, 67762-25-8, 68002-94-8.

The remaining substances in the category present a greater hazard for the environment (high acute toxicity to fish, daphnids and algae, in the range 0.1 - 1 mg/l, and/or high chronic toxicity). The substances in this subgroup biodegrade rapidly and environmental monitoring data from seven countries indicates exposures to the environment is anticipated to be low and are included in an Annex to the SIAR. The chemicals in this subgroup that should be candidates for further work by member countries, who are invited to perform an exposure assessment and, if necessary, a risk assessment, are CAS Numbers: 112-30-1, 112-42-5, 90583-91-8, 112-70-9, 112-72-1, 629-76-5, 68603-15-6, 67762-41-8, 68855-56-1, 63393-82-8, 66455-17-2, 68333-80-2, 75782-86-4, 75782-87-5, 80206-82-2, 68551-07-5, 85665-26-5.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substances

This SIAR addresses a family of primary aliphatic alcohols within a carbon chain length range of C6-C22. It covers 30 long chain alcohols, which in turn describe almost 100 commercial products in total (see Confidential Annex A). Commercial products generally include several aliphatic alcohol components, with a range of carbon chain lengths present. The family consists of alcohols with various compositions and structures. Composition depends on the route to manufacture and the related feedstocks. Most of the alcohols have linear carbon chains but certain manufacturing processes create branched structures. More details are provided below.

The commercial industrial processes used to produce alcohols in some cases necessarily result in a spread of carbon number, and some alkyl chain branching. In addition, a limited number of unsaturated substances very similar to the saturated analogues are included. The category justification is given in section 1.4.

Data are also available for eleven other similar substances, which support the category. Non-sponsored alcohols may not be HPV or may not be produced by members of the consortium, but have structures similar to sponsored linear alcohols.

Long chain aliphatic alcohols are manufactured by a number of processes, but these can be divided into two general categories:

> **Oleochemical** - the feedstocks for the most common oleochemical-based processes include plant or animal based oils or fats: coconut, palm kernel oil and tallow fat, or other triglycerides.
>
> **Petrochemical** - the most commonly used processes use different petroleum-based feedstocks - olefins (alpha and internal), ethylene, propylene oligomers.

Some commercially available products are blends of two or more specific chain length alcohols to produce mixtures.

Different manufacturing methods can lead to different compositional profiles: further details are given in section 1.1.1 below. In addition to this summary, detailed compositional data of the alcohols in this family have been provided in Confidential Annex A to this SIAR.

The basis of the environmental section of the SIAR will be an analysis with reference to carbon chain length, including cross-reference to commercial multi-component substances. The human health portion of this SIAR focuses on an analysis of commercial products.

1.1.1 Synthetic routes and associated structural characteristics

Production processes based on oleochemical feedstocks

There are two major commercial processes for converting oleochemicals to alcohols:

> **Methyl ester hydrogenation** – coconut and palm kernel oils and tallow fat are the major feedstocks for this route to alcohols. The triglycerides that compose the major raw materials are first subject to transesterification with excess methanol using an alkaline catalyst. The resulting fatty acid methyl esters are subject to distillation and then may be converted to alcohols by hydrogenation.
>
> **Fatty acid hydrogenation** – this process involves the hydrolysis of fats and oils to the corresponding fatty acids followed by the direct catalytic hydrogenation to alcohols.
>
> Alcohols manufactured by oleochemical processes have a linear structure and an even-numbered carbon chain usually in the range C6 to C22. Some members of this category may contain unsaturated primary alcohols.

Production processes based on petrochemical feedstocks

The commercial processes generally used for converting petrochemical feedstocks to alcohols are:

> **From ethylene via the Ziegler process** – like the alcohols manufactured by oleochemical processes those derived from ethylene via Ziegler chemistry have a linear structure and an even-numbered carbon chain usually in the range C6 to C22.
>
> **From olefins via OXO and modified-OXO synthesis -** the olefin precursors may be linear alpha-olefins (1-alkenes), or linear internal olefins, or mixtures of the two and are reacted with mixture of carbon monoxide and hydrogen. The alcohols produced have one more carbon than the olefin feed and consist of linear alcohols and their corresponding mono C2-alkyl isomers (predominantly methyl) and may fall in the range C7 – C17, contain even and odd numbered carbon chains. The proportion of linear alcohols ranges from approximately 90 to 50% depending on the feed selection and type of OXO process.
>
> In some cases the ca. 50% linear alcohols are further processed by physical separation techniques to obtain:
>
> a. alcohols of approximately 95% mono-branched at the 2-position, predominantly 2-methyl;
>
> b. alcohols of approximately 95% linearity
>
> **From olefins derived from the Fischer-Tropsch process** – the resulting C12-C13 alcohol consists of approximately 50% linear, 30% mono-methyl branched and 20% other unintended components.

A summary of the above is presented in Table 1.1 overleaf.

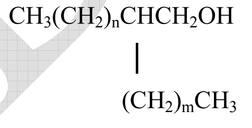
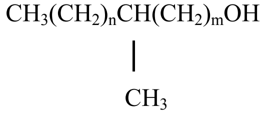
Table 1.1.Summary of alcohol production processes

Process	Feedstock	Carbon chain length range	Carbon chain length distribution	Typical linearity ranges
Methyl Ester Hydrogenation	Fats and oils	C6-C22	Even carbon numbers	Linear
Fatty Acid Hydrogenation	Fats and oils	C6-C22	Even carbon numbers	Linear
Conventional OXO	Olefin (alpha or internal or both)	C7-C15	Odd and even carbon numbers	50-60% linear, remainder mono-branched at the 2-position, predominantly 2-methyl
Further processing		C9-C15	Odd and even carbon numbers	5% linear, 95% mono-branched at the 2-position, predominantly 2-methyl *and* 95% linear, remainder mono-branched at the 2-position, predominantly 2-methyl
Modified OXO	Olefin (alpha or internal or both)	C7-C17	Odd and even carbon numbers	75-90% linear, remainder mono-branched at the 2-position, predominantly 2-methyl
Ziegler Oxidation	Ethylene	C6-C22	Even carbon numbers	Linear
Fischer-Tropsch	Syngas	C12-C13	Odd and even carbon numbers	50% linear, 30% mono-branched, 20% other unintended components

1.1.2 Overview of composition

The chemical structures of Category members (sponsored and supporting substances) are described in Table 1.2 below.

Table 1.2 Overview of composition

Molecular Formula:	**$C_xH_{(2x+1)}OH$ where x = 6 to 22**	
Structural Formulae:	$CH_3(CH_2)_nCH_2OH$	Linear n = 4 to 20
	 $CH_3(CH_2)_nCH(CH_2)_mCH_3)CH_2OH$	2-Alkyl branched n + m = 3 to 18, and m is predominantly = 0. Present in essentially-linear alcohols
	 $CH_3(CH_2)_nCH(CH_3)(CH_2)_mOH$	Other-methyl branching n + m= 9 or 10 Present in essentially-linear Fischer-Tropsch derived alcohols
	$CH_3(CH_2)_7CH{=}CH(CH_2)_7CH_2OH$	Unsaturated 9-*Z* unsaturated components are present in some commercial products.
Molecular Weight:	102 to 326	

The alcohols that have chiral centres are prepared as racemic mixtures. This is not considered to be relevant to the behaviour of the substances under standard test conditions, in the environment or *in vivo*.

The term 'mixture' in chemical terms can be interpreted specifically to mean a deliberate blend or preparation of substances. In general, for multi-component substances which are reaction products, the term 'complex mixture' is commonly used in the chemical industry. 'Mixture' in its more colloquial sense has been used by some authors to refer to multi-component alcohols, including complex reaction products. This term may appear in this report and its supporting documents in places and should not be over-interpreted.

1.1.3 Compositional types for sponsored substances

For certain CAS numbers in the long chain aliphatic alcohols Category, commercially available products are not necessarily of identical (or near-identical) composition. They may fall into two or more compositional types with different compositional characteristics, e.g. in terms of proportion of branched components or proportion of longer or shorter carbon chain lengths within the stated range.

In some cases these variations could mean that the different types of commercial products would have quite different properties, and so it is important to distinguish them, for the correct scientific interpretation of the data set. Therefore, for the purposes of this work, the types have been formally differentiated. These are referred to in the respective SIDS dossiers and in this SIAR as Type A, Type B etc. This approach provides a more detailed context than simply reporting test results by CAS number, it allows test results for different commercial products to be grouped, as appropriate, while maintaining confidentiality regarding more sensitive details such as more detailed compositional data for specific commercial products.

Please note that these Type notations apply specifically to the present work programme and are not used in commercial product specifications or the CAS registry system.

Compositional descriptions are presented in Table 1.3. Further data are confidential, and are presented in Confidential Annex A.

Table 1.3 Compositional information on members of the Category

CAS	CHEMICAL NAME	DESCRIPTION
Explanation of the format used for the Description: X% Linear; Y% specific chain lengths [range A-B]; Even/Odd X: the proportion of linear alcohol components across all chain lengths. The remainder are branched Y: the proportions of components present at 'significant' proportions. Components present at <5% w/w are omitted from this part of the description A – B: the stated 'range' includes all identified components present (including those present at <5%) 'Even' and 'Odd' refer to carbon chain lengths present		
111-27-3	1-Hexanol	100% Linear; >95% C6 [range C6-C10]; Even
111-87-5	Octyl alcohol	100% Linear; >90% C8 [range C6-C10]; Even
112-30-1	1-Decanol	100% Linear; >90% C10 [range C8-C12]; Even
112-42-5	Undecyl alcohol	>80% Linear; >95% C11 [C9-C14]; Even & odd
112-70-9	1-Tridecanol	>80% Linear; >90% C13, <10% C12 [range C12-14]; Even & odd
112-72-1	1-Tetradecanol	100% Linear; >95% C14 [range C12-C16]; Even
143-28-2	9-Octadecen-1-ol, (9Z)-	100% linear; >70% C16/18, <10% C14, including >70% C18 unsaturated [range C12-C20]; Even
36653-82-4	1-Hexadecanol	100% Linear; >=95% C16 [range C14-C18]; Even
629-76-5	1-Pentadecanol	>80% Linear; >90% C15, <10% C14 [range C14-15]; Even & odd
629-96-9	1-Eicosanol	>80% Linear; >=90% C20 [range C18-22]; Even
63393-82-8	C12-15 Alcohols	>40% Linear; >95% C12/13/14/15 range [range C10-C17]; Even & odd Type A. >80% Linear; >95% C12/13/14/15 range C10-C17]; Even & odd Type B. 40-50% Linear; >95% C12/13/14/15 [range C11-C16]; Even & odd
661-19-8	1-Docosanol	100% Linear; >95% C22; Even
66455-17-2	C9-11 Alcohols	>80% Linear; > 95% C9/10/11 [range C8-12]; Even & odd
67762-25-8	C12-18 Alcohols	100% Linear; >95% C12/14/16/18 [rangeC8-C20]; even Type A. 100% Linear; >50% C12/C14; >10% C16/C18 [range C8-C20]; even Type B. 100% Linear; >10% C12/C14; >60% C16/C18 [range C12-C20]; even
67762-27-0	C16-18 Alcohols	100% linear (or unstated); <10% C14, >=90% C16/18 [range C12-C20]; Even
67762-30-5	C14-18 Alcohols	100% Linear (or unstated); >95% C14/16/18 [rangeC10-C20]; Even Type A. 100% Linear (or unstated); >=95% C16/18 [rangeC12-C20]; Even Type B. 100% Linear (or unstated); >95% C14/16/18 [rangeC10-C20]; Even
67762-41-8	C10-16 Alcohols	5-100% Linear; C10-16 alcohols [range C8-18]; Even or Even & odd Type A. 100% Linear; >80% C10/12/14, <10% C16 [range C8-C18]; Even Type B. 5-50% Linear; >=95% C12/13 [range C11-C14]; Even & odd Type C. 80-95% Linear; >95% C12/C13 [range C11-15]; Even & odd Type D. 40-50% Linear; >95% C12/13/14/15 [range C11-C16]; Even & odd
68002-94-8	C16-18 and C18 Unsaturated	100% linear; >70% C16/C18, <10% C14, including 40-90% C18 unsaturated [range C12-C22]; Even
68155-00-0	Alcohols, C14-18 and C16-18-unsatd.	Linearity unspecified; 5-50% C16,18 saturated, 40-90% C16,18 unsaturated [range C14-C18]; Even
68333-80-2	C14-16 Alcohols	5-95% Linear; >95% C12/13/14/15 [range C11-16]; Even & odd Type A. 5-95% Linear; >95% C14/15 [range C12-17]; Even & odd Type B. <=5% Linear; >95% C12/13/14/15 [range C11-C16]; Even & odd
68551-07-5	C8-18 ALCOHOLS	100% Linear; 5-30% C8/10, >60% C12/14/16/18 [range C8-20]; Even.

CAS	CHEMICAL NAME	DESCRIPTION
68603-15-6	C6-12 Alcohols	5-100% Linear; C6-12 alcohols [range C6-13]; Even or Even & odd, as follows: Type A. 5-95% Linear; >= 95% C11 [range C9-C13]; Even & odd Type B. >80% Linear; > 95% C9/10/11 [range C8-C12]; Even & odd Type C. >80% Linear; > 95% C7/8/9 [range C6-C10]; Even & odd Type D. 100% Linear; >=90% C8/10; <10% C6 [range C6-C12]; Even
68855-56-1	C12-16 Alcohols	40-100% Linear; C12-16 alcohols, >95% C12/13/14/15 [range C8-C18]; Even or Even & odd Type A. >40% Linear; >95% C12/13/14/15 [range C10-C17]; Even & odd Type B. 100% Linear; >80% C12/14, <20% C16 [range C8-C18]; Even Type C. 100% Linear; <10% C12, >90% C14/16 [range C10-C18]; Even
75782-86-4	C12-13 Alcohols	>80% Linear; >95% C12/13 [range C11-C15]; Even & odd
75782-87-5	C14-15 Alcohols	>80% Linear; >95% C14/15 [range C12-17]; Even & odd
80206-82-2	C12-14 Alcohols	100% Linear; >95% C12/14/16 [rangeC6-C18]; Even Type A. 100% Linear; >90% C12/14 (C12>14), <10% C16 [range C6-C18]; Even Type B. 100% Linear; >95% C12/14 (C12<14) [range C8-C18]; Even
85566-12-7	C8-10 Alcohols	100% Linear; > 80% C8/10, <=5% C6, <10% C12 [range C6-C12]; Even
85665-26-5	Alcohols, C10-12	100% Linear; >90% C10/12, <=5% C14 [range C8-C16]; Even
90583-91-8	Tridecanol, branched and linear	5% Linear; >95% C13; Odd
97552-91-5	C18-22 Alcohol	100% Linear; >95% C18/20/22 [range C16-C24]; Even

The single-component alcohols form a homologous series of increasing carbon chain length. The multi-component substances are reaction-products containing these single substances.

Note regarding data tables in this report:

For presentation in data tables, the alcohols are ranked in order of increasing chain length. Products which are multi-component substances, containing alcohols of various different chain lengths, have been positioned in the tables based on the component with lowest carbon chain length present, above a level of ≥5% w/w. The variation between compositional 'types' means in some cases that values for different 'types' of the same CAS number are not presented sequentially in the tables.

1.1.4 Supporting substances

In order to support some areas of both human health and environmental assessment, data from some alcohols that are not part of the sponsored family have been included. Some of these substances support specifically the environmental or human health data sets, or only relate to a few endpoints. Data for supporting substances is used primarily to assist in filling of data gaps for sponsored substances, as follows:

- in the validation of property prediction for physicochemical and environmental properties, and
- to allow read-across for human health data.

Full substance-specific dossiers have not at this stage been prepared for these substances.

It is not the intention of this report to draw conclusions for the supporting substances, and it would be wrong to read the conclusions of this report across to them in the absence of a similarly in-depth review of the full data sets of those substances specifically.

The supporting substances are as follows:

Supporting (environment and human health):

111-70-6	1-Heptanol
112-53-8	1-Dodecanol
112-92-5	1-Octadecanol
143-08-8	1-Nonanol

Supporting (human health only):

104-76-7	1-Hexanol, 2-ethyl-
123-51-3	1-Butanol, 3-methyl- *(Isoamyl alcohol)*
85566-14-9	Alcohols, C7-11-branched and linear
123607-66-9	Alcohols, C24-34 *(D002 (C24, C26, C28, C30, C32, C34))*

Supporting (environment only):

68516-18-7	Decene, hydroformylation products
68527-05-9	Octene, hydroformylation products
70955-11-2	Hexene, hydroformylation products

1.2 Purity/Impurities/Additives

The substances in this category have a range of purity. Some information is confidential. Non-confidential data are summarised in Table 1.3 above.

Some of the substances contain other alcohols (e.g. decanol may be present in commercial dodecanol). In the context of the category, these are considered to be by-products rather than impurities. True impurities, possessing a chemical structure different from the definition of the category, are not present in these substances.

1.3 Physico-chemical properties

Measured physicochemical property data are presented in Tables 1.4 to 1.10. Please note that the dissociation constant pKa is omitted. Long chain aliphatic alcohols are extremely weak acids and only dissociate under strongly basic conditions (pH >16 approximately). In the range of pH usually considered relevant to the environment, i.e. pH 4-9, these substances will be non-ionised.

The search strategy used to collect data on physicochemical and other endpoints is shown in Section 7.

In this section, measured values are given first, with their sources. Annex I gives the detail of how quantitative structure-activity relationship ((Q)SAR) methods have been used to fill data gaps. At the end of Section 1.3, Table 1.11 presents a set of recommended values for all the properties, from measurement or (Q)SAR. For multi-component substances, the value appropriate to a particular property has usually to be represented as a range. For substances with more than one compositional 'type', values for key properties such as solubility, log K_{ow} and vapour pressure have been estimated for each compositional type where measured data are not available. It was not considered necessary to do this for all physicochemical properties as it was not essential for understanding of the data set.

Since many of the measured physicochemical data are in the form of secondary literature, the validity has been judged based on the reference given. Values from authors such as Yalkowsky (water solubilities) and Daubert and Danner (vapour pressures) are judged to be highly reliable and have been accorded reliability 2. Values from other authors, when taken from sources known to use a high standard of peer review in the compilation process (e.g. the CRC handbook) have also been given reliability 2.

1.3.1 General trends in the data

The general trends in the data show properties that vary with the carbon chain length in accordance with normal expectations: as it increases, then the following generalisations apply:

- Melting point, boiling point increase and vapour pressure decreases, because molecular weight is higher and intermolecular forces in the substance are all higher; one consequence of this is that flash point temperatures increase at higher molecular weight;

- Water solubility decreases because the free energy required for a molecule to dissolve becomes less favourable for larger molecules;

- Similarly, the octanol-water partition coefficient increases with molecular weight, since each additional CH_2 group makes the octanol phase more preferable in terms of relative solvation energy.

Table 1.4 Measured melting point data

CAS No	Chemical Name	Comment[1]	Melting Point (°C)	Reliability	Source
111-27-3	1-Hexanol		-44 to -51	4	Verschueren, 1996
111-70-6	1-Heptanol	Supporting	-34	4	Verschueren 1996
111-87-5	1-Octanol		-15.5 to -17	2	Budavari, 1996
143-08	1-Nonanol	Supporting	-5	4	Verschueren, 1996
112-30-1	1-Decanol		6.4	2	Lington and Bevan, 1994, Budavari, 1996,
112-42-5	1-Undecanol		14.3 11 to 19	4 4	Lington and Bevan 1994 Verschueren, 1996
112-53-8	1-Dodecanol	Supporting	22.6 to 24	4	Budavari, 1996
112-70-9	1-Tridecanol		30.6 32 to 33	4 4	Lington and Bevan, 1994 Verschueren, 1996
112-72-1	1-Tetradecanol		39-40	2	CRC - Lide 1999
629-76-5	1-Pentadecanol		44 45-46	4 4	Lington & Bevan, 1994 SRC, on-line database
36653-82-4	1-Hexadecanol		50	2	CRC - Lide 1999
112-92-5	1-Octadecanol	Supporting	58 59.5	4 4	Lington and Bevan, 1994 SRC on-line, database

CAS No	Chemical Name	Comment[1]	Melting Point (°C)	Reliability	Source
143-28-2	9-Octadecen-1-ol, (9Z)-		13-19	2	Budavari, 1989
629-96-9	1-Eicosanol		66.0 64-68	4 4	Lington and Bevan, 1994 Condea technical data sheet
661-19-8	1-Docosanol		72.5	2	CRC - Lide 1999
66455-17-2	C9-11 Alcohols		Ca. -21	4	unreferenced; IUCLID 2000 CD-ROM
67762-41-8	C10-16 Alcohols	Type B	0	1	Sasol, Sastech Research and Development, 1998
67762-41-8	C10-16 Alcohols	Generic/not possible to determine which Type	18.5	4	IUCLID datasheet, 1995a
80206-82-2	C12-14 Alcohols	Generic/not possible to determine which Type	Solidification point 17-23	4	Henkel MSDS
68855-56-1	C12-16 Alcohols	Generic/not possible to determine which Type	21	4	IUCLID datasheet, 1995c
67762-25-8	C12-18 Alcohols	Generic/not possible to determine which Type	Solidification range 25-28	4	IUCLID 2000 CD-ROM
68333-80-2	C14-16 Alcohols	Generic/not possible to determine which Type	29 to 32	4	IUCLID 2000 CD-ROM
67762-27-0	C16-18 Alcohols		Ca. 49-56 Solidification range 48-52	4 4	unreferenced; IUCLID 2000 CD-ROM Henkel MSDS
68002-94-8	C16-18 and C18 Unstd.		Solidification range 28-34 Solidification range 2-21	4 4	Henkel MSDS Henkel MSDS
97552-91-5	C18-22 Alcohol		Ca. 55-67	4	Henkel undated

Note: 1 – Compositional Types are described in section 1.1.3.

Table 1.5 Measured boiling point data (ambient pressure)

CAS No	Chemical Name	Comment[1]	Boiling Point (°C)	Reliability	Source
111-27-3	1-Hexanol		158	4	Verschueren 1996
111-70-6	1-Heptanol	Supporting	176	4	Budavari, 1996
111-87-5	1-Octanol		194 to 195	2	Gerarde and Ahlstrom 1966, Budavari 1996
143-08	1-Nonanol	Supporting	194 to 213	4	Verschueren, 1996

CAS No	Chemical Name	Comment[1]	Boiling Point (°C)	Reliability	Source
112-30-1	1-Decanol		229	2	Beilstein
112-42-5	1-Undecanol		245	4	Lington and Bevan, 1994
112-53-8	1-Dodecanol	Supporting	259 255 to 269	4 4	Budavari, 1996 Verschueren, 1996
112-70-9	1-Tridecanol		276	4	Lington and Bevan, 1994
112-72-1	1-Tetradecanol		289	2	Lide, 1999
36653-82-4	1-Hexadecanol		334 to 344	2	Lide 1999
112-92-5	1-Octadecanol	Supporting	210 at 15 mm Hg	4	Budavari, 1996
143-28-2	9-Octadecen-1-ol, (9Z)-		333	4	Sax & Lewis, 1987
629-96-9	1-Eicosanol		309	2	Lide, 1999
661-19-8	1-Docosanol		Only available measured value is at reduced pressure.	-	
68603-15-6	C6-12 Alcohols		180 to 214 at 1013 hPa	4	IUCLID datasheet, 1995h
85566-12-7	C8-10 Alcohols		190-260	4	Sidobre Sinnova SDS
66455-17-2	C9-11 Alcohols		ca. 216 – 251	4	unreferenced; IUCLID 2000 CD-ROM
67762-41-8	C10-16 Alcohols		265 to 280 at 1013 hPa	4	IUCLID 1995a
80206-82-2	C12-14 Alcohols	Type A	255-295	4	Henkel MSDS
68855-56-1	C12-16 Alcohols		255 to 310 at 1013 hPa 265-295 at 1013 hPa	4 4	IUCLID 1995c IUCLID 2000 CD-ROM
67762-25-8	C12-18 Alcohols		260-350	4	Henkel MSDS
68333-80-2	C14-16 Alcohols		280 to 295	4	IUCLID 2000 CD-ROM
67762-27-0	C16-18 Alcohols		Ca. 300-360 310-360	4 4	unreferenced; IUCLID 2000 CD-ROM Henkel MSDS
68002-94-8	C16-18 and C18 Unstd.		315-360 330-360	4 4	Henkel MSDS Henkel MSDS
97552-91-5	C18-22 Alcohol		Ca. 340-400	4	Henkel undated

Note: 1 – Compositional Types are described in section 1.1.3.

Table 1.6 Measured density data

CAS No	Chemical Name	Comment	Density (g/cm^3 at 20°C unless otherwise stated)	Reliability	Source
111-27-3	1-Hexanol		0.82	4	http://chemfinder.cambridgesoft.com/
111-70-6	1-Heptanol	Supporting	0.82	4	Verschueren, 1996
111-87-5	1-Octanol		0.826	4	http://chemfinder.cambridgesoft.com/
143-08	1-Nonanol	Supporting	0.83	4	Verschueren, 1996
112-30-1	1-Decanol		0.8297	4	Beilstein
112-42-5	1-Undecanol		0.83	4	Verschueren, 1996
112-53-8	1-Dodecanol	Supporting	0.83	2	SIDS dossier on 1-Dodecanol, 1993a
112-70-9	1-Tridecanol		0.82	4	Verschueren, 1996
112-72-1	1-Tetradecanol		0.8236 at 38°C	4	Henkel, 1971
36653-82-4	1-Hexadecanol		0.818	4	http://chemfinder.cambridgesoft.com/
112-92-5	1-Octadecanol	Supporting	0.812 at 59°C	4	SIDS dossier on octadecanol, 1993b
143-28-2	9-Octadecen-1-ol, (9Z)-		0.8489	2	Lide, 1999
629-96-9	1-Eicosanol		0.8405	2	CRC
661-19-8	1-Docosanol		0.805-0.809	4	NACOL MSDS
68603-15-6	C6-12 Alcohols		0.83	4	IUCLID datasheet, 1995h
85566-12-7	C8-10 Alcohols		0.825	4	Sidobre Sinnova SDS
66455-17-2	C9-11 Alcohols		ca. 0.831	4	unreferenced; IUCLID 2000 CD-ROM
67762-41-8	C10-16 Alcohols	Type B	0.844	4	Sasol, Sastech Research and Development 1998
67762-41-8	C10-16 Alcohols		0.831	4	IUCLID CD-ROM
80206-82-2	C12-14 Alcohols	Type A	0.82 to 0.83 at 30°C	4	IUCLID datasheet, 1995b
68855-56-1	C12-16 Alcohols		0.831 0.82 to 0.83 at 30°C	4 4	IUCLID 2000 CD-ROM IUCLID 2000 CD-ROM
67762-25-8	C12-18 Alcohols		0.81 to 0.82 at 40°C	4	IUCLID datasheet, 1995d
68333-80-2	C14-16 Alcohols		0.815 - 0.825 at 40°C	4	IUCLID 2000 CD-ROM
67762-30-5	C14-18 Alcohols		0.79 to 0.8 at 80°C	4	IUCLID 2000 CD-ROM
67762-27-0	C16-18 Alcohols		0.8	4	unreferenced; IUCLID 2000 CD-ROM
68002-94-8	C16-18 and C18 Unstd.		0.83-0.84 at 40°C	4	Henkel MSDS
97552-91-5	C18-22 Alcohol		0.8 - 0.81 at 70°C	4	Henkel undated

Note: 1 – Compositional Types are described in section 1.1.3.

Table 1.7 Measured vapour pressure data

CAS No	Chemical Name	Comment	Vapour Pressure (hPa at 25°C unless otherwise stated)	Reliability	Source
111-27-3	1-Hexanol		1.22 hPa	2	Daubert and Danner, 1989
111-70-6	1-Heptanol	Supporting	0.28 hPa	2	Daubert and Danner, 1989
111-87-5	1-Octanol		0.10 hPa	2	Daubert and Danner, 1989
143-08	1-Nonanol	Supporting	0.03 hPa 0.0133 hPa	2 4	Daubert and Danner, 1989 Clayton and Clayton, 1994
112-30-1	1-Decanol		0.0113 hPa	2	Daubert and Danner, 1989
112-42-5	1-Undecanol		0.0039	2	Daubert and Danner, 1989
112-53-8	1-Dodecanol	Supporting	0.0011 hPa 0.0087 hPa at 20°C	2 4	Daubert and Danner, 1989 Verschueren, 1996
112-70-9	1-Tridecanol		0.00057 hPa	2	Daubert and Danner, 1989
112-72-1	1-Tetradecanol		0.00014 hPa	2	Daubert and Danner, 1989
629-76-5	1-Pentadecanol		0.0000512 hPa	2	Daubert & Danner, 1989
36653-82-4	1-Hexadecanol		0.000014 hPa	2	Daubert and Danner, 1989
112-92-5	1-Octadecanol	Supporting	0.0000033 hPa	2	Daubert and Danner, 1989
629-96-9	1-Eicosanol		0.00000015 hPa	2	Daubert and Danner, 1989
661-19-8	1-Docosanol		Only available measured value is a limit value.	-	
68603-15-6	C6-12 Alcohols		< 0.04 hPa at 20°C	3	IUCLID datasheet, 1995h
66455-17-2	C9-11 Alcohols		Two measurements at elevated temperatures.	-	
67762-41-8	C10-16 Alcohols		0.68 hPa[1]	2	Sasol, Sastech Research and Development 1998
75782-86-4	C12-13 Alcohols		Limit value only.	-	
63393-82-8	C12-15 Alcohols		Limit value only.	-	
68333-80-2	C14-16 Alcohols		A measurement at elevated temperature only.	-	

Notes: 1: this value is out of line with expectations; although it was a valid study, the method used (the static method) is susceptible to giving values that are too high, due to the presence of trace impurities such as water.

Table 1.8 Measured octanol-water partition coefficient data

CAS No	Chemical Name	Comment [1]	log Kow	Reliability	Source
111-27-3	1-Hexanol		2.03	2	Tewari *et al*., 1982
111-70-6	1-Heptanol	Supporting	2.57	2	Tewari *et al*., 1982
111-87-5	1-Octanol		3.15	2	Hansch *et al*. 1989 [2]
143-08	1-Nonanol	Supporting	3.77	2	Tewari *et al*., 1982
112-30-1	1-Decanol		4.57	2	Hansch *et al*., 1995
112-42-5	1-Undecanol		4.72	4	Abraham *et al*., 1994
112-53-8	1-Dodecanol	Supporting	5.36	2	Burkhard, Kuehl and Veith, 1985
112-70-9	1-Tridecanol		5.51	2	Hansch and Leo, 1979; Veith *et al*., 1980
112-72-1	1-Tetradecanol		6.03	2	Burkhard *et al*., 1985
36653-82-4	1-Hexadecanol		6.65	2	Burkhard, Kuehl and Veith, 1985
112-92-5	1-Octadecanol	Supporting	7.19	2	Burkhard, Kuehl and Veith, 1985
629-96-9	1-Eicosanol		7.75	2	Burkhard, Kuehl and Veith, 1985
68603-15-6	C6-12 Alcohols	Type C	2.3 to 4.2	2	Pearson *et al*., 1984
67762-41-8	C10-16 Alcohols	Type B	4.8	2	Sasol, Sastech Research and Development 1998
67762-41-8	C10-16 Alcohols	Type C	6	4	Shell, 2000a
68855-56-1	C12-16 Alcohols	Type A	6.0	4	Shell, 2000b
68333-80-2	C14-16 Alcohols		6	4	IUCLID 2000 CD-ROM

Note:

1 – Compositional Types are described in section 1.1.3.

2 – Please note that there is no scientific problem in measuring an octanol-water partition coefficient for octanol.

Table 1.9 Measured water solubility data

CAS No	Chemical Name	Comment	Water Solubility (mg/L at 25°C unless otherwise stated)	Reliability	Source
111-27-3	1-Hexanol		5900 mg/L at 20°C	2	Yalkowsky and Dannenfelser, 1992
111-70-6	1-heptanol	Supporting	1313 mg/L at 20°C	2	Tewari *et al*., 1982
111-87-5	1-Octanol		551 mg/L at 25°C	2	Yalkowsky and Valvani, 1980
143-08	1-Nonanol	Supporting	128 mg/L at 20°C	2	Letinski *et al*. , 2002
112-30-1	1-Decanol		39.5 mg/L	2	Yalkowsky *et al*., 1980
112-42-5	1-Undecanol		8 mg/L at 20°C	2	Letinski *et al*., 2002
112-53-8	1-Dodecanol	Supporting	1.93 mg/L at 20°C	2	Letinski, 2002
112-70-9	1-Tridecanol		0.38 mg/L at 20°C	2	Letinski *et al*., 2002
112-72-1	1-Tetradecanol		0.191 mg/L	2	Yalkowsky *et al*., 1992

629-76-5	1-Pentadecanol		0.102 mg/L	2	Yalkowsky *et al*., 1980
36653-82-4	1-Hexadecanol		0.013 mg/L	2	Yalkowsky *et al*., 1992
112-92-5	1-Octadecanol	Supporting	0.0011 mg/L	2	SIDS dossier on 1-octadecanol, 1993b; Budavari, 1996
66455-17-2	C9-11 Alcohols		Only limit value available.	-	
67762-41-8	C10-16 Alcohols	Type B	2.9 mg/L	2	Sasol, Sastech Research and Development 1998
67762-41-8	C10-16 Alcohols	Type C	2.4 mg/L	2	Bridie, Winter and Wolff, 1973
68855-56-1	C12-16 Alcohols	Type A	0.8 mg/L at 20°C	2	Bridie, Winter and Wolff, 1973; IUCLID datasheet, 1995c
68333-80-2	C14-16 Alcohols	Type A	0.7 mg/L at 20°C	2	Bridie, Winter and Wolff, 1973

Note:

1 – Compositional Types are described in section 1.1.3.

Table 1.10 Measured hazard property data

For several of the substances, no data are available. These are omitted from the table.

CAS	Chemical Name	Flash Point (°C)	Reliability	Source	Flam-mability	Reliability	Source	Explosive Properties	Reliability	Source	Oxidizing Properties	Reliability	Source
111273	1-Hexanol	ca. 65	4	MSDS, Henkel	No data			No data			No data		
111875	1-Octanol	ca. 90	4	Safety data sheet, Henkel KGaA	non-flammable	4	IUCLID datasheet, 1995j	not explosive	4	IUCLID datasheet, 1995j	no oxidizing properties	4	IUCLID datasheet, 1995j
112301	1-Decanol	82 open cup value also available	4	http://chemfinder.cambridgesoft.com/	non-flammable	4	IUCLID datasheet, 1995i	not explosive	4	IUCLID datasheet, 1995i	no oxidizing properties	4	IUCLID datasheet, 1995i
112538	1-Dodecanol	No data			flammable	2	SIDS dossier on 1-dodecanol, 1993a	No data			No data		
112721	1-Tetra-decanol	140 open cup value also available	4	http://chemfinder.cambridgesoft.com/	non-flammable]	4	IUCLID datasheet, 1995k	not explosive	4	IUCLID datasheet, 1995k	no oxidizing properties	4	IUCLID datasheet, 1995k
112925	1-Octa-decanol	170	2	SIDS dossier on 1-octa-decanol, 1993b	moderate fire hazard	2	SIDS dossier on 1-octadecanol, 1993b	No data			No data		
36653824	1-Hexa-decanol	135	4	http://chemfinder.cambridgesoft.com/	No data			No data			No data		
67762258	C12-18 Alcohols	140	4	IUCLID datasheet, 1995d	non-flammable	4	IUCLID datasheet, 1995d	not explosive	4	IUCLID datasheet, 1995d	no oxidizing properties	4	IUCLID datasheet, 1995d

CAS	Chemical Name	Flash Point (°C)	Reliability	Source	Flam-mability	Reliability	Source	Explosive Properties	Reliability	Source	Oxidizing Properties	Reliability	Source
67762270	C16-18 Alcohols	>160 ca. 170 (both values open cup)	4 4	unreferenced IUCLID datasheet, 1995d	non-flammable	4	IUCLID datasheet, 1995g	not explosive	4	IUCLID datasheet, 1995g	no oxidizing properties	4	IUCLID datasheet, 1995g
67762305	C14-18 Alcohols	ca. 170	4	IUCLID datasheet, 1995f	non-flammable	4	IUCLID datasheet, 1995f	not explosive	4	IUCLID datasheet, 1995f	no oxidizing properties	4	IUCLID datasheet, 1995f
67762418	C10-16 Alcohols	>110	1	Sasol, Sastech Research and Development, 1998	auto-ignition temperature 242°C (i.e.non-flammable under typical operational conditions)	1	Sasol, Sastech Research and Development, 1998	not explosive	1	Sasol, Sastech Research and Development, 1998	No data		
68551075	Alcohols, C8-18	ca. 128 (open cup)	4	MSDS	No data			No data			No data		
68603156	C6-12 Alcohols	ca. 79	4	IUCLID datasheet, 1995h	No data			No data			No data		
68855561	C12-16 Alcohols	ca. 132 to 140	4	IUCLID datasheet, 1995c	No data			No data			No data		
80206822	C12-14 Alcohols	ca. 140 (Type A)	4	IUCLID datasheet, 1995b	non-flammable	4	IUCLID datasheet, 1995b	not explosive	4	IUCLID datasheet, 1995b	no oxidizing properties	4	IUCLID datasheet, 1995b

Note:

1 – Compositional Types are described in section 1.1.3.

Table 1.11 Summary of physicochemical properties for sponsored substances

Note: References are presented elsewhere in this section and are omitted from this table for clarity. All estimates are taken from Annex I.

Property	Value											
SUBSTANCE [1]:	111-27-3	111-87-5	112-30-1	112-42-5	112-70-9	90583-91-8	112-72-1	629-76-5	36653-82-4	629-96-9	661-19-8	143-28-2
	1-Hexanol	1-Octanol	1-Decanol	1-Undecanol	1-Tridecanol	Tridecanol, branched and linear	1-Tetradecanol	1-Pentadecanol	1-Hexadecanol	1-Eicosanol	1-Docosanol	9-Octadecen-1-ol, (9Z)-
Molecular weight	102.2	130.2	158.3	172.3	200.4	200.4	214.4	228.4	242.4	298.5	326.6	268.5
Physical state at 25°C (L=liquid, S=solid) [2]	L	L	L	L	S	[S]	S	S	S	S	S	S
Melting point (°C)	-44 to -51	-15.5 to -17	6.4	14.3 11 to 19	30.6 32 to 33	Ca. 29 [Estimate]	39-40	44 45-46	50	66.0 64-68	72.5	13-19
Boiling point (°C)	158	194 to 195	229	245	276	279 [Estimate]	289	317.7 [estimate]	334 to 344	309	Only available measured value is at reduced pressure. 401.1 [estimate]	333
Relative Density (g/ml at 20°C unless otherwise stated)	0.82	0.826	0.8297	0.83	0.82		0.8236 at 38°C	No data; not possible to estimate	0.818	0.8405	0.805-0.809	0.8489
Vapour pressure (hPa at 25°C unless otherwise stated)	1.22	0.10	0.0113	0.0039	0.00057	0.00057 [estimate]	0.00014	0.0000512	0.000014	0.00000015	Only available measured value is a limit value. 8.2E-08 [estimate]	0.0000198 [estimate]

Property	Value											
SUBSTANCE [1]:	111-27-3	111-87-5	112-30-1	112-42-5	112-70-9	90583-91-8	112-72-1	629-76-5	36653-82-4	629-96-9	661-19-8	143-28-2
	1-Hexanol	1-Octanol	1-Decanol	1-Undecanol	1-Tridecanol	Tridecanol, branched and linear	1-Tetra-decanol	1-Penta-decanol	1-Hexa-decanol	1-Eicosanol	1-Docosanol	9-Octa-decen-1-ol, (9Z)-
Water solubility (mg/L at 25°C unless otherwise stated)	5900 mg/L at 20°C	551	39.5	8 mg/L at 20°C	0.38 mg/L at 20°C	0.38 mg/L at a loading rate of 1000 mg/L [estimate]	0.191	0.102	0.013	0.0027 mg/L at a loading rate of 1000 mg/L [estimate]	0.0027 mg/L at a loading rate of 1000 mg/L [estimate]	0.042 mg/L at a loading rate of 1000 mg/L [estimate]
Partition coefficient (log Kow)	2.03	3.15	4.57	4.72	5.51	5.56 [estimate]	6.03	6.43 [estimate]	6.65	7.75	7.75 [estimate]	7.07 [estimate]

Property	Value								
SUBSTANCE [1]:	85566-12-7	68603-15-6	66455-17-2	75782-86-4	67762-41-8	80206-82-2	68855-56-1	63393-82-8	67762-25-8
	C8-10 Alcohols	C6-12 Alcohols	C9-11 Alcohols	C12-13 Alcohols	C10-16 Alcohols	C12-14 Alcohols	C12-16 Alcohols	C12-15 Alcohols	C12-18 Alcohols
Molecular weight	-	-	-	-	-	-	-	-	-
Physical state at 25°C (L=liquid, S=solid) [2]		L	L		L	L	L		S
Melting point (°C)	No data; not possible to estimate.	-16 to -4; chemical Type unclear. Not possible to estimate.	ca -21	No data; not possible to estimate.	Type B: 0 18.5	Solidification point 17-23	21	No data; not possible to estimate.	Solidification range 25-28
Boiling point (°C)	190-260	180 to 214^{o}C at 1013 hPa; chemical Type unclear. Not possible to estimate.	ca. 216 – 251	ca. 259-276 [estimate]	265 to 280^{o}C at 1013 hPa	Type A: 255-295	255 to 310^{o}C at 1013 hPa 265-295 deg C at 1013 hPa	Ca. 259-318 [estimate]	260-350
Relative Density (g/ml at 20°C unless otherwise stated)	0.825	0.83; chemical Type unclear. Not possible to estimate.	ca. 0.831	No data; not possible to estimate.	Type B: 0.844	Type A: 0.82 to 0.83 at 30^{o}C	0.831 0.82 to 0.83 at 30°C	No data; not possible to estimate.	0.81 to 0.82 at 40°C

Property	Value								
SUBSTANCE [1]:	85566-12-7	68603-15-6	66455-17-2	75782-86-4	67762-41-8	80206-82-2	68855-56-1	63393-82-8	67762-25-8
	C8-10 Alcohols	C6-12 Alcohols	C9-11 Alcohols	C12-13 Alcohols	C10-16 Alcohols	C12-14 Alcohols	C12-16 Alcohols	C12-15 Alcohols	C12-18 Alcohols
Vapour pressure (hPa at 25°C unless otherwise stated)	0.089 [estimate]	< 0.04 hPa at 20ºC Type A: 0.0044 [estimate] Type B: 0.013 [estimate] Type C: 0.17 [estimate] Type D: 0.16 [estimate]	Two measurements at elevated temperatures. 0.013 [estimate]	Limit value only. 8.3E-04 [estimate]	0.68 Type A: 0.0029 [estimate] Type B: 0.00083 [estimate] Type C: 0.00082 [estimate] Type D: 0.00053 [estimate]	Type A: 0.0050 [estimate] Type B: 0.0014 [estimate]	Type A: 0.00054 [estimate] Type B: 0.0016 [estimate] Type C: 0.00025 [estimate]	Limit value only. Type A: 0.00050 [estimate] Type B: 0.00053 [estimate]	Type A: 0.0016 Type B: 0.00026 [estimate]
Water solubility (mg/L at 25°C unless otherwise stated)	202 mg/L at a loading rate of 1000 mg/L. [Estimate]	Type A: 9.7 mg/L at a loading rate of 1000 mg/L. [estimate] Type B: 10 mg/L at 20ºC Type C: 510 mg/L at a loading rate of 1000 mg/L. [estimate] Type D: 293 mg/L at a loading rate of 1000 mg/L. [estimate]	Only limit value available. 44 mg/L at a loading rate of 1000 mg/L. [Estimate]	1.1 mg/L at a loading rate of 1000 mg/L. [Estimate]	Type A: 7.1 mg/L at a loading rate of 1000 mg/L. [estimate] Type B: 2.9 Type C: 2.4 Type D: 0.67 mg/L at a loading rate of 1000 mg/L. [estimate]	Type A: 4.6 mg/L at a loading rate of 1000 mg/L. [estimate] Type B: 2.8 mg/L at a loading rate of 1000 mg/L. [Estimate]	Type A: 0.8 mg/L at 20ºC Type B: 3.2 mg/L at a loading rate of 1000 mg/L. [estimate] Type C: 0.42 mg/L at a loading rate of 1000 mg/L. [estimate]	Type A: 0.63 mg/L at a loading rate of 1000 mg/L. [estimate] Type B: 0.67 mg/L at a loading rate of 1000 mg/L. [Estimate]	Type A: 1.7 mg/L at a loading rate of 100 mg/L. [Estimate] Type B: 0.35 mg/L at a loading rate of 1000 mg/L. [Estimate]
Partition coefficient (log Kow)	3.2-4.6 [Estimate]	Type C: 2.3 to 4.2	3.8-4.7 [Estimate]	5.4-5.5 [estimate]	Type A: 4.6-6.0 [Estimate] Type B: 4.8 Type C: 6 Type D: 5.4-6.4 [Estimate]	Types A and B: both 5.4-6.0 [estimate]	Type A: 6.0	Types A and B: both 5.3-6.4 [estimate]	Type A: 5.4-6.0 [estimate] Type B: 6.7-7.2 [estimate]

Property	Value								
SUBSTANCE [1]:	75782-87-5	68333-80-2	67762-30-5	67762-27-0	68002-94-8	97552-91-5	68155-00-0	85665-26-5	68551-07-5
	C14-15 Alcohols	C14-16 Alcohols	C14-18 Alcohols	C16-18 Alcohols	C16-18 and C18 Unsaturated	C18-22 Alcohol	Alcohols, C14-18 and C16-18-unsatd.	Alcohols, C10-13	Alcohols, C8-18
Molecular weight	-	-	-	-	-	-			
Physical state at 25°C (L=liquid, S=solid) [2]		S		S	S	S			
Melting point (°C)	No data; not possible to estimate	29 to 32	No data; not possible to estimate	ca 49-56 Solidification range 48-52	Solidification range 28-34 Solidification range 2-21	ca 55-67	No data; not possible to estimate	No data; not possible to estimate	No data; not possible to estimate
Boiling point (°C)	Ca. 289-318 [estimate]	280 to 295	No data; not possible to estimate	ca 300-360 310-360	315-360 330-360	ca 340-400	No data; not possible to estimate	Ca. 229-259 [estimate]	No data; not possible to estimate
Relative Density (g/ml at 20°C unless otherwise stated)	No data; not possible to estimate	0.815 - 0.825 at 40°C	0.79 to 0.8 at 80°C	0.8	0.83-0.84 at 40°C	0.8 - 0.81 at 70°C	No data; not possible to estimate	No data; not possible to estimate	No data; not possible to estimate
Vapour pressure (hPa at 25°C unless otherwise stated)	1.1E-04 [estimate]	A measurement at elevated temperature only. Type A: 0.00011 [estimate] Type B: 0.00051 [estimate]	Type A: 0.000017 [estimate] Type B: 0.00009 [estimate]	1.3E-05 [estimate]	3.7E-05 [estimate]	1.1E-06 [estimate]	1.9E-05 [estimate]	0.011 [estimate]	0.012 [estimate]
Water solubility (mg/L at 25°C unless otherwise stated)	0.15 mg/L at a loading rate of 1000 mg/L. [Estimate]	Type A: 0.7 mg/L at 20°C Type B: 0.64 mg/L at a loading rate of 1000 mg/L. [estimate]	Type A: 0.04 mg/L at a loading rate of 1000 mg/L. [Estimate] Type B: 0.12 mg/L at a loading rate of 1000 mg/L. [Estimate]	0.030 mg/L at a loading rate of 1000 mg/L. [Estimate]	0.045 mg/L at a loading rate of 1000 mg/L. [Estimate]	0.0056 mg/L at a loading rate of 1000 mg/L. [Estimate]	0.024 mg/L at a loading rate of 1000 mg/L. [Estimate]	34 mg/L at a loading rate of 1000 mg/L.. [Estimate]	26.52 mg/L at a loading rate of 1000 mg/L. [estimate]
Partition coefficient (log Kow)	6.0 - 6.4 [estimate]	6	Type A: 6.7-7.2 [estimate] Type B: 6.0-7.2 [estimate]	6.7-7.2 [estimate]	6.7-7.2 [estimate]	7.2-7.75 [estimate]	6.0-7.2 [estimate]	4.6-5.4 [estimate]	3.2-7.2 [estimate]

Notes:

1 – Compositional Types are described in section 1.1.3.

2 – In some cases where no measurement is available and estimation is not possible, the physical state has been left blank.

1.4 Category justification

The category must be justified firstly on the basis of structural features, and physicochemical, environmental (degradation, toxicity) and health properties. The relevant sections expand upon the relevant data sets and therefore only brief summaries are given here. Whilst this set exhibits a wide range of values for some of the properties, they share common modes of degradation and biological action, as well as many uses in common.

The long chain aliphatic alcohol family has at its centre a homologous series of increasing carbon chain length. In addition, certain branched and unsaturated structures are considered to have such similar properties that their inclusion in the category may be justified. Commercial products contain a range of alcohols, which in some products may include: unsaturated alcohol components; essentially linear (mono-alkyl branched) components as well as linear alcohols. All components of all commercial products relevant to this category are primary alcohol structures. Composition of category members is described in more detail in section 1.1.2.

The hydroxyl group in alcohols confers upon the hydrocarbon chain a considerable degree of polarity, and hence affinity for water. It is susceptible to oxidation by metabolic processes. Linear or essentially linear hydrocarbon chains are also readily oxidised metabolically. No highly branched structures are proposed for inclusion in the Category. Substances that contain a number of homologous components can be expected to behave in a way consistent with the carbon number distribution present.

1.4.1 Overview of measured physicochemical properties

This has been given in Section 1.3. It can be seen that there is a good coverage of the group.

Annexes I and II show that these properties are predicted well by various (Q)SAR methods. Whilst (Q)SAR techniques are always in part validated by the very measured data reported, they are validated across many other structural types. Their success in predicting properties for Category members for which measured data exist suggested that the members do not possess any particularly unusual features.

Substances comprising of a range of carbon chain lengths can be dealt with by appropriate addition of their individual contributions to the whole.

1.4.2 Overview of measured environmental effects

Effects on aquatic organisms

Detailed results are given in Section 4.

Alcohols, with the exception of some propargylic alcohols (Veith, Lipnick and Russom, 1989) that are excluded from this family, act by non-polar narcosis (Lipnick *et al*., 1985). As chain length increases, hydrophobicity increases resulting in greater toxicity, and in parallel, solubility decreases. At a critical point, solubility becomes lower than expected toxicity and longer chain lengths show no acute toxicity.

Chronic effects for such substances are also known; present data again indicate that effects are anticipated up to C15. For alcohols with carbon numbers higher than C15 there are significant experimental difficulties in producing, maintaining and quantifying exposures of the test substance.

Even so, it is unlikely that they would exhibit chronic toxicity because the relationship between carbon number and chronic toxicity, established from the test results that are available, suggests that the solubility of the alcohol would limit the bioavailable dissolved fraction to sub-toxic concentrations.

By considering the sponsored long chain aliphatic alcohols as a single family, these structure-activity trends are clearly illustrated; the assessment of any one member of the family is strengthened by reference to the other members. These trends are illustrated throughout this assessment. In this assessment, trends between aquatic toxicity and carbon chain length are based on normal alcohols, since data do not exist on single carbon chain length essentially-linear alcohols. However, the comparability of the toxicity of straight-chain and essentially-linear alcohols is shown by a comparison of commercial products.

Annex VIII shows that these properties are predicted well by (Q)SAR methods. Their success in predicting properties for Category members suggested that the members do not possess any particularly unusual features. Annex IX discusses how the ecotoxicological effects of the multi-component substances are described and interpreted. The properties of these substances can be understood in terms of the components present in them, and a predictive model has been developed to demonstrate this and fill some data gaps.

Substances comprising of a range of carbon chain lengths can be dealt with by appropriate addition of their individual contributions to the whole, described fully as needed.

1.4.3 Overview of measured degradation properties

Detailed results are summarised in Section 2.2.5. Similarly for biodegradation, the comparability of linear and essentially-linear alcohols is demonstrated by the consistency of data for biodegradability of commercial products containing branched, linear and unsaturated components.

Annex V shows that these properties are predicted well by various (Q)SAR methods. Whilst (Q)SAR techniques are always in part validated by the very measured data reported, they are validated across many other structural types. Their success in predicting properties for Category members suggested that the members do not possess any particularly unusual features.

The mammalian biotransformation of aliphatic alcohols involves an oxidation step of the alcohol function to the corresponding aliphatic carboxylic acid, with the aldehyde being a transient intermediate. These carboxylic acids (i.e. fatty acids) are subsequently broken down by stepwise removal of one or several C-2 units from the aliphatic carbon chain through the β-oxidation process. The stepwise breakdown of aliphatic alcohols results in common intermediate metabolites with shorter chain lengths, providing further justification that the aliphatic alcohols under consideration can be regarded as a single category and explains the similarity in toxicological profile for systemic effects. Aliphatic alcohols are generally highly efficiently metabolised and there is limited potential for retention or bioaccumulation for the parent alcohols and their biotransformation products.

1.4.4 Overview of health effects

A review of the toxicological database for the category of the aliphatic alcohols demonstrates that these materials are of a low order of toxicity upon single or repeated exposure. Overall, the data show an inverse relationship between chain length and toxicity. The shorter chain alcohols tend to induce more pronounced effects when compared to materials with a longer chain length. This is illustrated most clearly by the degree of local irritation in studies involving single or repeat administration. Aliphatic alcohols have no skin sensitisation potential, are not mutagenic and have not shown any adverse effects on fertility, development and reproduction. On the basis that a clear relationship exists between chain length and toxicological properties, substances with chain lengths exceeding the upper range tested can be expected to possess toxicological properties similar to those tested.

The health effect of the aliphatic alcohols has been considered for two sub-categories: linear and essentially linear alcohols. The overall toxicological profile of the sub-categories is fully comparable for all of the end points assessed. The relationship between chain length and toxicological properties is present for both sub-categories of the aliphatic alcohols. In the evaluation some 100% branched alcohols were included as surrogate materials to assess in more detail the potential impact of branching on the overall toxicological properties.

Taken together, a comparison of the SIDS, irritation and sensitisation endpoints demonstrates that the toxicological properties of the classes of linear and essentially linear alcohols are fully comparable and justify the combination of this group as a single category within the ICCA/HPV programme.

1.4.5 Summary of category justification

Key points are that the members share:

- The same structural features
- Similar metabolic pathways
- Common mode of ecotoxicological action
- Common levels and mode of human health related effects.

This allows multi-component reaction products to be considered within the Category.

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production volumes and use pattern

The estimated global production volume by region of this family of long chain aliphatic alcohols is presented in Table 2.1, based on a 2002 survey of the Consortium member companies.

Table 2.1 Production data

	North America	Europe	Asia Pacific	Total
Total Production (metric tonnes)	624,261	710,389	245,779	1,580,429

These data are supplemented by public domain information, as follows. Across all ‘sponsored’ and ‘supporting’ category members:

- US: production plus import ca. 650 000 - 2 000 000 tonnes in 2002 (US IUR ('Inventory Update Rule') volumes)
- Western Europe: consumption ca. 700 000 tonnes in 2004 (APAG/CEFIC annual statistical data)
- Japan: production + import total ca. 150 000 tonnes per year (Modler RF, Gubler R, and Inoguchi Y., 2004)
- Consumption in the Nordic countries ca. 1500 tonnes in 2002 (SPIN database)

Commercial production figures for specific CAS numbers, or narrow ranges of chain length, are confidential. The SPIN database, which represents only a small fraction of European consumption of these substances, indicates that the most significant products in the Nordic countries are C6-12 alcohols and C16-18 alcohols, each having a >20% share of alcohols consumed in Nordic countries in 2002.

Globally, across all Category member substances, approximately 50% of the total production volume is used directly in final products, the remainder is processed as an intermediate (with approximately 65% of the intermediate volume being site limited). The Consortium has conducted a survey amongst producers, formulators and users in 2002 to establish the main uses and formulation data for the category of the long chain aliphatic alcohols. On the basis of this survey it is expected that these alcohols would have widespread and dispersive uses in the industrial, commercial and consumer applications identified below. The survey results are summarised in the following sections. The conclusions can be substantiated from public sources such as company web sites, although there is no need to reference those in this document.

2.1.1 Intermediates

The use of the long chain aliphatic alcohols as synthetic intermediates for surfactants is the main application area. Chemical reactions include ethoxylation, propoxylation, and sulfation. Esterification and oxidation may also be employed, giving rise to products used in a wide range of products such as lubricant and plastics additives.

2.1.2 Industrial and commercial uses (non-intermediate)

Long-Chain Aliphatic Alcohols have widespread and dispersive use in several industrial sectors and find many commercial uses mainly for their lubricant and emulsifying properties.

Examples of –(formulated) industrial products include:

- Flotation agents
- Lubricants
- Emulsifiers
- Formwork oils
- Rolling oils
- Oilfield chemicals
- Defoamers

Examples of commercial uses include:

Processing aids in paper, plastics, textile and leather industry

Formulation aids in agrochemicals, pharmaceuticals and medicines

Additive in plastics, plaster, paper products

Typical levels of Long Chain Aliphatic Alcohols in products used in industry and commerce are shown in Table 2.2. The levels as shown in Table 2.2 represent long chain aliphatic alcohol concentrations in the formulated product and do not take into account any dilution prior to or during use. Ranges are provided for the level in product as reported in a survey conducted by the SDA for the Long Chain Alcohols in 2002 (SDA, 2002). It should be pointed out that many marketed products in these categories may not contain long chain aliphatic alcohols. Applications where the maximum concentration is 1% or below have been omitted from this table.

Table 2.2 Summary of typical levels of aliphatic alcohols in use in industry and commerce

Product Category	**Product Formulations (%)**					
	USA		**EU**		**AP**	
	Mean	**Range**	**Mean**	**Range**	**Mean**	**Range**
Paints	3	1 - 5	3	1 - 5	3	1 - 5
Lubricants			87.5	75-100		
Paper products and processing	37.5	25–50	37.5	25-50	37.5	25-50
Plastic processing			62.5	25-100		
Textile processing			87.5	75-100		
Leather Processing			87.5	75-100		
Plaster Additives			27.5	10 -50		
Formwork Oils			17.5	10 - 25		
Other - Pharmaceuticals	3	1 - 5	3	1 - 5	3	1 - 5

2.1.3 Consumer uses

The main uses of long chain aliphatic alcohols in consumer products include the product categories shown in Table 2.3. The levels in products shown indicate long chain aliphatic alcohol concentration in the formulated product and does not take into account any dilution prior to or during use. Ranges are provided for the level in product as reported in a survey conducted by the SDA for the Long Chain Alcohols in 2002 (SDA, 2002). It should be pointed out that many products on the market in these categories do not contain long chain aliphatic alcohols. Applications where the maximum concentration is 1% or below have been omitted from this table.

Table 2.3 Summary of typical levels of aliphatic alcohols in use in consumer products

Product Category	**Product Formulations (%)**					
	USA		**EU**		**AP**	
	Mean	**Range**	**Mean**	**Range**	**Mean**	**Range**
Household Products						
Laundry detergents: Powder	3	1 - 5	3	1 - 5	3	1 - 5
Fabric softener	3	1 - 5	3	1 - 5	0.75	0.5 - 1
General and Hard Surface Cleaners	3	1 - 5	-	-	3	1 - 5
Personal Care and Cosmetic products						
Hair						
conditioners gel,	3	1-5	3	1-5	1.88	0.5 – 5
mousse					3	1 - 5
dye					7.5	5-10
Skin lotions, creams, cleaners	3	1 - 5	3	1 - 5	1.88	0.5 - 5
Antiperspirants (solid)	17.5	10-25	17.5	10-25	17.5	10-25
Face/Eye Cosmetics						
Liquid	3	1 – 5	3	1 - 5	3	1 - 5
Powder	3	1 – 5			0.75	
Mascara					3	1 - 5

2.1.4 Product Register data

Data from the Nordic countries product registers, obtained via the SPIN database, supports the above data. A wide range of applications are identified, including:

- Synthetic intermediates
- Food/feedingstuff additives
- Cleaning/washing agents
- Paints
- Pesticides
- Surfactants
- Surface treatments

- Adhesives
- Colouring agents
- Lubricants
- Antifreezes
- Cosmetics
- Pharmaceuticals

The full set of information is presented in Annex III. It is not helpful to attempt to present a breakdown of different uses based on the SPIN database, since the data vary from substance to substance, and in many cases tonnages are not available. Based on the available figures, the SPIN data do appear to indicate that use as a synthetic intermediate is the most significant application in the Nordic countries. However, almost half of the Nordic countries' consumption tonnage was unaccounted for in the applications breakdown.

The most significant identified use categories, based on non-confidential stated tonnages for different applications in Nordic countries in 2002, were lubricants and additives, and surface-active agents. However it should be noted that considerably higher tonnages were reported for unspecified use categories ('others'), and that almost two-thirds of the Nordic countries' consumption tonnage was unaccounted for in the use categories breakdown.

2.2 Environmental exposure and fate

2.2.1 Sources of environmental exposure

Exposure could arise in association with production, formulation and industrial use of these substances. There would also be exposure from consumer uses.

The main uses of alcohols are as manufacturing intermediates for consumer products. Discharge of these products is expected to be primarily to water, through disposal to drain.

The situation for multi-component substances is complicated by the fact that, given a particular route of exposure, each component will behave independently on release to the environment. The concentrations in each environmental compartment are based on the chemical properties of each individual component.

2.2.2 Photodegradation

Two measurements of atmospheric degradation rate are available for sponsored substances, for hexanol and octanol. To fill data gaps for this SIDS endpoint, the rate of degradation by hydroxyl radicals in the atmosphere has been estimated using the SRC AOPWIN v1.91 program (part of the EPIWIN suite v3.12). The best available data for category members are presented in Table 2.4.

The half-life for photo-oxidation in air, based on a hydroxyl radical concentration of 5E+05 molecules/cm^3 varies between 12 hours (estimated for 1-docosanol) to approximately 30 hours (measured for 1-hexanol). See Annex V for a detailed discussion of the estimation and validation.

Available measured data for relevant linear and branched structures suggest that the estimated half-lives are likely to be realistic and slightly conservative. 2-Alkyl branched structures and unsaturated structures are both predicted to be photo-degraded at a faster rate than saturated, linear structures of equivalent carbon number.

Table 2.4 Atmospheric photodegradation data

CAS	Chemical Name	Comment	Photodegradation rate or half-life	Relia-bility	Reference
111-27-3	1-Hexanol		Measured rate constant: 12.5E-12 cm^3/molecule.sec Half-life: 30.8 hours	2	Kwok, E.S.C. and Atkinson, R., 1994
68603-15-6	C6-12 Alcohols	Type C	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
111-87-5	1-Octanol		Measured rate constant: 14.4E-12 cm^3/molecule.sec Half-life: 26.7 hours	2	Atkinson, R., 1994
68603-15-6	C6-12 Alcohols	Type D	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
85566-12-7	C8-10 Alcohols		Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
68551-07-5	Alcohols, C8-18		Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
66455-17-2	C9-11 Alcohols		Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
68603-15-6	C6-12 Alcohols	Type B	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
112-30-1	1-Decanol		Estimated rate constant: 15.368E-12 cm^3/molecule.sec Half-life: 25.1 hours	2	Annex V
67762-41-8	C10-16 Alcohols	Generic/not possible to ascertain Type	Half life of 19.2 hours	4	unreferenced; IUCLID 2000 CD-ROM
67762-41-8	C10-16 Alcohols	Type A	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
85665-26-5	Alcohols, C10-12		Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
112-42-5	1-Undecanol		Estimated rate constant: 16.781E-12 cm^3/molecule.sec Half-life: 22.9 hours	2	Annex V
68603-15-6	C6-12 Alcohols	Type A	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
67762-41-8	C10-16 Alcohols	Type B	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
67762-41-8	C10-16 Alcohols	Type C	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
67762-41-8	C10-16 Alcohols	Type D	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
67762-25-8	C12-18 Alcohols	Type A	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
67762-25-8	C12-18 Alcohols	Type B	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
63393-82-8	C12-15 Alcohols	Type A	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V

CAS	Chemical Name	Comment	Photodegradation rate or half-life	Relia-bility	Reference
63393-82-8	C12-15 Alcohols	Type B	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
68855-56-1	C12-16 Alcohols	Generic/not possible to ascertain Type	Half life of 19.2 hours	4	Unreferenced; IUCLID 2000 CD-ROM
68855-56-1	C12-16 Alcohols	Type B	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
68855-56-1	C12-16 Alcohols	Type C	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
68855-56-1	C12-16 Alcohols	Type A	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
80206-82-2	C12-14 Alcohols	Type A	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
80206-82-2	C12-14 Alcohols	Type B	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
75782-86-4	C12-13 Alcohols		Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
68333-80-2	C14-16 Alcohols	Type B	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
112-70-9	1-Tridecanol		Estimated rate constant: 19.607E-12 cm3/molecule.sec Half-life: 19.6 hours	2	Annex V
90583-91-8	Tridecanol, branched and linear		Estimated rate constant: 19.884E-12 cm^3/molecule.sec Half-life: 19.4 hours	2	Annex V
112-72-1	1-Tetradecanol		Estimated rate constant: 21.021E-12 cm^3/molecule.sec Half-life: 18.3 hours	2	Annex V
68333-80-2	C14-16 Alcohols	Type A	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
75782-87-5	C14-15 Alcohols		Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
67762-30-5	C14-18 Alcohols	Type B	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
629-76-5	1-Pentadecanol		Estimated rate constant: 22.434E-12 cm^3/molecule.sec Half-life: 17.2 hours	2	Annex V
36653-82-4	1-Hexadecanol		Estimated rate constant: 23.847E-12 cm^3/molecule.sec Half-life: 16.2 hours	2	Annex V
			3.1% mineralisation and ~0.5% organic fragments after 17 hours exposure in microphotoreactor (UV lamp at 290 nm)	4	Freitag et al., 1982
67762-30-5	C14-18 Alcohols	Type A	Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V

CAS	Chemical Name	Comment	Photodegradation rate or half-life	Relia-bility	Reference
67762-27-0 (Also mixture of 36653-82-4 and 112-92-5)	C16-18 Alcohols		Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
143-28-2	9-Octadecen-1-ol, (9Z)-		Estimated rate constant: 79.718E-12 cm^3/molecule.sec Half-life: 4.8 hours	2	Annex V
68002-94-8	C16-18 and C18 Unstd.		Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
68155-00-0	Alcohols, C14-18 and C16-18-unsatd.		Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
97552-91-5	C18-22 Alcohol		Half-lives ranging between ca. 10-30 hours (estimate)	2	Annex V
629-96-9	1-Eicosanol		Estimated rate constant: 29.499E-12 cm^3/molecule.sec Half-life: 13.1 hours	2	Annex V
661-19-8	1-Docosanol		Estimated rate constant: 32.325E-12 cm^3/molecule.sec Half-life: 11.9 hours	2	Annex V

Note:

1 – Compositional Types are described in section 1.1.3.

2.2.3 Stability in water

All of the alcohols in this group would be expected to be stable in respect of abiotic degradation in water. Photo-oxidation in aqueous systems will not be significant. Alcohols have no hydrolysable groups and are therefore not susceptible to hydrolysis (Lyman, Reehl and Rosenblatt, 1990). Oxidation would not be expected under normal environmental conditions.

2.2.4 Transport between environmental compartments

2.2.4.1 Henry's Law constant

The Henry's Law constant (HLC) describes the potential for volatilisation from water. No measured values are available, hence the HLC can be estimated, e.g. from the values of vapour pressure and water solubility. Values calculated in this way range between approximately 0.7 – 80 Pa.m^3/mol (for 1-docosanol and 1-octadecanol respectively). Other category members have intermediate values. Whilst these values cannot in themselves be considered very low, fugacity modelling shows that a negligible proportion of the substance will be volatilised in the environment, as described below. There is no need for the present purpose to provide a full set of values.

2.2.4.2 Adsorption

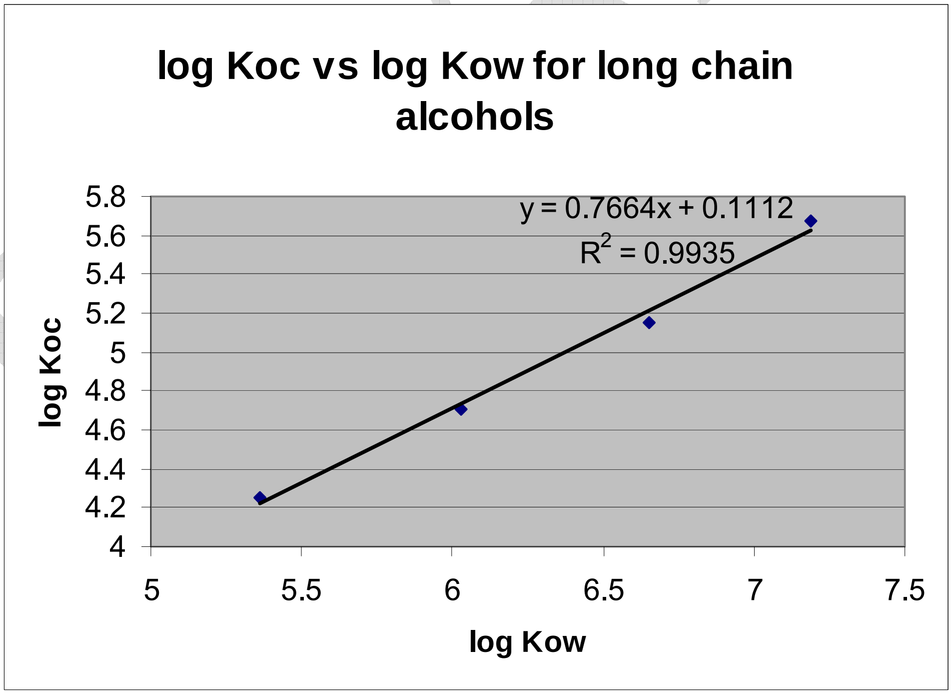
No fully-published valid measured adsorption data are available for long chain aliphatic alcohols. However, Van Compernolle *et al.* (2006) report the adsorption of several long chain alcohols (C_{12}, C_{14}, C_{16}, and C_{18}) to wastewater treatment plant solids in a manuscript devoted to developing a sorption (Q)SAR for alcohol ethoxylates. Alcohol sorption coefficients showed some time dependence, reaching a plateau by 72 h. Pentadecanol (C_{15}) was found to be an unexplained outlier. The 72-h results are presented in Table 2.5, below.

Table 2.5 Adsorption data from wastewater treatment plants

Carbon chain length	12	14	15	16	18
Kd	3000±80	8490±920	3080±270	23800±3200	78700±5400
Koc	17980	50830	-	143000	471000
log Koc	4.25	4.71	-	5.15	5.67

Based on the alcohol-only subset of data, as shown in Table 2.5, the following (Q)SARs are derived (data in Annex VII, Table A VII-2):

$\text{Log } K_d$ = Chain Length x 0.235 + 0.642 $R^2 = 0.999$, n = 4
$\text{Log } K_{oc}$ = Chain Length x 0.235 + 1.420 $R^2 = 0.999$, n = 4
$\text{Log } K_{oc}$ = log K_{ow} x 0.766 + 0.111 $R^2 = 0.994$, n = 4



A (Q)SAR based on four points should not be over-interpreted, but it is of interest to note that the (Q)SAR method from the TGD[2] (EC, 2003), for hydrophobics is:

Log K_{oc} = log K_{ow} x 0.81 + 0.10

which is very similar to that found for the four substances measured. While this method is not intended for use with alcohols, the similarity to the (Q)SAR developed from the above measured data suggests that this method is relevant for these substances.

Therefore, K_{oc} values have been predicted using particularly-relevant (Q)SAR methods from the TGD[3] (EC, 2003): for hydrophobics, non-hydrophobics, and for alcohols. The SRC PCKOCWIN v1.66 method (part of the EPIWIN suite v3.12) has also been used, since it does not use log K_{ow} as input. Full details of the property prediction are set out in Annex V. The predicted value of K_{oc} varies from 8.3 (hexanol) to 149,000 (docosanol) using the PCKOCWIN method; and 20 (hexanol) to 219 (undecanol) using the TGD Alcohols (Q)SAR, which is only valid up to log K_{ow} = 5.

The best available data for category members are presented in Table 2.6. All of the predicted values are of reliability (2).

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[2] EC Technical Guidance Document for risk assessment of New and Existing Substances

[3] EC Technical Guidance Document for risk assessment of New and Existing Substances

Table 2.6 Predicted adsorption data

CAS	Chemical Name	Comment[1]	Adsorption: soil-water partition coefficient - Koc			
			TGD Alcohols method[2]	TGD Hydrophobics method	TGD Non-hydrophobics method	SRC PCKOCWIN method
111-27-3	1-Hexanol		19.6	56	119.0	8.3
68603-15-6	C6-12 Alcohols	TYPE C	30 - 90	152 - 1430	230 - 960	15 – 50
111-87-5	1-Octanol		53.5	448	455.0	28.3
68603-15-6	C6-12 Alcohols	Type D	50 - 190	56 - 6330	450 - 2500	30 - 100
85566-12-7 (Also mixture of 111-87-5 & 112-30-1)	C8-10 Alcohols		54 – 190	56 - 27600	460 – 2490	28 – 96
68551-07-5	Alcohols, C8-18		54 - 2010	448 - 839000	460 - 57400	28 – 12900
66455-17-2	C9-11 Alcohols		90 - 220	1430 - 8380	960 - 2980	50 - 180
68603-15-6	C6-12 Alcohols	Type B	90 - 220	1430 - 8380	960 - 3000	50 - 180
112-30-1	1-Decanol		190	6330	2490	96
67762-41-8	C10-16 Alcohols	Type A	190 – 1240[3]	6330 - 307000	2490 – 30100	90 – 3790
85665-26-5	Alcohols, C10-12		190 – 390 [3]	6330 - 96500	2900 – 6400	96 – 330
112-42-5	1-Undecanol		220 [3]	8380	2980	180
68603-15-6	C6-12 Alcohols	Type A	ca. 220	CA. 7270	ca. 3000	ca. 180
67762-41-8	C10-16 Alcohols	Type B	390 - 450	27600 - 40100	6420 - 7680	330 - 600
67762-41-8	C10-16 Alcohols	Type C	390 - 450 [3]	27600 - 36600	6420 - 7680	330 - 600
67762-41-8	C10-16 Alcohols	Type D	390 - 1020 [3]	27600 - 177000	6420 - 23100	330 - 2050
67762-25-8	C12-18 Alcohols	Type A	389 - 2010 [3]	27600 - 839000	6420 - 57400	327 – 12900
67762-25-8	C12-18 Alcohols	Type B	389 - 2010 [3]	27600 - 839000	6420 - 57400	327 – 12900
63393-82-8	C12-15 Alcohols	Type A	390 – 1020 [3]	27600 - 203000	6420 – 23100	330 – 2050

CAS	Chemical Name	Comment[1]	Adsorption: soil-water partition coefficient - Koc			
			TGD Alcohols method[2]	TGD Hydrophobics method	TGD Non-hydrophobics method	SRC PCKOCWIN method
63393-82-8	C12-15 Alcohols	Type B	390 – 1020 [3]	27600 – 177000	6420 – 23100	330 – 2050
68855-56-1	C12-16 Alcohols	Type B	390 - 1240 [3]	27600 - 307000	6400 - 30100	330 - 3790
68855-56-1	C12-16 Alcohols	Type C	390 - 1240 [3]	27600 - 307000	6400 - 30100	330 - 3790
68855-56-1	C12-16 Alcohols	Type A	390 - 1020 [3]	27600 – 177000	6400 - 23100	330 - 2050
80206-82-2	C12-14 Alcohols	Type A	390 - 1240 [3]	27600 - 307000	6420 - 30100	330 - 3790
80206-82-2	C12-14 Alcohols	Type B	390 - 710 [3]	27600 - 96500	6420 - 14300	330 - 1110
75782-86-4	C12-13 Alcohols		390 – 450 [3]	27600 - 36600	6420 – 7680	330 – 600
68333-80-2	C14-16 Alcohols	Type B	390 - 1020 [3]	27600 - 177000	6420 - 23100	330 – 2050
112-70-9	1-Tridecanol		450 [3]	36600	7680	600
90583-91-8	Tridecanol, branched and linear		470 [3]	40100	8150	530
112-72-1	1-Tetradecanol		710 [3]	96500	14300	1110
68333-80-2	C14-16 Alcohols	Type A	710- 1020 [3]	96500 - 177000	14300 - 23100	1110 – 2050
75782-87-5	C14-15 Alcohols		711 – 1020 [3]	96500 - 203000	14300 – 23100	1110 – 2050
67762-30-5	C14-18 Alcohols	Type B	710 - 2010 [3]	96500 - 839000	14300 - 57400	1110 - 12900
629-76-5	1-Pentadecanol		1020 [3]	203000	23100	2050
36653-82-4	1-Hexadecanol		1240 [3]	307000	30100	3790
67762-30-5	C14-18 Alcohols	Type A	1240 - 2010 [3]	307000 - 839000	30100 - 57400	3790 - 12900
67762-27-0 (Also mixture of 36653-82-4 and 112-92-5)	C16-18 Alcohols		1240 - 2010 [3]	96500 - 839000	30100 - 57400	3790 - 12900
143-28-2	9-Octadecen-1-ol, (9Z)-		1810 [3]	671000	49700	12900
68002-94-8	C16-18 and C18 Unstd.		1240 – 2010 [3]	96500 - 839000	30100 – 57400	3790 – 12900

CAS	Chemical Name	Comment[1]	Adsorption: soil-water partition coefficient - Koc			
			TGD Alcohols method[2]	TGD Hydrophobics method	TGD Non-hydrophobics method	SRC PCKOCWIN method
68155-00-0	Alcohols, C14-18 and C16-18-unsatd.		711 – 2010 [3]	96500 - 839000	14300 – 57400	1110 – 12900
97552-91-5	C18-22 Alcohol		2010 – 3330 [3]	839000 – 2390000 [3]	57400 – 112000	12900 – 149000
629-96-9	1-Eicosanol		3330 [3]	2390000 [3]	112000	43800
661-19-8	1-Docosanol		3330 [3]	2390000 [3]	112000	149000

Notes:

1. Compositional Types are described in section 1.1.3.
2. These are two relevant (Q)SAR methods from the TGD (EC, 2003), for non-hydrophobics and alcohols
3. The TGD Alcohols method is valid up to log Kow = 5. The TGD Hydrophobics method is valid up to log Kow = 7.5. The result is presented for comparison only.

2.2.4.3 Fugacity modelling

Two models have been used:

- The 1997 Level I model implemented as 'EQC'
- The 1999 Level III model, available on the Canadian government web site.

Both models use key property data as inputs (molecular weight; melting point, vapour pressure, water solubility, log K_{ow}) and also use degradation half lives. The purpose of this modelling is to gain an overview of relative exposure, not any absolute values of predicted concentration.

In modelling the long chain aliphatic alcohols, some degradation has been allowed for in both the Level I and Level III models. The half-life for degradation in air is estimated using the SRC AOPWIN v1.91 model (as described in section 3.2.2), which predicts the rate of reaction with hydroxyl radicals in the atmosphere. This is converted into a half-life using the standard EU atmospheric concentration of hydroxyl radicals. The half-lives in soil and in water are both set to 720 hours, i.e. 30 days, for all of the alcohols, to reflect that they are all aerobically biodegradable. Whilst some of the alcohols might be expected to degrade much faster than this, for the purpose of this comparative study the input value is not critical. Further discussion is given in Annex VI.

The modelling shows that, for release via water, a maximum of 0.021% of alcohol (C8) will partition to soil. The distribution ratio between water and sediment decreases from 99.9 : 0.1 for hexanol to 2.5 : 97.5 for docosanol. The results of level I modelling are presented in Table 2.7 below. The results of Level III modelling are shown in Table 2.8 based on an assumption of 100% discharge to air, water and soil.

Distribution modelling for wastewater treatment plants

The distribution in a sewage treatment plant has been estimated using the SimpleTreat model (implemented in EUSES v2.03). The outputs, summarised in Tables 2.9 and 2.10 below, are based on two sets of properties. The assignation of biodegradability is discussed in section 2.2.5, and the physicochemical properties are as given above for the fugacity modelling of distribution. In Table 2.9 standard biodegradation rates and the ‘alcohols’ (Q)SAR is used. In Table 2.10, much higher degradation rates have been applied, and a different (Q)SAR (the ‘non-hydrophobics’) is used at higher C numbers. These details are discussed in sections 2.2.4, 2.2.5 and 2.2.8. The second set of predictions is more in line with field measurements.

Table 2.7 Environmental distribution predicted by Level I model

CAS number	Name	% air	% soil	% water	% fish	% sediment
111-27-3	1-hexanol	28	6.2	65.6	3.52E-04	0.14
111-87-5	1-octanol	17.3	45.4	36.3	2.56E-03	1.01
112-30-1	1-decanol	2.57	92.5	2.81	5.22E-03	2.06
112-42-5	1-undecanol	3.37	92.5	1.99	5.22E-03	2.06
112-70-9	1-tridecanol	2.02	95.5	0.33	5.39E-03	2.12
112-72-1	1-tetradecanol	0.33	97.3	0.10	5.50E-03	2.16
629-76-5	1-pentadecanol	0.10	97.6	0.04	5.51E-03	2.17
36653-82-4	1-hexadecanol	0.13	97.6	0.03	5.51E-03	2.17
143-28-2	9z-octadecenol	0.13	97.6	9.38E-03	5.51E-03	2.17
629-96-9	1-eicosanol	1.61E-03	97.8	1.96E-03	5.52E-03	2.17
661-19-8	1-docosanol	1.05E-03	97.8	1.96E-03	5.52E-03	2.17

Table 2.8 Environmental distribution predicted by Level III model

Name	CAS	Release to air				Release to water				Release to soil			
		% to air	% to water	% to sediment	% to soil	% to air	% to water	% to sediment	% to soil	% to air	% to water	% to sediment	% to soil
1-Hexanol	111-27-3	66.8	8.11	7.28E-03	25.1	0.0375	99.9	0.0897	0.0141	0.0379	14.6	0.0131	85.3
1-Octanol	111-87-5	63.6	4.02	0.0504	32.3	0.0407	98.7	1.24	0.0207	4.46E-03	1.6	0.02	98.4
1-Decanol	112-30-1	71.9	3.18	3.74	21.2	0.0324	45.9	54.0	9.54E-03	2.87E-04	0.0674	0.0792	99.9
1-Undecanol	112-42-5	77.9	2.67	4.64	14.8	0.0414	36.6	63.4	7.84E-03	3.34E-04	0.0458	0.0794	99.9
1-Tridecanol	112-70-9	69.1	1.36	13.1	16.4	0.018	9.38	90.6	4.28E-03	1.71E-04	0.0121	0.117	99.9
1-Tetradecanol	112-72-1	38.4	1.57	32.5	27.6	3.95E-03	4.61	95.4	2.84E-03	3.30E-05	0.0106	0.219	99.8
1-Pentadecanol	629-76-5	21.1	1.47	42.7	34.7	1.28E-03	3.32	96.7	2.11E-03	1.12E-05	0.0107	0.310	99.7
1-Hexadecanol	36653-82-4	9.88	1.25	40.7	48.2	1.25E-03	2.98	97.0	6.09E-03	1.34E-05	0.0103	0.335	99.7
Octadecen-1-ol, 9Z	143-28-2	8.01	1.17	42.9	47.9	5.79E-04	2.65	97.3	3.47E-03	9.86E-06	0.0105	0.383	99.6
1-Eicosanol	629-96-9	0.639	1.22	47.5	50.6	2.52E-05	2.50	97.5	1.99E-03	2.41E-07	0.0111	0.433	99.6
1-Docosanol	661-19-8	0.582	1.22	47.5	50.7	1.72E-05	2.50	97.5	1.49E-03	1.71E-07	0.0111	0.434	99.6

Table 2.9 Distribution in waste water treatment plant (WWTP) predicted by SimpleTreat model (default degradation rate)

Substance	Molecular weight	Water solubility	log Kow	Vapour pressure	Koc predicted by TGD (Q)SAR:	Biodegradability class	Rate constant per hour	Fate in WWTP:			
								Fraction to air	Fraction to water	Fraction to sludge	Fraction degraded
		mg/L		Pa				Fstp_air	Fstp_water	Fstp_sludge	
1-Hexanol	102	5900	2.03	1.22E+02	Alcohols	Ready deg. inside window	1.00	0.008	0.123	0.005	0.863
1-Heptanol	116	1313	2.57	2.80E+01	Alcohols	Ready deg. inside window	1.00	0.010	0.122	0.014	0.854
1-Octanol	130	551	3.15	1.00E+01	Alcohols	Ready deg. inside window	1.00	0.009	0.119	0.040	0.832
1-Nonanol	144	128	3.77	3.00E+00	Alcohols	Ready deg. inside window	1.00	0.011	0.110	0.113	0.765
1-Decanol	158	39.5	4.57	1.10E+00	Alcohols	Ready deg. inside window	1.00	0.010	0.088	0.326	0.576
1-Undecanol	172	8	4.72	3.90E-01	Alcohols	Ready deg. inside window	1.00	0.016	0.082	0.376	0.526
1-Dodecanol	186	1.93	5.36	1.10E-01	Alcohols	Ready deg. inside window	1.00	0.011	0.067	0.577	0.344
1-Tridecanol	200	0.38	5.51	5.70E-02	Alcohols	Ready deg. inside window	1.00	0.024	0.063	0.614	0.300
1-Tetradecanol	214	0.191	6.03	1.40E-02	Alcohols	Ready deg. inside window	1.00	0.008	0.065	0.728	0.199
1-Pentadecanol	228	0.102	6.43 (est)	5.13E-03	Alcohols	Ready deg. inside window	1.00	0.004	0.069	0.796	0.131
1-Hexadecanol	242	0.013	6.65	1.40E-03	Alcohols	Ready deg. outside window	0.30	0.008	0.087	0.865	0.040
1-Octadecanol	270	0.0011	7.19	3.30E-04	Alcohols	Ready deg. outside window	0.30	0.009	0.081	0.894	0.015
1-Eicosanol	298	0.0011 (est)	7.75	1.50E-05	Alcohols	Inherent deg.	0.10	0.000	0.082	0.916	0.002
1-Docosanol	326	0.001 (est)	7.75 (est)	8.20E-06 (est)	Alcohols	Inherent deg.	0.10	0.000	0.082	0.916	0.002

Table 2.10 **Distribution in waste water treatment plant (WWTP) predicted by SimpleTreat model (rapid degradation rate)**

Substance	Koc predicted by TGD (Q)SAR:	Fate in WWTP:			
		Fraction to air	Fraction to water	Fraction to sludge	Fraction degraded
		Fstp_air	Fstp_water	Fstp_sludge	
1-Hexanol	TGD Alcohols	0.004	0.001	0.002	0.993
1-Heptanol	TGD Alcohols	0.005	0.001	0.003	0.991
1-Octanol	TGD Alcohols	0.004	0.001	0.005	0.990
1-Nonanol	TGD Alcohols	0.006	0.0014	0.0083	0.984
1-Decanol	TGD Alcohols	0.0076	0.0014	0.017	0.974
1-Undecanol	TGD Alcohols	0.013	0.0014	0.019	0.967
1-Dodecanol	Van Compernolle *et al*.	0.0048	0.0038	0.47	0.521
1-Tridecanol	Van Compernolle *et al*.	0.00755	0.00417	0.498	0.490
1-Tetradecanol	Van Compernolle *et al*.	0.00277	0.0077	0.597	0.393
1-Pentadecanol	Van Compernolle *et al*.	0.00136	0.012	0.648	0.339
1-Hexadecanol	Van Compernolle *et al*.	0.00172	0.0152	0.671	0.312
1-Octadecanol	Van Compernolle *et al*.	0.00163	0.0273	0.729	0.242
1-Eicosanol	Van Compernolle *et al*.	1.36E-04	0.045	0.796	0.159
1-Docosanol	Van Compernolle *et al*.	0.000094	0.045	0.796	0.159

2.2.5 Biodegradation

2.2.5.1 Aerobic biodegradation

Many biodegradation assays have been carried out on this family of alcohols. Table 2.15 lists the best quality data (Klimisch reliability score of 1 or 2) generated on single carbon chain length alcohols for tests that conform most closely to ready test biodegradability methods (OECD 301 series). In all cases the inoculum was not acclimated; tests which allowed adaptation are considered to have significant methodological deficiencies for the present purpose, and are accordingly considered to be Klimisch reliability 3: Invalid. These data show that alcohols with chain lengths up to C18 are readily biodegradable. At carbon chain lengths ≤ 14, most tests showed that pass levels for ready biodegradation were reached within the 10 day window. Chain lengths of C16-18 achieved ready test pass levels, but not within the 10 day window. The one test on a single carbon chain length greater than C18 (docosanol) showed degradation of 37%.[4]

The data in this table were generated on linear alcohols with the exception of the data on C11, which relate to a 50% linear alcohol. These data on single carbon-chain lengths are supplemented in Table 2.16 with data generated on commercial products that contain more than one component. Many of these commercial products contain essentially-linear alcohol. The data expand the range of carbon chain lengths for which biodegradation data are available. The conclusions drawn from all these studies, which were used in the fugacity modelling, are shown in Table 2.13.

Table 2.11 below summarises the conclusions for tests of ready biodegradation carried out in standard studies. This summary applies equally to the 2-branched components and the linear ones.

Table 2.11 Summary of aerobic biodegradation under 'ready test' conditions

Carbon chain length	Results
<16	Readily biodegradable meeting the 10 day window
16-18	Rapidly biodegradable but unclear that the 10 day window is passed
>18	Degradation of 21-60% in ready tests, considered to be equivalent to inherent biodegradability

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[4] Some of the data were generated using the BODIS test methodology (ISO 10708). This method is equivalent to the OECD 301 A-F series and is a 2 phase closed bottle test for poorly water soluble compounds. The comparability of the BODIS method to tests in the OECD A-F series is shown by data on dodecanol which showed:

- 71% in 28 days at 20 mg/L (60% in 10 d window), in 301-B test (Morris, Filler and Nielsen, 1991)
- 79% in 28 d at 2 mg/L (60% in 10 d window) in 301 D test (Henkel, 1999d)
- 100% in 28 d at 100 mg/L (>60% in 10 d window) in BODIS test (Henkel, 1992c)
- 50% after 28 d at 26 mg/L; <60% in 10 d in 301B test [Mead, 1997a]
- 41% after 31 d at 20 mg/L; <60% in 10 d in 301B test [Vista Chemical Co., 1994].

And data on octadecanol which showed:

- 69% in 28 d at 2 mg/L (<60% in 10 d window, 60% in 14 d) in 301D test (Henkel, 1992f);
- 67% in 28 d (<60% in 10 d window, 60% in 20 d) in BODIS test (Henkel, 1992g)
- 67% after 28 days at 20 mg; <60% in 14d in 301B test (Vista Chemical Company, 1994)
- 43% after 28 days at 20 mg/L; <60% in 10d in 301B test [Mead, 1997d]

Several non-standard studies are useful in the overall understanding of the biodegradability of the category members. Federle and Itrich (Ecotox. Environ. Safety, 2006) have studied the fate of free and linear alcohol-ethoxylate-derived fatty alcohols in activated sludge, in a non-standard study conducted to a scientifically sound method. This has been assigned reliability 2, but has not been included in the summary table. Radiolabelled (^{14}C) C12, C14 and C16 alcohols were used. The study was a batch-mode activated sludge die-away system. Two treatments consisting of 1 litre each of biologically active sludge were prepared for each test substance. The 14-C alcohols were dissolved in methanol, which was diluted in water and dosed into the sludge in 2-litre flasks. Disappearance of parent, formation and disappearance of metabolites, uptake into biomass and mineralization to 14-C CO2 were monitored over time. Activated sludge from a municipal WWTP was obtained, and used at 2500 mg/L. The test substance was dosed at 0.05 µM: this is equivalent to 9.3µg/L (C12), 10.0 µg/L (C14), 10.7 µg/L (C16); added to flasks at 20ºC. This concentration is low relative to standard studies, but relevant to environmental conditions. Recoveries were high.

After 48 h incubation, concentrations were as shown in Table 2.12 below:

Table 2.12 Removals and fate of linear alcohols in a non-standard study

	Form that the radiolabelled carbon is present in (%)				
C	**Parent**	**metabolites**	**Water**	**Solids**	**CO_2**
C12	0.8	5.9	3.5	20.7	73.9
C14	1.3	6.3	2.0	21.0	76.7
C16	2.6	11.5	2.1	17.0	65.3

Concentration time-dependence data were modelled with the equation:

$$C = Ae^{-k_1 t} + Be^{-k_2 t}$$

(A two compartment first order decay model) and the fitted results were as shown in Table 2.13 below:

Table 2.13. Model parameters for degradation of linear alcohols in a non-standard study

C	**A**	**k_1 (h^{-1})**	**B**	**k_2 (h^{-1})**
C12	82±2	113±8	9±1	0.36±0.1
C14	82±2	87±5	12±1	0.30±0.1
C16	41±3	103±23	48±2	0.43±0.04

The results show the high biodegradability of C12 to 16 alcohols in activated sludge. The trend in the fitted parameters suggests a very rapid removal of dissolved substance as the dominant process, with a slower removal of adsorbed substance (although this proposal has not been proven). Such a trend would be consistent with the pattern of the ready-test data. In the TGD, the SIMPLETREAT model uses a rate constant of 1 h^{-1} for readily biodegradable substances meeting the 10-day window. The significance of these data is discussed further in the context of monitoring data (section 2.2.8 and Annex VII). However, there is further evidence that very high rates are appropriate.

Other recent data on ethoxylated alcohols also suggest that the rate of degradation could be higher than usually assigned to readily-biodegradable substances. In a study of the fate of alcohol ethoxylate homologues in a laboratory continuous activated sludge unit (Wind, *et al*., 2006) useful data about the properties and environmental exposures of alcohols are presented, although the paper describes mainly the properties of alcohol ethoxylates (AE). The waste water organisms were exposed principally to ethoxylates, but the alcohols would be generated by the degradation of the ethoxylates. A mixed chain length test substance was used at 4 mg/L in the influent.

Results are shown in Table 2.14 below:

Table 2.14. Removal of alcohols during an activated sludge test on alcohol ethoxylates.

Alcohol	Conc in effluent ng/L	Conc in sludge µg/g	%removal
C12	18	0.6	98.6
C13	21	0.7	99.5
C14	5.5	0	99.6
C15	2.9	1.1	99.8
C16	1.6	0.01	99.5
C18	58	0.7	99.1
Total	130	2	99.4

This shows that most of that which does not degrade (itself a small amount) was found in the solids in recovery at the end of the study. This study is important in that it indicates that the extent of removal of alcohols is high, from an exposure route that can realistically be anticipated based on the known life cycle.

Rapid degradation is also indicated by the difficulties encountered in chronic aquatic toxicity tests for the lower solubility substances, caused by rapid removal of the substance from the test medium, presumably by biodegradation by micro-organisms.

Predicted data from the SRC BIOWIN v4.00 program (part of the EPIWIN suite v3.12) supports rapid degradation for the linear alcohols (discussed in Annex V), but cannot be used quantitatively. However, the extent of measured data means that it is not necessary to rely upon any form of (Q)SAR: interpolation to fit data gaps can be done by expert judgement across the data set.

Reliable studies for decanol and tetradecanol that show low levels of degradation are considered to be unexplained outliers. It is usual in the interpretation of such data to take the highest levels of degradation as the key study.

2.2.5.1.1 Structural issues

Branched alcohols are present in many of the commercial products. No measured results are available for branched alcohols specifically. It is possible that branched components might be slightly less rapidly biodegradable than linear ones due to the slightly more complex chemical structure, but this would not be picked up in a standard study. Prediction by (Q)SAR (SRC BIOWIN v4.00) allows for a screening assessment of persistence and some findings using this method are discussed here. (Q)SAR (BIOWIN) indicates that as a general rule mono-branched structures degrade at essentially the same rate as the linear unsaturated alcohol of equivalent carbon number. These conclusions are supported by reliable measured data for branched alcohols which are members of the Oxo Alcohols Category. For full details please refer to the Oxo alcohols draft SIAR and SIDS dossiers.

Unsaturation does not appear to be detrimental to biodegradation rate; in two ready tests, a commercial multi-component substance (C16-18 components, containing C18 unsaturated components) was found to be readily biodegradable in a reliable study (using a non-standard inoculum; garden soil micro-organisms), and in several studies of non-assignable reliability. This substance was also found to be rapidly biodegradable under anaerobic conditions in a reliable study. C18 unsaturated alcohol was predicted by (Q)SAR (BIOWIN) to degrade at essentially the same rate as the linear unsaturated alcohol, as described in Annex V.

It is concluded that in studies where both linear and essentially-linear components are present, all would degrade rapidly.

2.2.5.2 Biodegradation under anaerobic conditions

The anaerobic biodegradability of C8, C16 (three reliable studies) and C16-18 + C18 unsaturated (one reliable study), has been investigated. Table 2.17 shows that all test substances were anaerobically degradable.

Table 2.15 Ready biodegradation data on single component alcohols

CAS	Chemical Name	Comment	Method	Result		Reliability	Reference
				% degradation	10 day window		
111-27-3	1-Hexanol		OECD 301-D	77% in 30 days at 2 mg/L 61% in 30 days at 5 mg/L	>60% in 14 days	2	Richterich, 2002a
111-27-3	1-Hexanol		Non-standard	- half life of 8.7 hours	-	2	Yonezawa and Urushigawa 1979
111-87-5	1-Octanol		ISO ring test (CO2 headspace biodegr. test)	92% in 28 days at 20 mg/L	>60%	2	Procter & Gamble, 1996
111-87-5	1-Octanol		OECD 301-B	59 % in 29 days at 10 mgC/L	-	2	Huntingdon Life Sciences Ltd. 1996a
111-87-5	1-Octanol		Non-standard	- half life of 1.9 hours	-	2	Yonezawa and Urushigawa 1979
112-30-1	1-Decanol		301-D	88% in 30 days at 2 mg/L	>60%	2	Richterich, 2002c
112-30-1	1-Decanol		301-B	29 % after 29 day(s) at 10 mg/L COD	-	2	Huntingdon Life Sciences Ltd. 1996b
112-53-8	1-Dodecanol	Supporting	301-D	79% in 28 days at 2 mg/L	>60% in 14 days	1	Richterich, 1993
112-72-1	1-Tetradecanol		BODIS ~ISO 10708	92% in 28 days at 100 mg/L COD	>60%	1	Henkel, 1992d
112-72-1	1-Tetradecanol		301-B	28 % after 28 day(s) at 25.4 mg/L	-	1	Mead 1997b
36653-82-4	1-Hexadecanol		301B	62% after 28 days at 17.1 mg/L	<60%	1	Mead, 1997c
36653-82-4	1-Hexadecanol		BODIS	76 % after 28 day(s) at 100 mg/L COD	<60% after 14 d	2	Henkel KGaA 1992a
112-92-5	1-Octadecanol	Supporting	301D	38% in 29 days at 5 mg/L 69% in 29 days at 2 mg/L	<60%	1	Henkel, 1992f
661-19-8	1-Docosanol		301B	37% after 28 days at 12.4 mg/L	<60%	1	Mead, 2000

Table 2.16 Biodegradation of commercial alcohol products

CAS	Chemical name	Comment	Method	Result		Reliability	Reference
				% degradation	10 day window		
68603-15-6	Alcohols, C6-12	Type C	301B	64-79% in 28 days at 20 mg/L	>60%	2	Miller and Watkinson, 1984
68603-15-6	Alcohols, C6-12	Type C	301D	53-54% at 2 mg/L	-	2	Miller and Watkinson, 1984
68603-15-6	Alcohols, C6-12	Type A	301-F	83% in 26 days at 38 mg/L	>60%	2	Instituto Guido Donegani, 1993a
67762-41-8	Alcohols, C10-16	Type B	301-B	86-87% in 28 days at 13 & 26 mg/L	>60%	1	Sasol, Sastech Research and Development 1998a
67762-41-8	Alcohols, C10-16	Type B	301-F	91% in 26 days at 45 mg/L	>60%	2	Instituto Guido Donegani, 1993b
67762-41-8	Alcohols, C10-16	Type B	301-F	80% in 28 days at 46 mg/L	>60%	2	Instituto Guido Donegani, 1993b
67762-41-8	Alcohols, C10-16	Type C	301-F	84% in 28 days at 35&54 mg/L	>60%	2	Instituto Guido Donegani, 1993d
67762-25-8	Alcohols, C12-18	Type B	301-D	79% in 28 days at 2 mg/L	58% in 7 days, >60% in 14 days	1	Henkel, 1992b
63393-82-8	Alcohols, C12-15	Type B	301-D	100% in 30 days at 2 mg/L	>60%	1	Richterich 2002b
68855-56-1	Alcohols, C12-16	Type B	301-B	61% in 29 days at 10 mg/L COD	45%	2	Huntingdon Life Sciences, 1996c
80206-82-2	Alcohols, C12-14	Type A	BODIS	79-97% in 28 days at 100 mg/L	>60%	1	Henkel 1997
68333-80-2	Alcohols, C14-16	Type A	301-F	82% in 28 days at 45 mg/L	>60%	1	Instituto Guido Donegani, 1995
68333-80-2	Alcohols, C14-16	Type A	301-F	75% in 28 days at 45& 52 mg/L	<60%	2	Instituto Guido Donegani, 1993c
Mixture of 36653-82-4 +112-92-5 (67762-27-0)	Alcohols, C16-18	-	Modified Sturm	21-65% in 28 days at 20 mg/L	<60% (60% in 15 days)	2	Morris, Filler and Nielsen, 1991
68002-94-8	Alcohols, C16-18 and C18 Unsaturated	-	301-D	87% in 28 days at 2 mg/L	>60	2	Borner, 1999 garden soil inoculum study

Note:

1 – Compositional Types are described in section 1.1.3.

Table 2.17 Anaerobic degradation of alcohols

CAS	Chemical name	Comment	Method	Source of sludge	Concentration of test substance	Duration	% degradation at end of test	Reliability	Reference
111-87-5	1-Octanol		Serum bottle, gas production + GC analysis	1º or 2º digesters	50 ug/ml	8 weeks	>75%	2	Shelton and Tiedje, 1984
36653-82-4	1-Hexadecanol		Batch test using ^{14}C labelled test material	Municipal digester sludge fortified with activated sludge	1 mg/L	28 days	90%	2	Nuck and Federle, 1996
36653-82-4	1-Hexadecanol		Batch test using ^{14}C labelled test material	Municipal sewage digester	10 mg/L	28 days	97%	2	Steber and Wierich, 1987
68002-94-8	Alcohols, C16-18 & C18 unsaturated		ECETOC screening test	Municipal sewage digester	50 mg/L	8 weeks	89%	2	Steber *et al*. 1995

2.2.6 Bioaccumulation

No reliable guideline-standard measured bioconcentration data are available. Chain lengths C11 and above have log K_{ow} >4.5 and so could be considered to be potentially bioaccumulative. Annex V discusses the strategy for property prediction in detail. However, the rapid degradation described above, combined with evidence of rapid metabolism in mammalian studies, suggests that this would be an overly conservative interpretation, and that it is unlikely that bioaccumulation would be seen in studies.

Bioconcentration factors (BCF) calculated on the basis of log K_{ow} range from 7.0 for C6 to a maximum of 46000 for C16 reducing to 1100 for C22 (Technical Guidance Document, 1996 after Veith *et al*. 1979 and recalculated from Connell and Hawker, 1988). For hexadecanol, the BCF (Q)SAR estimates a value of 46000, but there is a measured value of 56 (Freitag *et al*., 1982) and a range of values from another study, 507-1550 (Unilever, 1995). These measured values are all from poor quality studies in which measurements were made on total radioactivity, no attempt was made to determine if steady-state conditions had been established and exposure concentrations were above the limit of solubility. There are no measured BCF values for any other member of the alcohol family. However, BCF data for alcohols similar to those in this family but with 2.1-2.9 branches per molecule also indicate that BCF (Q)SAR overestimate BCF (ExxonMobil, 2001). All these data suggest that log K_{ow}-based (Q)SAR overestimate BCF, which is to be expected since they take no account of biotransformation and alcohols are considered to be metabolised, at least in mammals (refer to chapter 3 on human health hazards).

These expectations are supported by reliable measured data for similar alcohols which are members of the Oxo Alcohols Category, which further substantiate the lower-than-predicted BCFs. These data wil need to be considered once they are in the public domain. For full details please refer to the Oxo alcohols draft SIAR and SIDS dossiers.

The data set cannot be considered as definitive for this property. The best available data are presented in Table 2.18.

Table 2.18 Bioaccumulation factors

All of these calculated BCF values are discussed in Annex V to the SIAR.

CAS	Chemical Name	Comment	Bioaccumulation
111-27-3	1-Hexanol		BCF = 11 calculated (Veith *et al*., 1979)
68603-15-6	C6-12 Alcohols	TYPE C	BCF = 31-320 calculated (based on values of components)
111-87-5	1-Octanol		BCF = 95 calculated (Veith *et al*., 1979)
68603-15-6	C6-12 Alcohols	TYPE D	BCF = 10-1530 calculated (based on values of components)
85566-12-7 (Also mixture of 111-87-5 & 112-30-1)	C8-10 Alcohols		BCF = 90-1500 calculated (based on values of components)
68551-07-5	Alcohols, C8-18		BCF = 95 - 43800 calculated (based on values of components)
66455-17-2	C9-11 Alcohols		BCF = 300 – 2050 calculated (based on values of components)
68603-15-6	C6-12 Alcohols	TYPE B	BCF = 320-2050 calculated (based on values of components)
112-30-1	1-Decanol		BCF = 1530 calculated (Veith *et al*., 1979)
67762-41-8	C10-16 Alcohols	TYPE A	BCF = 1530 - 45300 calculated (based on values of components)

CAS	Chemical Name	Comment	Bioaccumulation
85665-26-5	Alcohols, C10-12		BCF = 1500 – 7200 calculated (based on values of components)
112-42-5	1-Undecanol		BCF = 2050 calculated (Veith *et al*., 1979)
68603-15-6	C6-12 Alcohols	TYPE A	BCF = 1800-2050 calculated (based on values of components)
112-53-8	1-Dodecanol - SUPPORTING		BCF = 3,801 (calculated) [SIDS dossier on 1-dodecanol, 1993a]
67762-41-8	C10-16 Alcohols	TYPE B	BCF = 4500 - 9600 calculated (based on values of components)
67762-41-8	C10-16 Alcohols	TYPE C	BCF = 7200 - 9600 calculated (based on values of components)
67762-41-8	C10-16 Alcohols	TYPE D	BCF = 4500 - 42600 calculated (based on values of components)
67762-25-8	C12-18 Alcohols	TYPE A	BCF = 7200 – 43800 calculated (based on values of components)
67762-25-8	C12-18 Alcohols	TYPE B	BCF = 7200 – 43800 calculated (based on values of components)
63393-82-8	C12-15 Alcohols	TYPE A	BCF = 7200 - 42600 calculated (based on values of components)
63393-82-8	C12-15 Alcohols	TYPE B	BCF = 4500 - 42600 calculated (based on values of components)
68855-56-1	C12-16 Alcohols	TYPE B	BCF = 7200 - 45300 calculated (based on values of components)
68855-56-1	C12-16 Alcohols	TYPE C	BCF = 7200 - 45300 calculated (based on values of components)
68855-56-1	C12-16 Alcohols	TYPE A	BCF = 4500 - 42600 calculated (based on values of components)
80206-82-2	C12-14 Alcohols	TYPE A	BCF = 7200 – 45300 calculated (based on values of components)
80206-82-2	C12-14 Alcohols	TYPE B	BCF = 7200 – 33900 calculated (based on values of components)
75782-86-4	C12-13 Alcohols		BCF = 4500 – 9600 calculated (based on values of components)
68333-80-2	C14-16 Alcohols	TYPE B	BCF = 4500 – 42600 calculated (based on values of components)
112-70-9	1-Tridecanol		BCF = 9630 calculated (Veith *et al*., 1979)
90583-91-8	Tridecanol, branched and linear		BCF = 10600 calculated (Veith *et al*., 1979)
112-72-1	1-Tetradecanol		BCF = 33900 calculated (recalculated from Connell and Hawker, 1988)
68333-80-2	C14-16 Alcohols	TYPE A	BCF = 33900 – 42600 calculated (based on values of components)
75782-87-5	C14-15 Alcohols		BCF = 24000 – 42600 calculated (based on values of components)
67762-30-5	C14-18 Alcohols	TYPE B	BCF = 33900 – 45300 calculated (based on values of components)
629-76-5	1-Pentadecanol		BCF = 42600 calculated (recalculated from Connell and Hawker, 1988)
36653-82-4	1-Hexadecanol		BCF = 45300 calculated (recalculated from Connell and Hawker, 1988) Available measured data are invalid
67762-30-5	C14-18 Alcohols	TYPE A	BCF = 43800 - 45300 calculated (based on values of components)
67762-27-0 (Also mixture of 36653-82-4 and 112-92-5)	C16-18 Alcohols		BCF = 43800 – 45300 calculated (based on values of components)
143-28-2	9-Octadecen-1-ol, (9Z)-		BCF = 45200 calculated (recalculated from Connell and Hawker, 1988)
68002-94-8	C16-18 and C18 Unstd.		BCF = 43800 – 45100 calculated (based on values of components)
68155-00-0	Alcohols, C14-18 and C16-18-unsatd.		BCF = 33900 – 43800 calculated (based on values of components)

CAS	Chemical Name	Comment	Bioaccumulation
112-92-5	(1-Octadecanol) - SUPPORTING		BCF = 100,000 (calculated) [SIDS dossier on 1-octadecanol, 1993b]
97552-91-5	C18-22 Alcohol		BCF = 32000 – 43800 calculated (based on values of components)
629-96-9	1-Eicosanol		BCF = 31800 calculated (recalculated from Connell and Hawker, 1988)
661-19-8	1-Docosanol		BCF = 31800 calculated (recalculated from Connell and Hawker, 1988)

Note:

1 – Compositional Types are described in section 1.1.3.

2.2.7 Other Information on Environmental Fate

No additional data are available.

2.2.8 Measured environmental concentrations

2.2.8.1 Sources of Environmental Exposure

Sources of environmental exposure to long chain aliphatic alcohols can be broken down into several broad classes: natural sources and occurrence, distribution from manufacturing and production facilities by discharge to surface water, and distribution from domestic wastewater treatment plants as a result of consumer use.

Natural Sources of Long Chain Aliphatic Alcohols

The published and grey literature on the environmental occurrence, fate and behavior of fatty alcohols has been reviewed (Mudge, 2005). The principal focus of this review was on the natural production of aliphatic alcohols, which occurs in all living organisms from bacteria to man, and the profiles and concentrations of these compounds in water, soils and sediments. The major production mechanism is from the reduction of fatty acids, through aldehyde intermediates, to fatty alcohols and in many organisms to esters with fatty acids to form waxes (Metz et al., 2000). These waxes are used for a variety of purposed from the prevention of desiccation in the terrestrial environment to energy reserves in the marine environment (Sargent et al., 1976; Buckner et al., 1996; Nelson et al., 1999; Ishige et al., 2003; Dahl et al., 2005). They are ubiquitous and occur in most environments around the world including the deep ocean and in sediment cores. Due to the nature of the synthetic pathway using acetyl-CoA, most long chain aliphatic alcohols are of an even chain length. Terrestrial plants utilize fatty alcohols as waxy coating and these compounds are dominated by long chain moieties with chain lengths from C_{22} to C_{32}; in contrast marine organisms synthesize smaller compounds with peak chain lengths of C_{14} to C_{16}. Bacteria also produce fatty alcohols but these can also be odd chain lengths and contain branches. This aspect of their occurrence enables them to be used as biomarkers for organic matter sources. As well as their natural production and occurrence, fatty alcohols are also utilised in detergent formulations principally as polyethoxylates. The analytical method used to measure the concentration of the ethoxylates involves direct derivatisation with a pyridinium complex and quantification via LC-MS. This technique will detect free fatty alcohols as well as the ethoxylates but will not detect any of the compounds such as the waxes that are highly chemically related to alcohols. Upon biodegradation or under certain metabolic conditions, alcohols could be derived from waxes. The concentration of individual fatty alcohols in the environment ranges from low values in old (several thousand year) deep cores from the open ocean floor (undetectable to 12 ng/g dry weight for C_{16}) to high values near natural sources and especially in suspended particulate matter (2.7 mg/g dry weight for C_{16}); this is almost a factor of 106 difference in their concentrations. The short chain compounds have been found to be more readily degradable than the longer chain compounds and in many cases are removed first as a food source for bacteria. The longer chain compounds may also degrade to short chain compounds with time but, in general, the $>C_{20}$ class of alcohols are better preserved in sediments than the $<C_{20}$ class.

The rates of production of long chained aliphatic alcohol from natural waxes and fatty acids in environmental conditions are not known (Mudge, 2005). These include release rates and mass contributions from microbial senescence, household consumption of animal and vegetable matter, and the like. For example, Leeming et al. (1994) established that long chain aliphatic alcohols (C_{14}-C_{32}) are measurable components of human feces in wastewater treatment. The sum of C_{14} to C_{18} chain lengths ranged from 217-1825 µg/g. It is clear that measurements of long chain alcohol in environmental matrices will reflect the combination of both natural and anthropogenic sources.

While a number of measurements of long chain alcohol in wastewater effluents and aquatic sediments have been made, but there has been little effort devoted to understanding their sources. A review of the literature by Mudge (2005) suggests that additional research is needed to clearly quantify the relative levels of natural and anthropogenic alcohol inputs to and presence in surface water and sediment compartments. To do so will require new analytical, sampling, and monitoring approaches (Mudge, 2005). Based on present literature it is already clear that long chained aliphatic alcohols are present in environments without anthropogenic influences.

Sources of Long Chain Alcohols from Manufacturing Discharges

Release of long chain aliphatic alcohols as a result of manufacturing has not been empirically demonstrated, but can be assumed present due to process and handling losses, cleaning of equipment and lines and the like. Releases are often minimized by the utilization of “fat traps” which capture aliphatic substances from being released. Model predictions for potential release of long chain aliphatic alcohols to the environment from manufacturing is consistent with measurements made in domestic wastewater treatment plant effluents (Annex VII, Tables A VII-4 and VII-6).

Sources of Long Chain Aliphatic Alcohols From Consumer Use

Release of long chain aliphatic alcohols as a result of consumer use has not been empirically demonstrated, but assumed from measurements of long chain aliphatic alcohols in domestic wastewater effluents. The ubiquitousness of long chain aliphatic alcohols in food, human waste, and as a result of natural biochemical processes present in influents to wastewater, are combined with disposal from consumer uses. The uses of free alcohols are a result of applications utilizing their emollient, emulsifying, solubilizing or lubricating properties. Long chain aliphatic alcohols are therefore found in various cosmetic and toiletry goods, surface lubricants (rolling oils), and pharmaceutical applications (Modler *et al.* 2004).

The presence of long chain aliphatic alcohols in domestic wastewater has also been tied to their use as a building block for alcohol-based anionic and nonionic detergents. For example, the nonionic alcohol ethoxylate (AE) surfactants are synthesized from long chain aliphatic alcohols and ethylene oxide. Biodegradation of AE has multiple pathways including ether cleavage releasing the free alcohol and polyethoxylate moieties (Federle and Itrich, 2006). Alcohol ethoxysulfates (AES), an anionic surfactant, is synthesized by sulfating the terminal member of an alcohol ethoxylate. Desulfation followed by ether cleavage will also potentially release free long chain aliphatic alcohols. Alcohol sulfate (AS), another anionic surfactant, is both a component of AES (the unethoxylated component) and synthesized separately as a detergent surfactant. Desulfation of the sulfate group can also potentially release fatty alcohol. The group of alcohol based surfactants are universally highly removed in wasterwater treatment, are anaerobically and aerobically biodegraded, and have low bioaccumulation potential as a result of inherent metabolic capabilities of biota (Nuck and Federle, 1996a, b; Bernhard and Dyer 2005a, b; Federle and Itrich, 2006).

2.2.8.2 Measured environmental concentrations

Long Chain Aliphatic Alcohols in wastewater treatment plant influent and effluents

Several methods that measure long chain aliphatic alcohols in environmental matrices are available. Dunphy *et al*. (2001a, b) devised and executed a method whereby alcohols present in an environmental sample can be detected at extremely low concentrations, often less than 10 ng/L. The method involves extraction of wastewater effluent and associated solids followed by derivatization with 2-fluoro-N-methylpyridinium p-toluenesulfonate to a permanent cation for quantitation by HPLC/MS. Morrall *et al*. (2006) reported influent levels of long chain alcohols for 9 wastewater treatment plants across the United States and 3 additional plants were reported in MRI (2004) (data from Morrall is developed from Dunphy et al. 2001a, MRI 2000, MRI 2001). Influent concentrations ranged from 102.8 to 2332.6 µg/L (sum of C_{12-18} long chain aliphatic alcohols) and averaged 698.4 µg/L across all influents (Annex VII, Table A VII-1). Individual chain lengths averaged 64.0 µg/L (C_{13}) to 160.0 µg/L (C_{18}). When considering these data further, it should be clear that the analytical procedure includes both free and adsorbed alcohol in the measurement. For further consideration of measured exposures in the environment, it is important to understand the amount that is adsorbed.

Van Compernolle *et al*. (2006) report the adsorption of several long chain alcohols (C_{12}, C_{14}, C_{16}, and C_{18}) to wastewater treatment plant solids in a manuscript devoted to developing a sorption (Q)SAR for alcohol ethoxylates. Based on the alcohol only subset of data, the following (Q)SARs are derived (data in Annex VII, Table A VII-2):

Log Kd = Chain Length x 0.235 + 0.642 $R^2 = 0.999$, n = 4
Log Koc = Chain Length x 0.235 + 1.420 $R^2 = 0.999$, n = 4
Log Koc = log Kow x 0.766 + 0.111 $R^2 = 0.994$, n = 4

It is of interest to note that the third (Q)SAR is very similar to that for ‘hydrophobics’ in the EU RA TGD, as discussed in 2.2.4.

Measured levels of long chain aliphatic alcohol in municipal wastewater effluents have been made with the same methodology cited for influents above and have been reported by Eadsforth *et al*. (2006), Morrall *et al*. (2006), and MRI (2004). These studies have taken place in United States, Canada, and 5 countries in Western Europe (Annex VII, Table AVII-3). Due to extremely rapid and extensive degradation concentrations in effluent are quite low. For this reason the methods of Dunphy *et al.* (2001) were developed as individual analytes typically are well below 0.1 µg/L thereby requiring large extraction volumes (4 L) and accounting of both free and sorbed alcohol on wastewater solids.

Determination of average regional wastewater concentrations varies in relation to the amount of specific data available on types of treatment employed within different geographies. In Europe, only Activated Sludge (AS) treatment was monitored whereas in Canada, Activated Sludge and fixed film treatment (trickling filter and rotating biological contactor) were monitored. However, because the number of plants and their wastewater flow volumes in Canada are not available for the entire country is not known how to appropriately weight the individual measurements of long chain alcohol by treatment to achieve a national average. This data is available for the United States (USEPA, 1997). For example, AS treatment accounts for 80.6% of total US wastewater flow versus 7.1% for trickling filters. Therefore, individual measurements can be weighted to achieve a national average concentration. For the purpose of broad comparisons across US, Canadian, and European geographies, the average total long chain aliphatic alcohol concentrations (C_{12} to C_{18}) in effluent are 1.442, 2.811, and 2.169 µg/L, respectively. Individual chain length contributions to this total are presented in Annex VII Table A VII-3. The 90%centile (all measurements at this concentration or lower) for total long chain aliphatic alcohol detected in individual monitored effluent measurements worldwide, not accounting for treatment type and flow, is 4.407 µg/L and the global average (arithmetic mean of the three regional averages) is 2.141 µg/L. These values include both free alcohol and alcohol sorbed to wastewater solids. Perspective on individual chain lengths is also in Annex VII, Table A VII-3. For treatment plant effluents monitored within the US the average concentrations of C18 (0.587 µg/L) > C16 ≈ C12 > C14 ≈ C15 > C13 (0.035 µg/L). For treatment plant effluents monitored in Canada the average concentrations of C15 (0.619 µg/L) ≈ C16 > C14 > C18 > C12 > C13 (0.209 µg/L). For treatment plant effluents monitored within Europe the average concentrations of C16 (0.688 µg/L) > C18 > C12 > C14 > C15 > C13 (0.165 µg/L). The overall trend appears to be that effluents have higher concentrations of longer aliphatic alcohol chain lengths than shorter chain lengths. This is also consistent with an expectation of chain lengths that have greater association with natural sources in the environment.

Wastewater effluent measurements in the previously cited studies include the levels of long chain alcohol initially sorbed to wastewater solids. Using the bioavailability (Q)SAR above, adjusted to a common level of organic carbon for wastewater ($f_{oc} = 0.32$), free long chain alcohol in effluents can be estimated (Annex VII, Table A VII-4). For US, Canada and Europe, the average total long chain alcohol concentrations (C_{12} to C_{18}) following adjustment due to sorption are 0.644, 1.487, 1.041 µg/L. The 90%centile (all measurements at this concentration or lower) for individual monitored effluent measurements worldwide, not accounting for treatment type and flow, is 2.121 µg/L and the global average of regional measurements is 1.057 µg/L. A reduction in the longest chain lengths, with the highest K_{oc} values, account for the largest change in contribution to the total exposure. This observation in particular has high importance when considering the structure-activity-relationships for aquatic toxicity to the long chain alcohols.

Long Chain Aliphatic Alcohols in Sediments

Few reliable data are available for the sediment compartment. Dyer *et al.* (2006) recently performed a study to determine the appropriateness of the Dunphy *et al.* (2001) analytical method for measuring alcohol ethoxylate in coarse sediments. The method was applied at three sites of varying sediment composition. Further refinements to the methods were instituted to potentially measure free long chain alcohols and alcohol ethoxylates in pore water, surface waters, and chemical bound to coarse and fine sediments. Analytical results without further interpretation were recently reported by MRI (2004) to the Soap and Detergent Association (SDA). Three additional sites were considered in this latter study and considered points upstream of the discharge, in the immediate point of entry for the discharge, at the end of the mixing zone, downstream of the mixing zone and far downstream of the mixing zone (Table Annex VII, Table A VII-5) (MRI, 2004). Long chain alcohols were ubiquitous and primarily associated with fine particulate matter in river sediments. Measurements by chain length and location were variable and the highest measurements (up to 12 µg/g) were recorded far downstream of sewage treatment plant inputs (above that recorded in the mixing zones and discharge proper). Levels of alcohols upstream of sewage inputs highly overlapped those in discharge and mixing zone samples (circa 0.1 to 1 µg/g). These observations are indicative of and consistent with the widespread natural presence of alcohols in sediments reviewed by Mudge (2005).

Long Chain Aliphatic Alcohols in manufacturing discharges

No data are available for the presence of long chain alcohols in manufacturing discharges. Due to the rapid and extensive biodegradation known for of alcohols it has been viewed as a low priority for work. Typically, manufacturing sites are structured to minimize potential inadvertent loss of materials due to process or production inefficiency. Specifically, so-called “fat traps” are in use to capture aliphatic substances on-site and prior to any environmental release. However, as with any engineered process and design some loss to the environment is inevitable. Because long chain aliphatic alcohols are aerobically and anaerobically biodegradable, and rapidly mineralized by unacclimated microbial consortia they are expected to decline quickly even while in discharge systems and subsequently after release into surface waters and sediments.

In order to gain insight into potential for release from manufacturing discharges in a local situation, EUSES v. 2 (EU TGD Volume 4, 2004) with Emission Scenarios for chemical production in industrialized Western Europe was used (details in Annex IX Measured Environmental Exposure). Table A VII-6 summarizes SIMPLETREAT output for C6-C20 alcohols. Predicted in-stream concentrations range from 0.003 to 0.113 µg/L for individual chain lengths. If a dilution factor of 10 is assumed following effluent discharge from domestic wastewater treatment facilities in the monitoring studies where long chain aliphatic alcohols was directly measured, in stream concentrations would range from 0.010 to 0.024 µg/L for individual chain lengths. It is clear that in-stream predictions for wastewater treatment plant effluents and discharge from manufacturing are expected to be quite similar. Further, all of these predictions do not yet account for subsequent degradation in the receiving water. Given the rapid and extensive degradation rates confirmed in benchtop simulation studies (Federle and Itrich, 2006, Wind *et al,* 2006), high rates of removal demonstrated in sewage treatment (Eadsforth *et al.,* 2006; Morrall *et al,* 2006), inherent metabolism of long chain aliphatic alcohols by micro and macrobiota, and the ubiquitous presence of natural sources of long chain aliphatic alcohols in the environment (Mudge 2005) exposure to long chain aliphatic alcohols will be of low concern.

2.3 Human Exposure

The assessment of the human exposure to long chain aliphatic alcohols is based on the information provided by the members of the Long Chain Aliphatic Alcohols Consortium. The data provided allowed an assessment of the following scenarios:

1. Potential occupational exposures to aliphatic alcohols during
    - Manufacture
    - Use
    - Formulation
2. Potential exposures to the consumer from the use products containing long chain aliphatic alcohols. The exposures have been estimated via modeling using screening level inputs and the formulation data.

A full assessment of human exposure has been undertaken, which is presented in Annex IV. This section provides a summary.

2.3.1 Occupational exposure

2.3.1.1 Manufacture of Aliphatic alcohols

Aliphatic alcohols are manufactured in established chemical manufacturing facilities that have standard engineering controls and procedures in place to ensure safe handling and use of chemicals.

Manufacturers apply process conditions that require a closed reactor design; long chain aliphatic alcohols are manufactured in a continuous operation at elevated temperature and pressure. On-site, aliphatic alcohols are transported via pipelines and stored predominantly in fixed roof storage tanks with a nitrogen blanket. As rule aliphatic alcohols are transported in bulk by truck, barge or rail; loading systems may include vapour recovery techniques.

All production facilities use standard personal protective equipment to prevent direct skin and eye contact with long chain aliphatic alcohols: for routine operations, including those involving a breach of the closed system goggles or safety glasses, gloves, safety boots and helmets are worn. Long chained aliphatic alcohols have a low volatility and as a rule engineering controls are available that prevent the need for respiratory protection. For non-routine operations involving a break in the closed system a higher level of protection is applied and usually extra measures are taken to prevent breathing of vapours, if (local) ventilation is inadequate. Operations with a potential for significant exposure require a permit to work system and a case-by-case assessment is made for appropriate protective measures.

2.3.1.2 Use of Aliphatic alcohols

The majority of the production of Long Chain Aliphatic Alcohols (LCAA) is used in processing of major anionic and ionic surfactants. This takes place in established chemical manufacturing facilities that have standard engineering controls and procedures in place to ensure safe handling and use of chemicals. The manufacture of these surfactants involves the use of reactive chemicals (e.g. ethylene oxide, sulphuric acid) that are of a higher order of acute, local and repeated dose toxicity than long chain aliphatic alcohols. Detergents based on long chain aliphatic alcohols are manufactured in a totally enclosed system in a batch process. On such sites LCAA are stored predominantly in fixed roof storage tanks with a nitrogen blanket are transported via pipelines. As rule, supply of aliphatic takes place via bulk transport by truck, barge or rail.

Facilities involved in the manufacture of major anionic and ionic surfactants or in the formulation of products for industrial, commercial or consumer use standard personal protective equipment to prevent direct skin and eye contact with chemicals handled during for routine operations; as a rule goggles or safety glasses, gloves, safety boots and helmets are worn. Activities involving a breach of the closed system also rely on similar standard protective equipment provided no reactive/corrosive substances are being handled. LCAA are of a low volatility and as a rule engineering controls are available preventing the need for respiratory protection. For non-routine operations involving a break in the enclosed system a higher level of protection is applied and sometimes measures are taken to prevent breathing of vapours, if (local) ventilation is inadequate. Operations with a potential for significant exposure require a permit to work system and a case-by-case assessment is made for appropriate protective measures

2.3.1.3 Formulation of Aliphatic alcohols

In the formulation of products for industrial, commercial or consumer use Long Chain Aliphatic Alcohols are typically formulated in established chemical manufacturing facilities that have standard engineering controls and procedures in place to ensure safe handling and use of a wide variety chemicals, including chemicals that are of a higher order of acute, local and repeated dose toxicity than long chain aliphatic alcohols.

Formulation of large volumes of product occurs frequently in a continuous process using a closed system. For formulating smaller volumes, a batch process is used. Closed reactors and/or mixing tank with closed charging systems are typically used for the formulation of LCAA. Products containing aliphatic alcohols are typically packaged and transported in drums and bags, whereas products produced in higher volumes are stored in tanks and transported in bulk by truck, barge or rail.

Exposure to aliphatic alcohols through the use of formulated products in industry and commerce is mitigated by following the recommended use and precaution instructions detailed in the material safety data sheet (MSDS). MSDS' reflect the hazard potential of the chemical ingredients in the product and provide details on the precautions necessary when handling these products and the instructions for first aid in case of an accidental exposure.

2.3.2 Consumer exposure

Aliphatic alcohols are extensively formulated in consumer laundry, cleaning and personal care products. Consumer exposures through the use of these products have been modeled using screening level inputs.

Use of consumer products containing aliphatic alcohols results predominantly in skin contact. The models used to estimate the consumer exposure are limited to an assessment of dermal exposures, except for a scenario addressing potential inhalational exposure through the use of spray cleaners. Table 2.19 summarises the modelled dermal and inhalational exposures by using aliphatic alcohols for personal care and in house hold laundry and cleaning products.

Table 2.19 Summary of Consumer Exposure Scenarios and Estimated Exposures

Exposure Scenario	Estimated Exposure (mg/kg/day)
Dermal Modeling	
Cleaning Products	
Laundry pre-treatment (undiluted)	5.5E-4 to 2.8E-3
Hand-wash of laundry (diluted)	4.3E-5 to 2.2E-4
Hard surface cleaner (diluted)	1.3E-4 to 6.5E-4
Hard surface cleaner (undiluted)	9.2E-4 to 4.6E-3
Laundry product residual on clothing	
Liquid detergent	1.9E-3 to 9.2E-3
Fabric Conditioner	1.7E-3 to 8.6E-3
Personal Care product residual after use	
Antiperspirants	3.7E-0 to 9.2E-0
Body moisturiser	2.8E-0 to 2.8E 1
Cleansing products	2.6E-3 to 2.6E-2
Face/Eye cosmetics	8.1E-1 to 4.1E-0
Hair conditioner	9.7E-3 to 9.7E-2
Hair styling tonic/gel	2.1E-1 to 2.1E-0
Inhalation Modeling	
Spray cleaner	3.6E-6 to 1.8E-5

3 HUMAN HEALTH HAZARDS

3.1 Effects on human health

Category Description

A description of the category of the Long Chained Alcohols (C6-C22 aliphatic alcohols) is presented in Annex 1 (Synthetic Routes and associated structural characteristics) of this SIAR; in this chapter this category may also be referred to as the aliphatic alcohols.

Briefly, the category of Long Chained alcohols under consideration covers a group of alcohols in the range of C6 – C22, consisting of two sub categories linear alcohols and essentially linear alcohols.

1. Linear alcohols are saturated primary -non-branched- aliphatic alcohols containing an even number of carbon atoms and may be derived from oleochemical or petrochemical feedstocks. Some alcohols derived from oleochemical sources may also contain unsaturated primary –non-branched- aliphatic alcohols.

2. Essentially linear alcohols consist of saturated, primary linear aliphatic alcohols and their saturated, mono branched primary alcohol isomers of corresponding carbon chain length. The alcohols of this sub-group may fall in the range C7 – C17 and contain even and odd numbered carbon chains. The proportion of linear alcohols ranges from 90 to around 50%. The mono-branched isomers have a linear backbone. This sub-category contains a closely related product containing saturated C12-C13 primary alcohols derived from Fischer-Tropsch olefins consisting of approximately 50% linear, 30% mono-methyl branched and 20% other unintended components. This product is referred to as C10-16 alcohols Type B [CAS 67762-41-8].

Table 3.1 presents an overview of the category of aliphatic alcohols and its key composition; the table is subdivided into the two sub-categories of linear alcohols and essentially linear alcohols and they are ranked in order of increasing chain length. Products containing alcohols with different chain lengths have been positioned in this table based on the component of significance with lowest carbon chain length (>5%; indicated in column 1) and share a common background shading. For further compositional details see the Long Chained Alcohols Data Matrix.

A separate overview of the detailed composition of the category of the Long Chained alcohols will be presented in confidential Annex A.

Table 3.1 Category of linear alcohols

	Linear Alcohols			Essentially Linear Alcohols		
	CAS	CHEMICAL NAME	CHAIN LENGTH DISTRIBUTION and COMMENTS	CAS	CHEMICAL NAME	CHAIN LENGTH DISTRIBUTION
C5				123-51-3	Isoamyl alcohol	Supporting substance
C6	111-27-3	1-Hexanol	>95% C6 [range C6-C10]; Even			
C7	111-70-6	1-Heptanol	Supporting substance	68603-15-6	C6-12 Alcohols	Type C. >80% Linear; > 95% C7/8/9 [range C6-C10]; Even & odd
C7				70955-11-2	Hexene, hydroformylation products	Supporting substance for ecotox endpoints. This entry is not shown in subsequent data summary tables.
C7				85566-14-9	Alcohols, C7-11-branched and linear	Supporting substance; 65% linear; range C7-C11; Odd
C8	111-87-5	1-Octanol	>90% C8 [range C6-C10]; Even	104-76-7	1-Hexanol, 2-ethyl-	Supporting substance
C8	68603-15-6	C6-12 Alcohols	Type D. >=90% C8/10; <10% C6 [range C6-C12]; Even			
C8	85566-12-7	C8-10 Alcohols	> 80% C8/10, C6<=5%, C12<10% [range C6-C12]; Even			
C8	68551-07-5	C8-18 Alcohols	5-30% C8/10, >60% C12/14/16/18 [range C8-20]; Even			
C9	143-08-8	1-Nonanol	Supporting substance	66455-17-2	C9-11 Alcohols	>80% Linear; > 95% C9.10, 11 [range C8-12]; Even & odd
C9				68603-15-6	C6-12 Alcohols	Type B. >80% Linear; > 95% C9/10/11 [range C8-C12]; Even & odd
C9				68527-05-9	Octene, hydroformylation products	Supporting substance for ecotox endpoints. This entry is not shown in subsequent data summary tables.
C10	112-30-1	1-Decanol	>90% C10 [range C8-C12]; Even			
C10	67762-41-8	C10-16 Alcohols	Type A. >80% C10/12/14, <10% C16 [range C8-C18]; Even			

	Linear Alcohols			Essentially Linear Alcohols		
	CAS	CHEMICAL NAME	CHAIN LENGTH DISTRIBUTION and COMMENTS	CAS	CHEMICAL NAME	CHAIN LENGTH DISTRIBUTION
C10	85665-26-5	Alcohols, C10-12	>90% C10/12, <=5% C14 [range C8-C16]; Even			
C11				112-42-5	1-Undecanol	>80% Linear; >95% C11 [C9-C14]; Even & odd
C11				68603-15-6	C6-12 Alcohols	Type A. 5-95% Linear; >= 95% C11 [range C9-C13]; Even & odd
C11				68516-18-7	Decene, hydroformylation products	Supporting substance for ecotox endpoints This entry is not shown in subsequent data summary tables.
C12	112-53-8	1-Dodecanol	Supporting Substance; assessed previously by OECD	67762-41-8	C10-16 Alcohols	Type B. 5-50% Linear; >=95% C12/13 [range C11-C14]; Even & odd Type C. 80-95% Linear; >95% C12/C13 [range C11-15]; Even & odd Type D. 40-50% Linear; >95% C12/13/14/15 [range C11-C16]; Even & odd
C12	67762-25-8	C12-18 Alcohols	Type A.; >50% C12/C14; >10% C16/C18 [range C8-C20]; even Type B. >10% C12/C14; >60% C16/C18 [range C12-C20]; even	63393-82-8	C12-15 Alcohols	Type A. >80% Linear; >95% C12/13/14/15 range C10-C17]; Even & odd Type B. 40-50% Linear; >95% C12/13/14/15 [range C11-C16]; Even & odd
C12	68855-56-1	C12-16 Alcohols	Type B. >80% C12/14, <20% C16 [range C8-C18]; Even Type C. <10% C12, >90% C14/16 [range C10-C18]; Even	68855-56-1	C12-16 Alcohols	Type A. >40% Linear; >95% C12/13/14/15 [range C10-C17]; Even & odd
C12	80206-82-2	C12-14 Alcohols	Type A; >90% C12/14 (C12>14), <10% C16 [range C6-C18]; Even Type B. >95% C12/14 (C12<14) [range C8-C18]; Even	75782-86-4	C12-13 Alcohols	>80% Linear; >95% C12/13 [range C11-C15]; Even & odd
C12				68333-80-2	C14-16 Alcohols	Type B. <=5% Linear; >95% C12/13/14/15 [range C11-C16]; Even & odd
C13				112-70-9	1-Tridecanol	>80% Linear; >90% C13, <10% C12 [range C12-14]; Even & odd
C13				90583-91-8	Tridecanol, branched and linear	5% Linear; >95% C13; Odd

	Linear Alcohols			Essentially Linear Alcohols		
	CAS	CHEMICAL NAME	CHAIN LENGTH DISTRIBUTION and COMMENTS	CAS	CHEMICAL NAME	CHAIN LENGTH DISTRIBUTION
C14	112-72-1	1-Tetradecanol	>95% C14 [range C12-C16]; Even	68333-80-2	C14-16 Alcohols	Type A. 5-95% Linear; >95% C14/15 [range C12-17]; Even & odd
C14	67762-30-5	C14-18 Alcohols	Type A. 100% Linear (or unstated); >=95% C16/18 [rangeC12-C20]; Even Type B. 100% Linear (or unstated); >95% C14/16/18 [rangeC10-C20]; Even	75782-87-5	C14-15 Alcohols	>80% Linear; >95% C14/15 [range C12-17]; Even & odd
C15				629-76-5	1-Pentadecanol	>80% Linear; >90% C15, <10% C14 [range C14-15]; Even & odd
C16	36653-82-4	1-Hexadecanol	>=95% C16 [range C14-C18]; Even			
C16	67762-30-5	C14-18 Alcohols	Type A. 100% Linear (or unstated); >=95% C16/18 [rangeC12-C20]; Even			
C16	67762-27-0	C16-18 Alcohols	<10% C14, >=90% C16/18 [range C12-C20]; Even			
C16	143-28-2	9-Octadecen-1-ol, (9Z)-	>70% C16/18, <10% C14, including >70% C18 unsaturated [range C12-C20]; Even			
C16	68002-94-8	C16-18 and C18 Unsaturated	>70% C16/C18, <10% C14, including 40-90% C18 unsaturated [range C12-C22]; Even			
C16	68155-00-0	Alcohols, C14-18 and C16-18-unsatd	Linearity unspecified; 5-50% C16,18 saturated, 40-90% C16,18 unsaturated [range C14-C18]; Even			
C18	112-92-5	1-Octadecanol	Supporting substance; assessed previously by OECD			
C18	97552-91-5	C18-22 Alcohol	100% Linear; >95% C18/20/22 [range C16-C24]; Even			
C20	629-96-9	1-Eicosanol	>=90% C20 [range C18-22]; Even			
C22	661-19-8	1-Docosanol	>95% C22; Even			
C24	123607-66-9	Alcohols, C24-34	Supporting substance			

3.1.1 Toxicokinetics, metabolism and distribution

Aliphatic alcohols are expected to be absorbed by all common routes of exposure. Based on comparative in vitro skin permeation data and dermal absorption studies in hairless mice, aliphatic alcohols show an inverse relationship between absorption potential and chain length with the shorter chain alcohols having a significant absorption potential (Iwata *et al*., 1987).

The initial step in the mammalian metabolism of primary alcohols is the oxidation to the corresponding carboxylic acid, with the corresponding aldehyde being a transient intermediate. These carboxylic acids are susceptible to further degradation via acyl-CoA intermediates by the mitochondrial β-oxidation process. This mechanism removes C2 units in a stepwise process and linear acids are more efficient in this process than the corresponding branched acids. In the case of unsaturated carboxylic acids, cleavage of C2-units continues until a double bond is reached. Since double bonds in unsaturated fatty acids are in the cis-configuration, whereas the unsaturated acyl-CoA intermediates in the β-oxidation cycle are trans, an auxiliary enzyme, enoyl-CoA isomerase catalyses the shift from cis to trans. Thereafter, β-oxidation continues as with saturated carboxylic acids (WHO, 1999).

An alternative metabolic pathway for aliphatic acids exists through microsomal degradation via ω- or ω–1 oxidation followed by β-oxidation. This mechanism provides an efficient stepwise chain-shortening pathway for branched aliphatic acids (Verhoeven, *et al*., 1998).

The acids formed from the longer chained aliphatic alcohols can also enter the lipid biosynthesis and may be incorporated in phospholipids and neutral lipids (Bandi *et al*, 1971a&b and Mukherjee *et al*. 1980). A small fraction of the aliphatic alcohols may be eliminated unchanged or as the glucuronide conjugate (Kamil *et al*., 1953).

Similar to the dermal absorption potential, it is expected that orally administered aliphatic alcohols also show a chain-length dependant potential for gastro-intestinal absorption, with shorter chain aliphatic alcohols having a higher absorption potential than longer chain alcohols.

With regards to the blood-brain barrier a chain-length dependant absorption potential exists with the lower aliphatic alcohols and acids more readily being taken up than aliphatic alcohols/acids of longer chain-length (Gelman, 1975). Taking into account the efficient biotransformation of the alcohols and the physico-chemical properties of the corresponding carboxylic acids the potential for elimination into breast milk is considered to be low.

The long chain aliphatic carboxylic acids are efficiently eliminated and aliphatic alcohols are therefore not expected to have a tissue retention or bioaccumulation potential (Bevan, 2001). Longer chained aliphatic alcohols within this category may enter common lipid biosynthesis pathways and will be indistinguishable from the lipids derived from other sources (including dietary glycerides) (Kabir, 1993; 1995a,b).

A comparison of the linear and branched aliphatic alcohols shows a high degree of similarity in biotransformation. For both sub-categories the first step of the biotransformation consists of an oxidation of the alcohol to the corresponding carboxylic acids, followed by a stepwise elimination of C2 units in the mitochondrial β-oxidation process. The metabolic breakdown for both the linear and mono-branched alcohols is highly efficient and involves processes for both sub-groups of alcohols. The presence of a side chain does not terminate the β-oxidation process, however in some cases a single Carbon unit is removed before the C2 elimination can proceed.

In summary, long chained alcohols are generally highly efficiently metabolised and there is limited potential for retention or bioaccumulation for the parent alcohols and their biotransformation products.

3.1.2 Acute Toxicity

3.1.2.1 Oral

Data Availability.

Using the same layout as the compositional data table (Table 3.1), the acute oral toxicity data, including the reliability scores, have been summarised in Table 3.2. In this table the available LD_{50} values in the rat are presented; data in other species are limited and are not discussed here. Inspection of this table, presenting only valid studies (reliability score 1 or 2), shows that a comprehensive data set is available for the whole category (linear and essentially linear) under consideration, justifying read-across to non-tested members of the category for this endpoint.

Linear Alcohols. Considering the data for linear alcohols in the range 1-octanol to 1-docosanol and including unsaturated alcohols, the oral LD_{50} values range from > 5000 mg/kg to well over 10,000 mg/kg, with most of values representing the maximum administered dose. 1-Hexanol is also of a low order of acute oral toxicity, however the data suggest that it's LD_{50} value (*ca.*3000 – 4000 mg/kg) is somewhat lower than that of the linear alcohols with a chain length of C_8 and higher (Sc. Assoc., 1965a; 1977c).

In line with current testing guidelines, more recent studies report oral LD_{50} values > 2,000 mg/kg, the limit dose. However, no significant signs of toxicity were noted in these studies and taking into account the high degree of consistency observed within this category for this endpoint, it appears justified to conclude that the sub-category of linear alcohols materials can be considered as practically non-toxic.

Clinical Signs. Few, if any signs of toxicity were reported following oral administration of the linear alcohols ranging from C6 to C22 alcohols. At doses approaching acute lethality loss of appetite, lethargy and diarrhoea was reported for most members of the linear alcohols. Animals surviving a large oral dose showed no evidence of any delayed or irreversible effects following acute administration of any of these alcohols. In decedents irritation of the gastro-intestinal tract and typical agonal changes were observed, however no substance specific observations could be recognised for any of the materials of this sub-category. There are no observations reported to suggest a potential for CNS depression following administration of a single oral dose of a linear alcohol within this category.

Intratracheal installation studies in rats suggested that linear aliphatic alcohols with chain lengths up to C13 may have an aspiration potential. In these studies alcohols with a chain length up to C10 induced immediate respiratory or cardiac arrest. Alcohols in the range C10 – C13 caused significant pneumonitis (Gerarde and Alhstrom, 1966).

Essentially Linear Alcohols. The essentially linear alcohols are also of a low order of acute toxicity with oral LD_{50} values well in excess of 2,000 mg/kg across the category of products. Most reported values represent the highest dose tested instead of lethality. There was consistency in the LD_{50} values across the whole range of the essentially linear alcohols.

Acute oral toxicity data in species other than the rat are limited, but appear to confirm the non-toxic properties of this category of alcohols, regardless of the carbon chain length and the detailed composition. Nevertheless, substances with LD_{50} values within this range can be regarded as practically non-toxic following acute exposure.

Clinical signs. Few, if any signs of toxicity were reported following oral administration of the essentially linear alcohols ranging from C6 to C15 alcohols. At doses approaching acute lethality loss of appetite, lethargy and diarrhoea was reported for most members of the essentially linear alcohols. Animals surviving a large oral dose showed no evidence of any delayed or irreversible effects following acute administration of any of these alcohols. In decedents irritation of the gastro-intestinal tract and typical agonal changes were observed, however no substance specific observations could be recognised for any of the materials in each of the sub-classes considered. There are no observations reported to suggest a potential for CNS depression following administration of a single oral dose of essentially linear alcohol within this category.

A comparison of the toxicity data and the clinical observations for the linear and essentially linear alcohols indicates that the acute toxicity of these sub-categories is qualitatively and quantitatively similar.

Conclusion: The category of the long chained aliphatic alcohols (linear and essentially linear) is of a low order of acute toxicity upon oral administration.

3.1.2.2 Inhalation

Data Availability. The acute inhalation LC_{50} data in the rat are summarised in Table 3.3. This table shows that the available data cover the lower (1-hexanol and 1-octanol), intermediate (1-decanol, 1-dodecanol) and higher (1-tetradecanol, C16-18 alcohols) chain-lengths of the linear alcohols subcategory. For the essentially linear alcohols the data include data on C6 – 12 alcohols [Types C and B covering the range of C6 - C10 and C8 - C12 alcohols, respectively] and C_{12-16} alcohols [Type A, covering the range C10 - C18 alcohols]. This data coverage is considered representative of the whole range of products in this class and justifies read-across for this end point to untested members of this category. Most of the available data are regarded as reliable (reliability scores 1 or 2). Some of the data represent 1, 2 or 6-hour exposures and results have been presented as the corresponding 4-hr exposure values (assuming a linear time-effect relationship), allowing a comparison of the available information. In some of cases the exposure levels were reported as the maximum attainable levels at ambient conditions without analytical confirmation of the achieved concentrations; in this case the –calculated- saturated vapour pressure at ambient conditions was used as a surrogate for the actual test concentrations.

The following algorithm was used to calculate the saturated vapour concentration from the vapour pressure:

$$\text{Concentration (ppm)} = \frac{\text{vapour pressure (mbar)} \times 1000}{1.01325\ \text{(mbar)}}$$

The vapour pressure used in these calculations was either measured or calculated at 25°C, resulting in a worst-case estimate of the possible saturated vapour concentration. For the alcohols consisting of several components the available data only allowed calculation the airborne concentrations in ppm; due to the unavailability of the molecular weight a conversion to mg/L was not made.

Linear and Essentially Linear Alcohols. The volatility of the category of aliphatic alcohols as a whole is low. Saturated vapour pressures for the higher chain alcohols are extremely low; for example the calculated concentration of a saturated atmosphere of 1-dodecanol and 1-octadecanol at ambient conditions is in the order of 10^{-2} and 10^{-5} mg/L, respectively. Most experimental studies used the maximum achievable vapour concentrations or aerosols for the assessment of the acute lethal concentration. For all substances tested the LC_{50} values exceeded the maximum achievable vapour concentrations. Even the more volatile members of this category (e.g. 1-hexanol, C6-12 essentially linear alcohols [Types B and C], 1-heptanol and 1-undecanol) showed no evidence of toxicity after a single exposure for 1 – 6 hours (Sc. Assoc, 1977c; Blair, 1980a, 1981; Truhaut 1974; Younger Labs, 1977). For 1-hexanol and 1-decanol hypoactivity and/or ataxia, gasping, lethargy and prostration were reported during a 1-hour experiment; these non-specific signs are observed commonly during exposure to experimental test atmospheres and the symptoms did not persist after the termination of the exposure (Sc. Assoc. 1977a, 1977c). RD_{50} values in the order of 50 – 100 ppm were reported for 1-heptanol and 1-octanol (Hansen and Nielsen, 1994; Muller and Greff, 1987; Bos *et al*., 1992). None of the acute inhalation studies provided any evidence of a potential for CNS depression for the category of aliphatic alcohols. This conclusion is further supported by data in mice indicating that inhalation of high concentrations (up to *ca*. 10,000 ppm) of 1-heptanol for short periods of time did not induce anaesthesia (Hansen and Nielsen, 1994). *Conclusion:* Inhalation of vapours of long chained alcohols in the range C6-C22 at levels up to the saturated vapour pressure is unlikely to be associated with significant toxicity.

3.1.2.3 Dermal

Data Availability. The acute dermal toxicity of category of the aliphatic alcohols has been investigated comprehensively; mainly in rats or rabbits, but some data in guinea pigs have also been reported. Table 3.4 presents a summary of the acute dermal LD_{50} values recorded for the category of the long chained aliphatic alcohols and the reliability rating of these data (Note data with a reliability score of 3 or 4 were omitted from this table). The data coverage for this end point is comprehensive and justifies inter- and extrapolation within the category of the long chained alcohols.

Linear Alcohols. For the linear alcohols in the range, C6 - C10 most of the reported LD_{50} values in rabbits are in the range 2000 - 4000 mg/kg. For the alcohols C_{12} and higher the acute dermal LD_{50} values were 8000 mg/kg or higher. Although some incidental LD_{50} values below 2000 mg/kg were reported, these values generally represented the maximum dose tested. Substances with a chain length beyond C18 have not been tested but on the basis of the consistent low acute dermal toxicity for alcohols with a chain-length of C16 and below and the consistently low oral acute toxicity for the category as a whole it is expected that aliphatic alcohols in the range C18 – C22 are of a low order of acute dermal toxicity.

Clinical signs. Occluded exposure for 24 hours generally caused local dermal irritation. There was a clear (inverse) relationship between the chain length and the severity of the dermal effects. The severity of the irritation was graded as moderate – severe for the lower members of this category; typical observations included erythema, oedema, wrinkling, desquamation and cracking. The grading of the local effects for the aliphatic alcohols with a longer carbon chain was reported as slight-moderate. Animals showing signs of significant local irritation displayed signs of toxicity such as general weakness, anorexia, lethargy; it is not possible to ascertain if these findings were secondary to the irritation or evidence of direct systemic toxicity.

Essentially Linear Alcohols. For the essentially linear alcohols, dermal LD_{50} values were >2000 mg/kg, all representing the maximum dose tested (limit dose). For the higher (C12 and higher) members of this sub-category LD_{50} values were in the range of >2000 – 11,000 mg/kg.

Clinical signs. Occluded exposure for 24 hours generally caused local dermal irritation. There was a clear [inverse] relationship between the chain length and the severity of the dermal effects. The severity of the irritation was graded as moderate – severe for the lower members of this category;

typical observations included erythema, oedema, wrinkling, desquamation and cracking. The grading of the local effects for the longer carbon chain alcohols was reported as slight-moderate. Animals showing signs of significant local irritation displayed signs of toxicity such as general weakness, anorexia, lethargy; it is not possible to ascertain if these findings were secondary to the irritation or evidence of direct systemic toxicity.

The acute dermal toxicity and clinical observations for the linear and essentially linear alcohols following a 24-hour dermal exposure were qualitatively and quantitatively similar.

Conclusion: The category of the long chained aliphatic alcohols is of a low order of acute toxicity upon dermal administration.

Table 3.2 Acute oral toxicity

	Linear Alcohols				Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	LD$_{50}$ value- oral; rat mg/kg	Rel.[1]	CAS	CHEMICAL NAME	LD$_{50}$ value- oral; rat mg/kg	Rel.[1]
C5					123-51-3	Isoamyl alcohol	Supporting substance	
C6	111-27-3	1-Hexanol	3,210 [Sc. Assoc.,1965a] 4,420 [Sc. Assoc. 1977c]	2 2				
C7	111-70-6	1-Heptanol Supporting Substance	5500-6200 [Truhaut, 1974]	2	68603-15-6	C6-12 Alcohols Type C	>2,000 (>80% lin.) [Shell, 1996a] >8300 (>80% linear) [Cassidy, 1978b]	1 2
C7					85566-14-9	Alcohols, C7-11-branched and linear	Supporting substance	
C8	111-87-5	1-Octanol	18,240 [Sc. Assoc., 1965b] > 5,000 [Henkel, 1981a]	2 2	104-76-7	1-Hexanol, 2-ethyl-	Supporting substance	
C8	68603-15-6	C6-12 Alcohols	Type D Low toxicity expected; LD50 > 2000	2				
C8	85566-12-7	C8-10 Alcohols	>5000 [Potokar, 1979]	2				
C8	68551-07-5	C8-18 Alcohols	Low toxicity expected; LD50 > 2000	2				
C9	143-08-8	1-Nonanol	Supporting substance		66455-17-2	C9-11 Alcohols	> 4,000 (>80% lin) [Albert, 1981a]	1
C9					68603-15-6	C6-12 Alcohols	Type B: >8300 (>80% lin) [Cassidy, 1978a]	2
C10	112-30-1	1-Decanol	> 5,000-> 26,410 [Potokar, 1979; Sc. Assoc. 1965c; 1977d]	2				
C10	67762-41-8	C10-16 Alcohols	Type A: Low toxicity expected; LD50 > 2000	2				
C10	85665-26-5	Alcohols, C10-12	Low toxicity expected; LD$_{50}$ > 2000	2				
C11					112-42-5	1-Undecanol	>10,000 (lin not stated) [Younger Labs, 1977]	2
C11					68603-15-6	C6-12 Alcohols Type A	>5000 (50% lin.) [Biolab, undated d]	2
C12	112-53-8	1-Dodecanol Supporting Substance	> 5,000 [Henkel, 1981b] > 26,530 [Sc. Assoc., 1965d]	2 2	67762-41-8	C10-16 Alcohols	Type B: >2000] (50% lin.) [Sasol, 1998a Type C: > 10,000 (80% lin.) [Cassidy, 1978c] Type C: > 5000 (95%lin) [Biolab,1990a] Type D: Low toxicity expected; LD50 > 2000	1 2 2 2

	Linear Alcohols				Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	LD_{50} value- oral; rat mg/kg	Rel.[1]	CAS	CHEMICAL NAME	LD_{50} value- oral; rat mg/kg	Rel.[1]
C12	67762-25-8	C12-18 Alcohols	Type A: > 5,000 [Henkel, 1981e] Type B: Expected low toxicity; LD_{50} > 2000	2 2	63393-82-8	C12-15 Alcohols	Type A: 26,400] (85% lin.) [Shell, 1964] Type B : Low toxicity expected; LD_{50} > 2000	2 2
C12	68855-56-1	C12-16 Alcohols	Type B >2000 [HLS, 1996j] Type C: Low toxicity expected; LD_{50} > 2000	1 2	68855-56-1	C12-16 Alcohols	Type A: >8,300(84% lin) [Clark 1978] >5000 (95% lin) [Biolab, 1991a]	2 2
C12	80206-82-2	C12-14 Alcohols	Type A: > 10,000 [Henkel, 1980a] Type B: : Low toxicity expected; LD_{50} > 2000	2 2	75782-86-4	C12-13 Alcohols	28,200 (>80% lin) [Shell, 1966]	2
C12					68333-80-2	C14-16 Alcohols	Type B : Low toxicity expected; LD_{50} > 2000	2
C13					112-70-9	1-Tridecanol	13760 (85% lin) [Smyth, 1962]	2
C13					90583-91-8	Tridecanol, branched and linear	Low toxicity expected; LD_{50} > 2000	2
C14	112-72-1	1-Tetradecanol	> 20,000 [Sc. Assoc., 1977b] 26,975 [Smyth 1969]	2 2	68333-80-2	C14-16 Alcohols Type A:	> 5000 (5% lin] [Biolab, 1990b] >10,000 (80% lin)[Cassidy, 1978d] > 5000 (95% lin) [Biolab, undated d]	2 2 2
C14	67762-30-5	C14-18 Alcohols	Type B: Low toxicity expected; LD_{50} > 2000	2	75782-87-5	C14-15 Alcohols	>23,100 (85% lin) [Lifestream Lab,1966]	2
C15					629-76-5	1-Pentadecanol	Low toxicity expected; LD_{50} > 2000	2
C16	36653-82-4	1-Hexadecanol	>7960 [Sc. Assoc. 1965e] >5000 Henkel, 1981c] > 2,000 [Hempstock, 1996a]	2 1 1				
C16	67762-30-5	C14-18 Alcohols	Type A: >5000 [Henkel, 1977; mouse]	2				
C16	67762-27-0	C16-18 Alcohols	> 10,000 mg/kg [Carter, 1975; Cont.Oil, 1979]	2				
C16	143-28-2	9-Octadecen-1-ol, (9Z)-	Low toxicity expected; LD_{50} > 2000	2				
C16	68002-94-8	C16-18 and C18 Unsaturated	>5000 [Henkel, 1981h]	1				
C16	68155-00-0	Alcohols, C14-18 and C16-18-unsatd	Low toxicity expected; LD_{50} > 2000	2				

	Linear Alcohols				Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	LD_{50} value- oral; rat mg/kg	Rel.[1]	CAS	CHEMICAL NAME	LD_{50} value- oral; rat mg/kg	Rel.[1]
C18	112-92-5	1-Octadecanol Supporting Substance	> 5000 [Henkel, 1981g], > 7960 [Sc. Assoc., 1965f] > 2000 [Hempstock, 1996b]	1 2 1				
C18	97552-91-5	C18-22 Alcohol	Low toxicity expected; LD_{50} > 2000	2				
C20	629-96-9	1-Eicosanol	> 10,000 [LPT, 1987a] >53760 [Smyth, 1969]	1 2				
C22	661-19-8	1-Docosanol	> 10,000 [LPT, 1987b] > 2000 [Hempstock, 1997c]	1 1				
C24	123607-66-9	Alcohols, C24-34 Supporting Substance	>5000 [Aleman, 1998; >5000 [Rodiero, 1995]	2 2				

Note:

1 Rel. is the reliability score used in IUCLID.

Table 3.3 Acute inhalation toxicity

	Linear Alcohols				Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	LC$_{50}$ value- oral; rat ^{1}	Rel.	CAS	CHEMICAL NAME	LC$_{50}$ value- oral; rat ^{1}	Rel.
C5					123-51-3	Isoamyl alcohol	Supporting substance	
C6	111-27-3	1-Hexanol	> 21 mg/L(1 hr); [Sc.Assoc, 1977c] 4hr. equiv.> 5.25 mg/L ^{2} (1204 ppm)	2				
C7	111-70-6	1-Heptanol Supporting Substance	> 1.3 mg/L (4 hr) [Truhaut, 1974] ^{3} (276 ppm)	2	68603-15-6	C6-12 Alcohols	Type C >0.58 mg/L-4 hr (168 ppm) >80% lin. [Blair, 1980a]	2
C7					85566-14-9	Alcohols, C7-11-branched and linear	Supporting substance	
C8	111-87-5	1-Octanol	> 5.6 mg/L (4 hr) [Amoco, 1988] (99 ppm)	2	104-76-7	1-Hexanol, 2-ethyl-	Supporting substance	
C8	68603-15-6	C6-12 Alcohols	Type D: LC$_{50}$ expected to be > 158 ppm (substantially saturated atmospheric concentration)	2				
C8	85566-12-7	C8-10 Alcohols	LC$_{50}$ expected to be > 88 ppm (substantially saturated atmospheric concentration)	2				
C8	68551-07-5	C8-18 Alcohols	LC$_{50}$ expected to be > 11.8 ppm (substantially saturated atmospheric concentration)	2				
C9	143-08-8	1-Nonanol	Supporting substance		66455-17-2	C9-11 Alcohols	LC$_{50}$ expected to be > 12.8 ppm (substantially saturated atmospheric concentration)	2
C9					68603-15-6	C6-12 Alcohols	Type B: >0.24 mg/L-4 hr (12.8 ppm) >80% lin. [Blair, 1981]	2
C10	112-30-1	1-Decanol	>71 mg/L (1 hr) [Sc. Assoc. 1977a] 4hr equiv >17.8 mg/L ^{2} (11.2 ppm)	2				
C10	67762-41-8	C10-16 Alcohols	Type A: LC$_{50}$ expected to be > 2.9 ppm (substantially saturated atmospheric concentration)	2				
C10	85665-26-5	Alcohols, C10-12	LC$_{50}$ expected to be > 10.9 ppm (substantially saturated atmospheric concentration)	2				

	Linear Alcohols				Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	LC$_{50}$ value- oral; rat[1]	Rel.	CAS	CHEMICAL NAME	LC$_{50}$ value- oral; rat[1]	Rel.
C11					112-42-5	1-Undecanol	> 0.4 mg/L 6 hr [Younger, 1977] 4 hr eq. >0.6 mg/L (3.8 ppm); Lin not stated	2
C11					68603-15-6	C6-12 Alcohols	Type A: LC$_{50}$ expected to be > 4.3 ppm (substantially saturated atmospheric concentration)	2
C12	112-53-8	1-Dodecanol Supporting Substance	> 1.05 mg/L (6 hr) [Clayton, 1994]; 4hr eq. >1.57 mg/L[2] (1.1 ppm)	4	67762-41-8	C10-16 Alcohols	Type B, C, D: LC$_{50}$ expected to be > 0.5 – 1 ppm (substantially saturated atmospheric concentration)	2
C12	67762-25-8	C12-18 Alcohols	Type A,: LC$_{50}$ expected to be >1.6 ppm (substantially saturated atmospheric concentration) Type B: LC$_{50}$ expected to be >0.25 ppm (substantially saturated atmospheric concentration)	2	63393-82-8	C12-15 Alcohols	Type A, B: LC$_{50}$ expected to be > 0.5 ppm (substantially saturated atmospheric concentration)	2
C12	68855-56-1	C12-16 Alcohols	Type B, LC$_{50}$ expected to be > 1.6 ppm (substantially saturated atmospheric concentration) Type C: LC$_{50}$ expected to be > 0.25 ppm (substantially saturated atmospheric concentration)	2	68855-56-1	C12-16 Alcohols	Type A : > 0.0005 mg/L (4 hr) [3] (0.5 ppm) [Blair, 1980b] 84% lin.	2
C12	80206-82-2	C12-14 Alcohols	Type A,. LC$_{50}$ expected to be > 4.9 ppm (substantially saturated atmospheric concentration) Type B. LC$_{50}$ expected to be > 1.3 ppm (substantially saturated atmospheric concentration)	2	75782-86-4	C12-13 Alcohols	LC$_{50}$ expected to be > substantially saturated atmospheric concentration	2
C12					68333-80-2	C14-16 Alcohols	Type B: LC$_{50}$ expected to be > 0.50 ppm (substantially saturated atmospheric concentration)	2
C13					112-70-9	1-Tridecanol	LC$_{50}$ expected to be > 0.56 ppm (substantially saturated atmospheric concentration)	2
C13					90583-91-8	Tridecanol, branched and linear	LC$_{50}$ expected to be > 0.56 ppm (substantially saturated atmospheric concentration)	2

	Linear Alcohols				Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	LC_{50} value- oral; rat[1]	Rel.	CAS	CHEMICAL NAME	LC_{50} value- oral; rat[1]	Rel.
C14	112-72-1	1-Tetradecanol	> 1.5 mg/L (1-hr) [Sc. Assoc. 1977b] 4 hr. eq.> 0.375 mg/L [2] (0.14 ppm)	2	68333-80-2	C14-16 Alcohols	Type A: LC_{50} expected to be > 0.11 ppm (substantially saturated atmospheric concentration)	2
C14	67762-30-5	C14-18 Alcohols	Type B: LC_{50} expected to be > 0.09 ppm (substantially saturated atmospheric concentration)	2	75782-87-5	C14-15 Alcohols	LC_{50} expected to be > 0.11 ppm (substantially saturated atmospheric concentration)	2
C15					629-76-5	1-Pentadecanol	LC_{50} expected to be > 0.05 ppm (substantially saturated atmospheric concentration)	2
C16	36653-82-4	1-Hexadecanol	LC_{50} expected to be > 0.014 ppm (substantially saturated atmospheric concentration)	2				
C16	67762-30-5	C14-18 Alcohols	Type A: LC_{50} expected to be > 0.017 ppm (substantially saturated atmospheric concentration)	2				
C16	67762-27-0	C16-18 Alcohols	> 0.012 ppm [3] (6 hr) [Cont.Oil, 1979]	2				
C16	143-28-2	9-Octadecen-1-ol, (9Z)-	LC_{50} expected to be > 0.020 ppm (substantially saturated atmospheric concentration)	2				
C16	68002-94-8	C16-18 and C18 Unsaturated	LC_{50} expected to be > 0.037 ppm (substantially saturated atmospheric concentration)	2				
C16	68155-00-0	Alcohols, C14-18 and C16-18-unsatd	LC_{50} expected to be > 0.019 ppm (substantially saturated atmospheric concentration)	2				
C18	112-92-5	1-Octadecanol Supporting Substance	LC_{50} expected to be > 0.003 ppm (substantially saturated atmospheric concentration)	2				
C18	97552-91-5	C18-22 Alcohol	LC_{50} expected to be > 0.001 ppm (substantially saturated atmospheric concentration)	2				
C20	629-96-9	1-Eicosanol	LC_{50} expected to be > 0.0001 ppm (substantially saturated atmospheric concentration)	2				

	Linear Alcohols				Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	LC_{50} value- oral; rat[1]	Rel.	CAS	CHEMICAL NAME	LC_{50} value- oral; rat[1]	Rel.
C22	661-19-8	1-Docosanol	LC_{50} expected to be > 8.1 E-05 ppm (substantially saturated atmospheric concentration)	2				
C24	123607-66-9	Alcohols, C24-34	Supporting substance					

Notes:

1 All data reported in ppm were derived from saturated vapour pressure at ambient (25C) conditions as presented in Table A1: Matrix of SIDS/HPV endpoints and data for SDA-sponsored Aliphatic Alcohols; the following algorithm used was applied for the conversion of vapour pressure mbar -> ppm: .

$$\text{Concentration (ppm)} = \frac{\text{vap. pressure (mbar)}}{1.01325\ \text{(mbar)}} \times 1000$$

2 4 hour LC 50 values have been calculated and are shown for comparative purposes only. In the calculation it is assumed that: Exposure concentration x exposure time is constant. This has not been validated for this category.

3 Data calculated from the saturated vapour pressure;

Table 3.4 Acute dermal toxicity

	Linear Alcohols				Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	LD50 value- [mg/kg]; Species	Rel.	CAS	CHEMICAL NAME	LD50 value [mg/kg]; Species	Rel.
C5					123-51-3	Isoamyl alcohol	Supporting substance	
C6	111-27-3	1-Hexanol	2,330 (rabbit) [Sc Assoc. 1980] 1500-2000 (rabbit) [Sc Assoc 1977c]	2 2				
C7	111-70-6	1-Heptanol	supporting substance		68603-15-6	C6-12 Alcohols	Type C: >2,000 (rat) (>80% lin.) [Shell, 1996b] >1600 (rat) (>80% lin.) [Cassidy 1978b]	1 2
C7					85566-14-9	Alcohols, C7-11-branched and linear	Supporting substance	
C8	111-87-5	1-Octanol	2,000 – 4000 (rabbit) [Sc. Assoc. 1976a]	2	104-76-7	1-Hexanol, 2-ethyl-	Supporting substance	
C8	68603-15-6	C6-12 Alcohols	Type D: Low toxicity expected; LD_{50} > 2000	2				
C8	85566-12-7	C8-10 Alcohols	>1000 (rabbit) [Potokar, 1979]	2				
C8	68551-07-5	C8-18 Alcohols	Low toxicity expected; LD_{50} > 2000	2				
C9	143-08-8	1-Nonanol	Supporting Substance		66455-17-2	C9-11 Alcohols	>1660 (rabbit) [Albert,1981b] (>80% lin)	1
C9					68603-15-6	C6-12 Alcohols	Type B: >1,600 (rat) [Cassidy,1978a] (lin. >80%)	2
C10	112-30-1	1-Decanol	>1,000-4,000 (rabbit) [Sc. Assoc., 1976b ; Potokar, 1979] ;	2				
C10	67762-41-8	C10-16 Alcohols Type A	Type A: Low toxicity expected; LD_{50} > 2000	2				
C10	85665-26-5	Alcohols, C10-12	Low toxicity expected; LD_{50} > 2000	2				
C11					112-42-5	1-Undecanol	3160 - 5010 [Younger, 1977] rabbit lin. not stated	2
C11					68603-15-6	C6-12 Alcohols	Type A: Low toxicity expected; LD_{50} > 2000	
C12	112-53-8	1-Dodecanol Supporting Substance	1500-2000 (rabbit) [Sc. Assoc. 1975] 8000-12,000(rabbit) [Sc. Assoc. 1977f]	2 2	67762-41-8	C10-16 Alcohols	Type B: >2000 (rat) [Sasol, 1998b] (50% lin.) Type C: > 2000 (rat) [Cassidy, 1978c] (80% lin.) Type D: Low toxicity expected; LD_{50} > 2000	1 2 2
C12	67762-25-8	C12-18 Alcohols	Type A, B: Low toxicity expected; LD_{50} >	2	63393-82-8	C12-15 Alcohols	Type A: >10,200(rabbit) [Shell,1964](>80%	2

	Linear Alcohols				Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	LD50 value- [mg/kg]; Species	Rel.	CAS	CHEMICAL NAME	LD50 value [mg/kg]; Species	Rel.
			2000				lin) Type B: Low toxicity expected; LD_{50} > 2000	2
C12	68855-56-1	C12-16 Alcohols	Type B, C: Low toxicity expected; LD_{50} > 2000	2	68855-56-1	C12-16 Alcohols	Type A: > 3320 (rat) [Cassidy 1978] >80% lin.	2
C12	80206-82-2	C12-14 Alcohols	Type A, B: Low toxicity expected; LD_{50} > 2000	2	75782-86-4	C12-13 Alcohols	11,300 (rabbit) [Shell, 1966] (>80%lin)	2
C12					68333-80-2	C14-16 Alcohols	Type B: Low toxicity expected; LD_{50} > 2000	2
C13					112-70-9	1-Tridecanol	5797 (rabbit)[Smyth,1962] (85%lin)	2
C13					90583-91-8	Tridecanol, branched and linear	Low toxicity expected; LD_{50} > 2000	2
C14	112-72-1	1-Tetradecanol	5847 (rabbit) [Smyth, 1969] 8,000 (rabbit)[Sc. Assoc 1977b]	2 2	68333-80-2	C14-16 Alcohols	Type A: >2000 (rat) [Cassidy, 1978d] (>80% lin)	2
C14	67762-30-5	C14-18 Alcohols	Type B: Low toxicity expected; LD_{50} > 2000	2	75782-87-5	C14-15 Alcohols	6180 (rabbit) [Lifestream Labs,1966] (>80% lin)	2
C15					629-76-5	1-Pentadecanol	Low toxicity expected; LD_{50} > 2000	2
C16	36653-82-4	1-Hexadecanol	Low toxicity expected; LD_{50} > 2000	2				
C16	67762-30-5	C14-18 Alcohols	Type A: Low toxicity expected; LD_{50} > 2000	2				
C16	67762-27-0	C16-18 Alcohols	> 8,000 (rabbit) [Carter, 1975]	2				
C16	143-28-2	9-Octadecen-1-ol, (9Z)-	Low toxicity expected; LD_{50} > 2000	2				
C16	68002-94-8	C16-18 and C18 Unsaturated	Low toxicity expected; LD_{50} > 2000	2				
C16	68155-00-0	Alcohols, C14-18 and C16-18-unsatd	Low toxicity expected; LD_{50}> 2000	2				
C18	112-92-5	1-Octadecanol Supporting Substance	Low toxicity expected; LD_{50} > 2000	2				
C18	97552-91-5	C18-22 Alcohols	Low toxicity expected; LD_{50} > 2000	2				
C20	629-96-9	1-Eicosanol	>16,800 (rabbit) [Smyth, 1969]	2				
C22	661-19-8	1-Docosanol	Low toxicity expected; LD_{50} > 2000	2				
C24	123607-66-9	Alcohols, C24-34 Supporting Substance	Low toxicity expected; LD_{50}> 2000	2				

3.1.3 Irritation

The data for skin and eye irritation and skin sensitisation potential for the category of the linear and the essentially linear alcohols are summarised in Table 3.5; in this table only those studies were incorporated, for which sufficient details were available to allow a determination of the irritancy potency. Table 3.5 presents the test protocol, the reliability and the overall irritancy/sensitisation grading. Individual animal data are presented in the Robust Study Summaries.

3.1.3.1 Skin Irritation[5]

Studies in Animals

Data Availability. A comprehensive set of reliable test data in the rabbit is available for the linear and essentially linear alcohols, covering all representative chain lengths of the category and allow read-across to non-tested members within the category.

Linear Alcohols. The data demonstrate that lower members of the linear alcohols (C6 – C11) have a skin irritancy potential ranging from mild to irritant, when applied undiluted for 4 – 24 hours. Application of diluted materials resulted in a lower grade irritation. The skin irritation potential of linear alcohols in the range C12 and C16 is graded as mild - essentially non-irritant. Alcohols with a carbon chain length C18 and above were generally without evidence of a skin irritation potential. Human studies indicate that the skin irritation hazard for the aliphatic alcohols is lower than that observed in the rabbit and well below the response noted for a positive control substance (Griffith, 1997; Henkel, 1996, 1996a; for further details see the section studies in humans).

For read-across, alcohols in the range C6-C11 are considered as irritant, representing the worst case within this range. Similarly, the intermediate chain lengths C12 –C16 alcohols are considered to be mild irritants and non-irritant for chain lengths of C18 and above.

Unsaturated alcohols have a potential for mild skin irritation. For C16-C18 and C18 unsaturated alcohols [CAS 68002-94-8] one experiment (Henkel, 1990a) reported an irritant outcome. Human data on this sample using a method comparable to OECD 404 caused no dermal responses (Henkel 1996). Other animal data for a similar alcohol described under this CAS number indicated mild irritation (Henkel, 1987a). Furthermore, a similar unsaturated alcohol (9-octadecene-1-ol [CAS 1143-28-2]) also showed a minimal degree of skin irritation (Guillot, 1977 and Motoyoshi, 1979), allowing the conclusion that unsaturated alcohols can be regarded at most as mild skin irritants.

Essentially Linear Alcohols. For the essentially linear alcohols, a differentiation in the irritation similar to that of the linear alcohols can be identified. For the alcohols in the C6- C11 range the skin irritation potential can be categorised as mild - irritant. The skin irritation potential for the higher members of the essentially linear alcohols in the range C12 – C16 is mild - essentially non-irritant.

For read-across alcohols in the range C6-C11 are considered as irritant; representing the worst case within this range. Similarly, the intermediate chain lengths C12 – C15 alcohols are considered to be mild irritants.

Studies in Humans

Comparative studies have shown that the cutaneous responses following a single topical application of aliphatic alcohols in the range C6 – C22 decreased in the order rabbit, guinea pig, hairless mouse

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[5] Scores of the skin irritation response and grading of the irritation are presented in the Robust Study Summaries

and human, with the human responses being categorised as virtually non-irritant (Kaestner, 1977; Motoyoshi *et al.*, 1979). Human skin contact for periods up to 4 hours showed that alcohols in the range C6 – C10 were not classifiable as a skin irritant when compared to a positive control (i.e. classifiable) substance (sodium lauryl sulphate, SLS) (Griffith *et al.*, 1997).

An open application test according to Burckhardt C12, C14 and C16-18 and C18 Unsaturated alcohols a 60- minute application caused no cutaneous responses, except for a mild transient erythema observed for C14 alcohol immediately following the removal of the test substance (Henkel 1996a). Similarly, C12, C14 and C16-18 and C18 Unsaturated alcohols caused at most a minimal erythematous response following either a 4- hour semi-occluded patch test (comparable to OECD 404) or an open application test, justifying no classification when compared to a positive control substance (20% SLS) (Henkel, 1996). Sato et al. (1996) reported low irritancy in the range C12 – C18 alcohols, however 1-octanol was of a slightly higher order of irritation.

In scarified human skin slight to marked responses were reported following daily applications over a period of 3 days. The degree of irritation was inversely related with the carbon chain length with a marked response reported for C10 and C12 alcohol, a moderate response for C14 alcohol and a slight response for C16 alcohol (Frosch and Kligman, 1976).

Overall, human data indicate that the irritation responses for the category of the linear alcohols are of a lower order than those observed in rabbits.

Conclusion: Aliphatic alcohols in the range C6 – C11 are mild irritants, not anticipated to be corrosive. Aliphatic alcohols in the range C12 – C16 have a low degree of skin irritation potential; alcohols with chain lengths of C18 and above are non-irritant to skin.

3.1.3.2 Eye Irritation[6]

Studies in Animals

Data Availability. Table 3.5 shows a comprehensive set of eye irritancy data representative for the category of the linear and essentially linear alcohols. The data covers all representative chain lengths of the category allowing read-across to non-tested members within the category.

Conclusion: Linear and Essentially Linear Alcohols. The available eye irritation data indicate that both sub-categories of alcohols induce varying degrees of irritation within the lower chain lengths [C6 – C11]. The eye irritation potential for the linear and essentially linear alcohols with a chain length of C12 and above is minimal.

For read-across purposes linear and essentially linear alcohols in the range C6-C11 are regarded eye irritant; representing the worst case within this range. Alcohols with a chain length of C12 and above are expected to be non-irritant.

3.1.3.3 Respiratory Tract Irritation

There is no information available from single or repeated inhalation exposures in laboratory animals or from human experience allowing a conclusion on potential respiratory tract irritation of the aliphatic alcohols.

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[6] Mean scores of the eye irritation response and grading of the irritation response are presented in the Robust Study Summaries

3.1.4 Sensitisation[7]

3.1.4.1 Studies in Animals

Skin

A comprehensive set of skin sensitisation data covering a C-chain distributions representative for the category of long chained alcohols is available (summarised in Table 3.5). No skin sensitisation reactions were observed for the category of linear and essentially linear alcohols, with the exception of a single report [1-decanol, a commercial sample of unknown isomeric composition]. In a modified (non-adjuvant) Draize test 1-decanol did not show any responses in guinea pigs following an intra-dermal induction and a topical and/or a intradermal challenge, however after a re-induction (intra-dermal) and re-challenge a weak response was reported (Sharp, 1978). The significance of this single weakly positive result is very limited on the basis that the result was obtained in a non-standard test assay applying a material of unknown composition and origin. The weight of the evidence indicates that this category does not have a skin sensitisation potential in guinea pigs.

3.1.4.2 Studies in Humans

Skin

Repeated insult patch tests in groups of up to 200 human volunteers have not identified any sensitising properties for C16 and C18 alcohol (Gloxhuber, 1983). Patch testing of patients with contact dermatitis showed that several long chain aliphatic alcohols were implicated in contact allergies, however considerable variations in the incidence of responders was reported in these studies (range *ca*. 1 – 25%). There is evidence to suggest that some of the responders were atopics (Auth, 1984; Blondeel *et al*., 1978; Fisher *et al*., 1971; Goossens, 1999; Hjorth and Trolle-Lassen; 1963; Tosti, *et al*., 1996; Van Ketel, 1984). Given the wide dispersive use in consumer and occupational applications and the relatively low numbers of cases of allergy, it can be concluded that long chain alcohols have a very low allergenic potency.

Conclusion

Aliphatic alcohols do not have a skin sensitisation potential in animals. Based on human evidence, the allergenic potency of this category is very low.

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[7] Responses are presented in the Robust Study Summaries

Table 3.5 Irritation and sensitisation

	Linear Alcohols					Essentially Linear Alcohols				
	CAS	CHEMICAL NAME	Skin ^{1}	Eye ^{1}	SS ^{1}	CAS	CHEMICAL NAME	Skin ^{1}	Eye ^{1}	SS ^{1}
C5						123-51-3	Isoamyl alcohol	Supporting substance		
C6	111-27-3	1-Hexanol	**Mild** ^{3}; 2 [Jacobs 1987] **Irritant**; 2 [Sc Assoc, 1977c] 24 hr occl. **Non** ; 2 [Griffith, 1997] 4 hr human test	**Irritant** ^{3}; 1,2,2 [Ecetoc, 1998; Sc. Assoc, 1977c; Jacobs, 1987]	**Non** ^{2}; 2 [Sharp,1978] Other					
C7	111-70-6	1-Heptanol Supporting substance	**Non-irritant** ; 2 [Truhaut, 1974]	**Irritant**; 2 [Truhaut, 1974]		68603-15-6	C6-12 Alcohols Type C	**Irritant** ; 2, 1 >80% lin [Cassidy, 1978b; 24 hr occl.; Rees, 1996a]	**Irritant**; 1 >80%lin) [Rees,1996b] **Non-irritant**; 2 >80 % [Cassidy 1978b]	**Non**; 1, 2 >80% lin [Rees, 1996c; Cassidy, 1978b]
C7						85566-14-9	Alcohols, C7-11-branched and linear	Supporting substance		
C8	111-87-5	1-Octanol	**Mild** ; 1 [Johnson, 1996a] **Non** ; 2 [Griffith, 1997] 4 hr human test	**Irritant**; 1 [Johnson, 1996d] **Irritant**; 1, 2 [Ecetoc, 1998 ; Jacobs, 1987c]	Non expected; 2	104-76-7	1-Hexanol, 2-ethyl-	Supporting substance		
C8	68603-15-6	C6-12 Alcohols Type D	Expected to be **irritant**; 2	Expected to be **irritant**; 2	Non expected; 2					
C8	68551-07-5	C8-18 Alcohols	Expected to be **irritant**; 2	Expected to be **irritant**; 2	Non expected; 2					
C8	85566-12-7	C8-10 Alcohols	Expected to be **irritant**; 2	Expected to be **irritant**; 2	Non expected; 2					
C9	143-08-8	1-Nonanol Supporting substance	**Irritant**; 2 [Jacobs, 1992a]			66455-17-2	C9-11 Alcohols	**Irritant** ; 1 >80% lin [Cagen, 1981c] 24 hr occl.	**Non**; 1 >80% lin [Cagen 1981a], Draize	**Non** ; 1 Buehler >80% lin; [Cagen 1981b],

	Linear Alcohols					Essentially Linear Alcohols				
	CAS	CHEMICAL NAME	Skin ^{1}	Eye ^{1}	SS ^{1}	CAS	CHEMICAL NAME	Skin ^{1}	Eye ^{1}	SS ^{1}
C9						68603-15-6	C6-12 Alcohols (type B)	**Irritant** ; 2 >80% lin [Cassidy, 1978a] 24 hr occl.	**Irritant**; 2 >80% lin [Cassidy, 1978a] Draize	**Non** ; 2 >80%lin [Cassidy, 1978a],
C10	112-30-1	1-Decanol	**Non**; 2; 8hr. occl [Potokar, 1979] **Mild**; 1, [Johnson, 1996b] **Irritant**; 1, 1 [Bagley, 1996 ; ECETOC, 1995] **Non** ; 2 [Griffith, 1997; Robinson, 1998] 4 hr human test	**Irritant**; 1 [Johnson, 1996e]	**Weak Sensitiser** ^{4}; 2 after re-induction and re-challenge [Sharp, 1978] Mod.Draize					
C10	67762-41-8	C10-16 Alcohols, Type A	Expected to be **irritant**; 2	Expected to be **irritant**; 2	**Non** expected; 2					
C10	85665-26-5	Alcohols, C10-12	Expected to be **irritant**; 2	Expected to be **irritant**; 2	**Non** expected; 2					
C11						112-42-5	1-Undecanol	**Irritant**, 2 Lin. Not stated [Jacobs, 1992] **Irritant**, 2 Lin. Not stated [Younger, Labs 1977] 24 hr occl.	**Mild** 2 [Younger Labs 1977]	**Non** expected; 2
C11						68603-15-6	C6-12 Alcohols Type A	**Mild**; 2 50% lin [Biolab, 1985b]	**Irritant**; 2; 50% lin [Biolab, 1985a]	**Non** expected; 2

	Linear Alcohols					Essentially Linear Alcohols				
	CAS	CHEMICAL NAME	Skin ^{1}	Eye ^{1}	SS ^{1}	CAS	CHEMICAL NAME	Skin ^{1}	Eye ^{1}	SS ^{1}
C12	112-53-8	1-Dodecanol Supporting substance	**Mild**; 1 [Sanders, 1996a; **Non**; 1 [10%] Hempstock1997a **Non**, 1 [Henkel, 1996] 4 hr human test **Non** ; 2 [Griffith, 1997] 4 hr human test	**Non**;1 [Sanders, 1996d]	**Non**; 1 [Iihama, 1997a]	67762-41-8	C10-16 Alcohols	Type B: **Mild**; 2; 50% lin) [Biolab, 1984a; 1991b] **Mild**; 1 50% lin [Sasol, 1998c] **Non**; 2 5% lin LGC Biosc., 1998a, b Type C: **Non**, 2 95% lin [Biolab; 1991a] **Irritant**; 2 >80% lin [Cassidy 1978c] 24 hr occl Type D: Expected to be **Irritant**; 2	Type B: **Non Irritant**; 1 50%lin [Sasol, 1998d] **Non irritant**; 2 50% lin Biolab undated a **Non irritant**; 2 5% lin [Biolab, 1991g] Type C: **Non irritant**; 2 95% lin (Biolab, 1991f) **Non Irritant** ; 2 >80% lin [Cassidy, 1978c] Draize Type D Expected to be **Irritant**; 2	Type B: **Non**; 1 50% lin [Sasol, 1998e] Type C. **Non** ; 2 >80% lin [Cassidy, 1978c Type D: **Non** expected, 2
C12	67762-25-8	C12-18 Alcohols Type A, B	Expected to be **Mild**; 2	Expected to be **Non-irritant**; 2	**Non** expected, 2	63393-82-8	C12-15 Alcohols	Type A **Mild**; 2 >80% lin [Shell, 1964] 24 hr occl. Type B. Expected to be **Mild**; 2	Type A **Non**; 2 >80% lin. [Shell, 1964] Draize Type B Expected to be **Non-irritant**; 2	Type A, B **Non** expected, 2

	Linear Alcohols					Essentially Linear Alcohols				
	CAS	CHEMICAL NAME	Skin [1]	Eye [1]	SS [1]	CAS	CHEMICAL NAME	Skin [1]	Eye [1]	SS [1]
C12	68855-56-1	C12-16 Alcohols	Type B Non ; 1 [Johnson, 1996c] Type C Expected to be Mild; 2	Type B Non; 1 [Johnson, 1996f] Type C Expected to be Non-irritant; 2	Type B, Non expected, 2 Type C: Non expected, 2	68855-56-1	C12-16 Alcohols Type A	Non; 2 50, 95% lin. [Biolab, 1991, 1984d] Mild; 2 95% lin. [Biolab 1991, Irritant; 2 >80% lin [Clark, Coombs, 1978] 24 hr occl	Non; 2 95%lin. [Biolab, 1991h Non; 2 >80% lin [Clark, Coombs 1978]	Non, 2 >80% lin [Clark, Coombs,1978]
C12	80206-82-2	C12-14 Alcohols	Type A. Mild; 2 [Henkel, 1980a] 24hr occl. Non; 2 [25, 10%] [Henkel 1980a] 24 hr occl Human (Burkhardt assay) Non, 1 [Henkel, 1996] 4 hr human test Type B Expected to be Mild; 2	Type A Non; 2 [Henkel, 1980a] Type B Expected to be Non-irritant; 2	Type A Non expected, 2 Type B Non expected, 2	75782-86-4	C12-13 Alcohols	Mild; 2 [Shell. 1966] 24 hr occl.	Non; 2 [Shell, 1966]	Non expected, 2
C12						68333-80-2	C14-16 Alcohols Type B	Expected to be Mild; 2	Expected to be Non-irritant; 2	Non expected, 2
C13						112-70-9	1-Tridecanol	Expected to be Mild; 2	Expected to be Non-irritant; 2	Non expected, 2
C13						90583-91-8	Tridecanol, branched and linear	Expected to be Mild; 2	Expected to be Non-irritant; 2	Non expected, 2

	Linear Alcohols					Essentially Linear Alcohols				
	CAS	CHEMICAL NAME	Skin ^{1}	Eye ^{1}	SS ^{1}	CAS	CHEMICAL NAME	Skin ^{1}	Eye ^{1}	SS ^{1}
C14	112-72-1	1-Tetradecanol	**Mild**, 2 [Sc. Assoc.1977b] 24hr occl. **Non**, 1 [Henkel, 1996] 4 hr human test **Non** ; 2 [Griffith, 1997] 4 hr human test	**Irritant**; 1 [Sanders, 1996f] **Non**; 1, 2 [10%, Hempstock, 1997g ; Sc. Assoc. 1977b]	**Non** ; 1 [Iihama, 1997b]	68333-80-2	C14-16 Alcohols Type A	**Non**: 2 (5, 95 % lin.) [Biolab 1985b; 1991d] **Mild**; 2 40% lin [Biolab, 1985c] **Irritant**: 2 >80% lin [Cassidy, 1978d] 24 hr. occl	**Non**; 2 (5, 40, 95% lin) [Biolab, undated b, 1991i,,j] **Non Irritant**, 2 >80% lin [Cassidy, 1978d]	**Non**; 2 40% lin. [Biolab, undated c] **Non**, 2 >80% lin. [Cassidy. 1978d]
C14	67762-30-5	C14-18 Alcohols Type B	Expected to be **Mild**; 2	Expected to be **Non-irritant**; 2	**Non** expected, 2	75782-87-5	C14-15 Alcohols	**Mild**; 2 >80% lin [Lifestream, 1966] 24 hr occl.; 50%	**Non**; 2 >80% lin [Lifestream, 1966]	**Non** expected, 2
C15						629-76-5	1-Pentadecanol	Expected to be **Mild**; 2	Expected to be **Non-irritant**; 2	**Non** expected, 2
C16	36653-82-4	1-Hexadecanol	**Non**; 1 [Sanders 1996b]	**Non**;1 [Sanders, 1996g]	**Non** ; 1,2 [Driscoll, 1996a; Gloxhuber, 1983]					
C16	67762-30-5	C14-18 Alcohols Type A	Expected to be **Mild**; 2	Expected to be **Non-irritant**; 2	**Non** expected, 2					
C16	67762-27-0	C16-18 Alcohols	**Non**; 2 [Carter, 1975; Continent., 1979] 24hr occl.	**Non**; 2 [Carter, 1975; Continent., 1979]	**Non** expected, 2					
C16	143-28-2	9-Octadecen-1-ol, (9Z)-	**Mild**, 2 [Guillot, 1977] 23 h, occl **Non**, 2 [Guillot, 1977] 10%, 23 h **Non**, 2 [Motoyoshi 1979] human, 48 h	**Non**; 2 [Guillot, 1977]	**Non**; 2 [Guillot, 1977] rabbit, 60 day exposure					

	Linear Alcohols					Essentially Linear Alcohols				
	CAS	CHEMICAL NAME	Skin [1]	Eye [1]	SS [1]	CAS	CHEMICAL NAME	Skin [1]	Eye [1]	SS [1]
C16	68002-94-8	C16-18 and C18 Unsaturated	Irritant; 1 [Henkel, 1990a]; Mild ; 1 [Henkel, 1987a] Non, 1 [Henkel, 1996] 4 hr human test	Non; 1 [Henkel, 1990b, 1987b]	Non; 1 [Henkel, 1988f]					
C16	68155-00-0	Alcohols, C14-18 and C16-18-unsatd	Expected to be Mild; 2	Expected to be Non-irritant; 2	Non expected, 2					
C18	112-92-5	1-Octadecanol Supporting Substance	Non; 1 [Sanders, 1996c]	Non; 1 [Sanders, 1996h]	Non ; 1 [Driscoll, 1996b]					
C18	97552-91-5	C18-22 Alcohol	Expected to be Non irritant; 2	Expected to be Non-irritant; 2	Non expected, 2					
C20	629-96-9	1-Eicosanol	Expected to be Non irritant; 2	Expected to be Non-irritant; 2	Non expected, 2					
C22	661-19-8	1-Docosanol	Non; 1 [Hempstock, 1997d]	Non; 1 [Hempstock, 1997e]						
C24	123607-66-9	Alcohols, C24-34; Supporting Substance	Supporting substance							

Notes:

1 Data presented in the following order: Test result; reliability score; [Reference]; additional information (e.g. test protocol; if no information is provided standard OECD or equivalent protocol was used]

2 Skin sensitization data represent the results of a guinea-pig maximization procedure, unless indicated otherwise

3 The relevant mean or individual test scores, where available, are presented in the Robust Study Summaries

4 Test sample of unknown isomeric content

3.1.5 Repeated Dose Toxicity

3.1.5.1 Studies in Animals

Data Availability. An overview of the available data regarding repeat dose toxicity is presented in Table 3.6. The data for the lower end of the class of linear alcohols include repeated dose toxicity studies in the rat and dog with 1-hexanol. For the intermediate chain lengths linear alcohols (range C12- C16) test data from a combined repeat-dose repro/developmental screening study with 1-dodecanol in the rat are available. Several repeat-dose toxicity studies for the longer chain linear alcohols in the range C16 to C22 are available. In addition, C24-34 alcohols[8], were administered to rats and dogs for periods up to 52 weeks. Additional information regarding the repeat dose toxicity of this sub-category can be obtained from the developmental toxicity study with 1-octanol. These data are all of acceptable quality (reliability score 1 or 2) and overall the available data are considered to be adequately representative for the sub-category of the linear alcohols. For the essentially linear alcohols sub-acute studies by the oral route are available for two members of the C6-12 alcohols (Types C and B) and a short-term inhalation study for C9-11 alcohol. Key studies for this category are a repeat dose study for a C10-16 alcohol (Type B, linearity 50%) and C14-16 alcohol (Type A, linearity ca. 70%). Considering the data availability for the essentially linear alcohols, repeated dose toxicity data for the lower range of the C6-C12 alcohols only cover exposure periods up to two weeks. Therefore, data from appropriate surrogate substances is considered to assess the repeat-dose toxicity for the sub-category of essentially linear alcohols. A 17-week oral study for iso-amyl (C5) alcohol (a supporting substance for this category appears to be suitable to assess the repeated dose toxicity of the lower end of the essentially linear alcohols. Iso-amyl alcohol (IAA) is a branched, primary C5 alcohol; its metabolism (i.e. conversion to corresponding aldehyde and carboxylic acid) is common to other alcohols in this category [Holbrook, 1992; BIBRA, 1995]. The chain length of IAA is one C-atom below the lowest component of the alcohols of this sub-category. For the branched components present in the C6-C12 range of the essentially linear alcohols the sub-chronic toxicity of 2-ethylhexanol (2-EH) is considered a suitable surrogate being a 100% branched alcohol with an ethyl branch at the C2 position. It should be noted that the side chain of 2-EH consists of an ethyl group whereas the side chain of the branched components of the essentially linear alcohols consists predominantly of a methyl group. It's metabolism proceeds through the β, ω and ω-1 oxidation, the pathways common to the metabolism of the alcohols in this category [WHO, 1993].

For a typical essentially linear alcohol the degree of branching is usually in the order of 20-30%, with the branched fraction consisting predominantly of mono methyl-substituted alcohols, with the remainder being a complex distribution of isomeric branched alkyl alcohols. The surrogates IAA or 2-EH are 100% branched mono-alkyl alcohols and considered representative of the branched fraction of the essentially linear alcohols sub-category.

The data available for the essentially linear alcohols, including the information provided through supporting substances, is considered to be adequate to assess the repeat dose toxicity of the sub-category of the essentially linear alcohols and to read-across between the members of the sub-category.

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[8] Substance supporting the category

Linear Alcohols

Studies in rats – oral

1-Hexanol [CAS 111-27-3]. Rats exposed to 1-hexanol via the diet for 13 weeks showed no signs of significant toxicity when administered at nominal concentrations up to 1% (with staged increases at concentrations up to 6% during the last phase of the exposure period). There were no microscopic alterations recorded in the animals receiving concentrations of 1-6% (equivalent to 1127 mg/kg/day). Examination of testes and the ovaries did not show any abnormalities (Scientific Associates, 1966a).

Exposure of male rats to high dietary concentrations (up to 8%) of 1-hexanol for 2 weeks did not produce evidence of peroxisome proliferation (Moody and Reddy, 1978, 1982).

C6-12 Alcohol [Type D; CAS 68603-15-6]. A 2-week study showed no potential for peroxisomal proliferation for a C6-12 linear alcohol. No effect on weights of liver and testes, peroxisome proliferation and hypolipidaemic activity in male rats was recorded; an equivocal increase in palmityl CoA oxidase activity was noted in an *in vitro* assay (Rhodes *et al*., 1984).

1-Octanol [CAS 111-87-5]. In a developmental toxicity study administration of 1-octanol by daily gavage of doses in the range 130 - 1300 mg/kg to pregnant rats caused dose-related clinical signs of toxicity, including nasal discharge, pneumonia, and signs consistent with slight, transient CNS depression at levels of 650, 975 and 1300 mg/kg/day. Slight decreases in body weight gain and food consumption were observed. The severity of these effects may have been exacerbated by the pregnancy of the test animals. No detailed assessment of the maternal toxicity was included in the design of this study (Hellwig *et al*., 1997).

1-Dodecanol [CAS 112-53-8] was tested in rats in a combined repeated-dose and reproductive / developmental toxicity screen. Animals received dietary concentrations of 1500, 7500 or 30,000 ppm during all phases in the production of a single generation; the composition of the diet was adjusted to take account of the caloric incorporation of the test material. Male animals were exposed for a total of 37 days including the mating period. Females were allowed to litter naturally and were terminated at day 5 post-natally. In males, there were no effects recorded other than a reduction in mean white blood cell count (15, 38 and 32% reduction for the low mid or high dose group, respectively) and changes in free cholesterol (38% reduction in the mid dose group) and triglycerides (46% reduction at the top dose level). In the absence of any changes in the differential white cell count, the observed reduction in total WBC is considered of uncertain significance. A reduction in plasma cholesterol was observed in the middle dose group; this was considered a chance finding associated with 2 outlying values. Although the reduction in plasma triglycerides and cholesterol levels may be indicative of marginal effects in the liver, the differences in composition of the test diets between control and the treatment groups may have confounded some of the parameters measured in this study. The NOEL was <1500ppm (<100 mg/kg/day) based on the haematological (WBC) changes; the NOAEL was 30,000 ppm (2000 mg/kg/day) (Hansen, 1992a).

1-Hexadecanol [CAS 36653-82-4] was without toxic effects in a 28-day study in rats receiving daily oral [gavage] doses of 0 (control), 100, 500 and 1000 mg/kg/day (Henkel, 1985a).

In a 13-week study in rats **1-hexadecanol** was administered in the diet at concentrations of 0 (control), 1, 2.5 or 5%; the level in the highest dose group being increased stepwise to 10% during the last 3 weeks of the study. Reductions in body weight gain (82-90% of control values) and food consumption (76 – 90% of control values) in the highest dose group and, occasionally, at the 2.5% level were the main findings of this study. Relative liver weights were increased in males at the top dose level (124% of control values) but in the absence of any microscopic findings the significance of this change is uncertain. A NOAEL was established at a dietary concentration of 1% (equivalent to *ca.* 750 mg/kg/day) based on the reductions in body weight gain and food consumption (Scientific Assoc., 1966a).

C16-18 and C18 unsaturated alcohols [CAS 68002-94-8] were without adverse effects in rats upon daily administration of 1 ml/kg/day (*ca.* 850 mg/kg/day) for 4 weeks (Henkel, 1973).

1-Octadecanol [CAS 112-92-5] was tested in Wistar rats in a combined repeated dose and reproductive/developmental screen. Animals received dietary concentrations of 1500, 7500 or 30,000 ppm during all phases in the production of a single generation; the composition of the diet was adjusted to take into account the caloric value due to the incorporation of the test material. Male animals were exposed for 37 days including the mating period. Females were allowed to litter and were terminated at post-natal day 5. In male animals (females were not investigated) reductions were recorded in the levels of plasma glucose (>15% reduction in all treatment groups) and triglycerides (>37% reduction all treated level level); free cholesterol levels were increased 25% or more in all treated groups; these changes were without a clear dose-response. No treatment-related histopathological changes were recorded. The clinical chemical changes may be indicative of mild effects in the liver, the differences in the composition of the test diets may have contributed to these results. The NOAEL was 30,000ppm (2000 mg/kg/day); the NOEL was <1500 ppm (<100 mg/kg/day) based on the changes in the clinical chemistry (Hansen, 1992b).

In a 4-week oral study **1-octadecanol** was administered daily (5 times/week) in olive oil to groups of 10 male and female Sprague-Dawley rats at levels of 0 (control), 100, 500 and 1000 mg/kg/day. There were no adverse effects reported in this study during all stages of the study (Henkel, 1986a).

1-Docosanol [CAS 661-19-8; C22 alcohol] was administered daily to groups of rats at levels up to 1000 mg/kg for 26 weeks. Body weight and food consumption was not affected by treatment. Haematology, clinical chemistry and gross necropsy investigations showed no evidence of toxicity. There were no treatment related microscopic changes (Iglesias *et al*., 2002a).

C24-C34 Alcohols [CAS 123607-66-9] was dosed daily by oral gavage of rats for periods up of 12 months. No adverse effects were recorded in any of these studies. The NOAEL was 1000 mg/kg/day (highest dose tested) following a 52-week exposure period (Rodiero, 1998b).

Studies in rats – other routes.

1-Hexanol [CAS 111-27-3]. No potential for peripheral neuropathy was identified in rats upon i.p. administration of 1-hexanol at levels of 102.5 mg/kg for 30 weeks (6 days/week) (Perbellini *et al*., 1978).

Studies in dogs - oral

1-Hexanol [CAS 111-27-3] Daily administration of capsules containing 1000 mg/kg/day 1-hexanol to male and female dogs resulted in post-dose salivation, transient but marked CNS effects (ataxia, tremors and narcosis) and mortality. One animal died after the first dose (not examined microscopically); 3 of 5 animals after 3-5 weeks. In all decedents death was attibuted to aspiration while the animals were under substance-induced narcosis . Macroscopic and microscopic examination of the decedents showed severe inflammation of the upper gastro-intestinal tract and testicular atrophy and decreased oogenesis. The single surviving female showed signs of gastro-intestinal irritation; however there were no adverse effects on the ovaries.

Other groups of 2 dogs/sex received 1-hexanol incorporated in the daily ration at nominal concentrations of 0 (control), 0.5 or 1.0 %. Apart from local irritation of the gastro-intestinal tract in the 1.0% dose group, no adverse systemic effects were observed in these animals.

The testicular effects observed in the early decedents were attributed to the general ill health of these animals caused by the severe gastro-intestinal irritation. This likelihood is supported by the lack of gonadal effects in dogs exposed to 1% and 0.5% 1-hexanol in the dietary portion of the study that showed greatly diminished or absence of the gastro-intestinal irritation, respectively. No other significant effects were noted at the 0.5% dietary level. The threshold for local irritative effects was 190 mg/kg/day (0.5%). The NOAEL for systemic effects was established at 1.0%, equivalent to 370 mg/kg/day (the highest dose tested in this portion of the study) (Scientific Associates, 1966b).

1-Hexadecanol [CAS 36653-82-4] In a 13-week study groups of 2 dogs/sex/dose received dietary concentrations of 0 (control), 0.5, 1.0 or 3% 1-hexadecanol. There no were adverse effects reported except for elevations of AST at week 13 at all incorporation levels, without evidence of a clear dose response relationship. The small groups sizes used in this study preclude a definitive conclusion about the significance of these changed enzyme levels, especially in the absence of any further corroborating evidence of liver toxicity (liver weight and histology). A NOAEL of 1000 mg/kg (highest dose tested) is therefore proposed (Scientific Assoc., 1966b).

1-Docosanol [CAS 661-19-8; C22 alcohol] was administered daily to groups of dogs at levels up to 2000 mg/kg for 26 weeks. Body weight and food consumption was not affected by treatment. Haematology, clinical chemistry and gross necropsy investigations showed no evidence of toxicity. There were no treatment related microscopic changes (Iglesias *et al*., 2002a).

C24-C34 Alcohols [CAS 123607-66-9] Daily oral administration of 50 or 250 mg/kg to dogs (4 animals/group/sex) for 52 week was without effects. A NOAEL was established at 250 mg/kg/day (highest dose tested for 52 weeks) (Aleman *et al*., 2001)

In summary, The sub-category of the linear aliphatic alcohols is of a low order of toxicity upon repeated exposure. The alcohols at lower end of this group caused local irritation at the site of first contact and induced signs of CNS depression and respiratory effects when administered at very high dose levels and only as a bolus dose (C6, C8 alcohol) in the dog (C6 alcohol) and the rat (C8 alcohol). Other routes of exposure induced no apparent neurotoxicity either centrally or peripherally. Intermediate (>C8 to C12) and higher (>C12) linear alcohols are non-irritant at the site of first contact and are without a neurotoxic potential. At high dose levels some of the higher alcohols showed changes in clinical chemical changes and liver weight but without further evidence of systemic toxicity; this finding may be indicative of mild, sub-clinical effects in the liver. There are no species differences observed for this sub-category, based on a comparison of the results of parallel studies in the rat and the dog.

Essentially Linear Alcohols

Studies in rats - inhalation

Inhalation of saturated vapours C9-11 alcohols (CAS 66455-17-2, containing mainly C9, C10, C11 Alcohols, linearity > 80%) for 9-days caused no adverse effects (Darmer *et al*., 1982).

Studies in rats - oral

Iso-amyl alcohol [CAS 123-51-3] was administered daily by gavage for 17 weeks to rats with interim laboratory assessments at 3 and 6 weeks. No adverse effects, other than reduced body weight gain and food consumption were recorded at 1000 mg/kg (Carpanini et al., 1973).

C6-12 Alcohols [Type C, B; CAS 68603-15-6] In sub-acute studies, essentially linear alcohols in the range C7-9; (typeC) linearity >60%, when administered orally for 2 weeks did not show evidence of systemic toxicity, including effects on the liver and testes or signs of peroxisomal proliferation or hypolipidaemia (Rhodes *et al*., 1984). Administration (5 ml/kg/day) of C6 to12 alcohol (containing mainly C7, C8 and C9 alcohols -type C- and mainly C9, C10, C11 alcohols – type B-; linearity > 80%) to rats resulted in local irritation of the g.i.-tract and equivocal evidence of slight liver toxicity in some rats (Brown *et al*., 1970).

C7-11 Alcohols [CAS 85566-14-9] In a developmental toxicity study, the surrogate C7-11 alcohol [CAS 85566-14-9, linearity ca. 65%], was administered by daily oral gavage of rats during days 6-15 of pregnancy at dose levels of 0, 144, 720 or 1440 mg/kg/day. There were no treatment-related effects noted in body weight development, food consumption and clinical observations during the study. No further detailed assessment of maternal toxicity was included in the design of this study (Hellwig et al., 1997).

2-Ethyl-1-hexanol [CAS 104-76-7] Administration of 2-ethylhexanol to rats by daily gavage for 3 months caused evidence of liver toxicity and irritation of the stomach at dose levels of 250 and 500 mg/kg; no adverse effects were recorded at 125 mg/kg/day. The liver toxicity was expressed as increased organ weight, changes in clinical chemical parameters (decreases in AP, ALT, glucose and cholesterol) and decreased fat deposition/infiltration in the liver. The effect on fat deposition in the liver is likely to be associated with the decreased body weight. Separate investigations identified an equivocal potential for peroxisomal proliferation for 2-EH, based on slight changes in palmitoyl Co-A oxidase activity, a key marker enzyme for peroxisomal proliferation. This effect was only measurable at or beyond the highest level tested in the repeated dose toxicity studies (>500 mg/kg) (WHO, 1993; Rhodes *et al*., 1984).

C10-16 Alcohol [Type B ; CAS 67762-41-8] In a 28-day oral toxicity study in rats C10-16 alcohol (type B) induced slight body weight reductions in males receiving 1000 mg/kg/day (ca. 10% reduction in overall body weight gain). Further changes at 1000 mg/kg/day were consistent with slight liver toxicity: elevated levels of ALT, AP and cholesterol (increases of *ca* 50, 40, 30 % respectively-) in females but without any concurrent histopathological findings. There was a dose-related increased in relative kidney weights in males at 300 and 1000 mg/kg/day, however there were no toxicological findings associated with the renal weight changes and are considered not of toxicological significance. The level of 300 mg/kg is therefore regarded to be without adverse effects (NOAEL) based the body weight changes and liver effects at 1000 mg/kg/day. No changes were noted in testis and ovaries at 1,000 mg/kg/day, the highest dose tested. At 100 mg/kg/day no changes were observed (Sasol, 1999).

C14-16 alcohol [Type A; CAS 68333-80-2] In a 13-week rat study C14-16 alcohol (mainly C14 and C15 alcohols; linearity 70%) was administered via the diet at concentrations of 0, 0.2, 1 and

5%. The top and intermediate dose level (5 and 1%, respectively) had limited palatability and induced a considerable reduction in growth (> 30% and ca. 15% reduction in body weight in high and mid dose males, respectively). Biochemistry showed changes in AP, ALT and protein ratios at the 1 and/or 5% level. Organ weight changes were consistent with an increased liver weight. No treatment-related microscopic changes were observed, including both the testis and ovaries at this same dose level. Based on the effect on body weight a NOAEL was established at the 0.2% dietary incorporation level (ca. 200 mg/kg/day). The results of the clinical chemistry and the organ weight analysis are consistent with slight liver toxicity, however there were no correlating histopathological changes in the liver. These changes in the liver enzyme profile may well have been confounded by inanition (Ito, 1976).

Tridecanol [CAS 112-70-9] 1-tridecanol was shown to be without a potential for peroxisomal proliferation or hypolididaemia. No histological or weight changes were observed in the liver and testes after oral administration of 184 mg/kg/day for 2 weeks (Rhodes *et al*., 1984).

In summary, the data for the essentially linear alcohols, including the data from supporting substances, indicate a low order of toxicity upon repeated exposure. A consistent finding for this group is the effect on the liver: mild organ weight increases and/or slight clinical chemical changes but without evidence of significant histopathological effects. The clinical chemistry changes were generally of a slight grade but showed some inconsistencies, some of which relating to decreases in transferase activity, a change not normally associated with adverse hepatic effects. The [small] degree of the liver weight increases, the pattern of the clinical chemical changes and the absence of markers support the conclusion that this sub-category of alcohols lacks a potential for the induction of peroxisomal proliferation. There is evidence of irritation at the first site of contact for the lower members of this group.

Conclusion: The repeat dose toxicity of the category of long chained alcohols with chain lengths ranging from C6 to C22 indicates a low order of toxicity upon repeated exposure. Typical NOAEL's recorded for this category range between ca. 200 mg/kg/day to 1000 mg/kg/day in the rat upon sub-chronic administration via the diet. At the lower end, members of this category induce local irritation at the site of first contact. Other notable findings observed for several members within this group suggest mild changes consistent with low-grade liver effects with the changes in essentially linear alcohols being slightly more pronounced than in linear alcohols. Typical findings include: slightly increased liver weight, in some cases accompanied by clinical chemical changes but generally without concurrent histopathological effects. The significance of these effects for human health is not likely to be significant given that the aliphatic alcohols are efficiently metabolised and the biotransformation products are very similar or indistinguishable from those derived from common dietary sources (triglycerides) and that human intake from these dietary sources is likely to be considerably higher than the exposures from uses involving aliphatic alcohols.

Special studies demonstrated that this category does not have a potential for peroxisome proliferation. A potential for CNS depression as observed for short chain aliphatic alcohols (C1 to C4; not included in this category) was also identified for 1-hexanol and 1-octanol, however this effect was only expressed upon repeated administration of a bolus dose; CNS effects were absent upon inhalation or dietary administration. Similarly, 1-hexanol and 1-octanol induced respiratory distress upon repeated administration of a bolus dose. Aliphatic alcohols do not have a potential for peripheral neuropathy. Furthermore, the data from the substances supporting this category (i.e. isoamyl alcohol and 2-ethyl-hexanol), demonstrate that the toxicological profile of the repeated dose toxicity of 100% branched alcohols is qualitatively similar to that of the corresponding essentially linear alcohols.

Table 3.6 Repeated dose toxicity

Linear Alcohols							Essentially Linear Alcohols					
	CAS	CHEMICAL NAME	Species/ Study type/ Duration [1]	Route	NOAEL [Ref]	Rel.	CAS	CHEMICAL NAME	Species/ Study type/ Duration [1]	Route	NOAEL [Ref]	Rel.
C5							123-51-3	Isoamyl alcohol; Supporting Substance	Rat 17 wk	Gavage	500 mg/kg [Carpanini, 1973]	2
C6	111-27-3	1-Hexanol	Dog 13 wk Rat 13 wk	Diet Diet	370 mg/kg [Sc.Assoc.'66b] 1127 mg/kg [Sc.Assoc.'66]	2 2						
C7	111-70-6	1-Heptanol	Supporting substance			2	68603-15-6	C6-12 Alcohols (Type C)	Rat 1-wk Rat 1 wk	Gavage Gavage	<4175 mg/kg > 80% lin [Brown, 1970] 128 mg/kg > 80% lin. [Rhodes, 1984]	2 2
C7							85566-14-9	Alcohols, C7-11-branched and linear Supporting Substance	Rat Dev. Tox	Gavage	1300 mg/kg [Hellwig, 1997]	2

Linear Alcohols							Essentially Linear Alcohols					
	CAS	CHEMICAL NAME	Species/ Study type/ Duration ^{1}	Route	NOAEL [Ref]	Rel.	CAS	CHEMICAL NAME	Species/ Study type/ Duration ^{1}	Route	NOAEL [Ref]	Rel.
C8	111-87-5	1-Octanol	Rat Dev. Tox.	gavage	130 mg/kg [Hellwig, 1997]	2	104-76-7	1-Hexanol, 2-ethyl- Supporting Substance	Rat/mouse 13 wk Rat, 24 mo Mouse, 18 mo Rat 2 wk	gavage gavage gavage gavage	125 mg/kg [WHO, 1993 BASF 1992] 50 mg/kg [WHO, 1993] 200 mg/kg [WHO, 1993] 130 mg/kg [Rhodes'84]	2 2 2 2
	68603-15-6	C6-12 Alcohols Type D	Rat 2 wk	Gavage	133 mg/kg [Rhodes, 1984]	2						
C8	85566-12-7	C8-10 Alcohols			Low systemic toxicity expected	2						
C8	68551-07-5	C8-18 Alcohols			Low systemic toxicity expected	2						
C9	143-08-8	1-Nonanol	Supporting substance				66455-17-2	C9-11 Alcohols	Rat 9-day	Inhalat'n	>0.158 mg/l >80% lin. [Darmer, 1982]	1
C9							68603-15-6	C6-12 Alcohols (type B)	Rat 2 wk	Gavage	< 4150 mg/kg >80% lin. [Brown, 1970]	2
C10	112-30-1	1-Decanol			Low systemic toxicity expected	2						
C10	67762-41-8	C10-16 Alcohols Type A			Low systemic toxicity expected	2						

Linear Alcohols							Essentially Linear Alcohols					
	CAS	CHEMICAL NAME	Species/ Study type/ Duration [1]	Route	NOAEL [Ref]	Rel.	CAS	CHEMICAL NAME	Species/ Study type/ Duration [1]	Route	NOAEL [Ref]	Rel.
C10	85665-26-5	Alcohols, C10-12			Low systemic toxicity expected	2						
C11							112-42-5	1-Undecanol			Low systemic toxicity expected	2
C11							68603-15-6	C6-12 Alcohols Type A			Low systemic toxicity expected	2
C12	112-53-8	1-Dodecanol Supporting Substance	Rat 5wk	Diet	2000 mg/kg [Hanssen,1992a]	2	67762-41-8	C10-16 Alcohols	Type B Rat 4wk	Gavage	300 mg/kg; 50 % lin [Sasol, 1999]	1
									Type C		Low systemic toxicity expected	2
									Type D Rat 2 wk	Gavage	209 mg/kg 80%lin. [Rhodes, 1984]	2
C12	67762-25-8	C12-18 Alcohols Types A, B			Low systemic toxicity expected	2	63393-82-8	C12-15 Alcohols Type A, B			Low systemic toxicity expected	2
C12	68855-56-1	C12-16 Alcohols Types B, C			Low systemic toxicity expected	2	68855-56-1	C12-16 Alcohols Type A			Low systemic toxicity expected	2

Linear Alcohols							Essentially Linear Alcohols					
	CAS	CHEMICAL NAME	Species/ Study type/ Duration [1]	Route	NOAEL [Ref]	Rel.	CAS	CHEMICAL NAME	Species/ Study type/ Duration [1]	Route	NOAEL [Ref]	Rel.
C12	80206-82-2	C12-14 Alcohols Types A, B			Low systemic toxicity expected	2	75782-86-4	C12-13 Alcohols			Low systemic toxicity expected	2
C12							68333-80-2	C14-16 Alcohols Type B			Low systemic toxicity expected	2
C13							112-70-9	1-Tridecanol	Rat 2 wk	Gavage	184 mg/kg [Rhodes, 1984]	2
C13							90583-91-8	Tridecanol, branched and linear			Low systemic toxicity expected	2
C14	112-72-1	1-Tetradecanol			Low systemic toxicity expected	2	68333-80-2	C14-16 Alcohols Type A	Rat 90 day	Diet	167 mg/kg; 70%lin [Ito, 1978]	2
C14	67762-30-5	C14-18 Alcohols Type B			Low systemic toxicity expected	2	75782-87-5	C14-15 Alcohols			Low systemic toxicity expected	2
C15							629-76-5	1-Pentadecanol			Low systemic toxicity expected	2
C16	36653-82-4	1-Hexadecanol	Rat 4 wk Dog 13 wk Rat 13 wk	Diet Diet Diet	1000 mg/kg [Henkel, 1985a] 1054 mg/kg [Sc.Assoc1966b] 750 mg/kg [Sc.Assoc1966a]	2 2 2						

Linear Alcohols							Essentially Linear Alcohols					
	CAS	CHEMICAL NAME	Species/ Study type/ Duration [1]	Route	NOAEL [Ref]	Rel.	CAS	CHEMICAL NAME	Species/ Study type/ Duration [1]	Route	NOAEL [Ref]	Rel.
C16	67762-30-5	C14-18 Alcohols Type a			Low systemic toxicity expected	2						
C16	67762-27-0	C16-18 Alcohols	Rat 10 day	Inhalatn	0.56 mg/L [Sc.Assoc1966a]	3						
C16	143-28-2	9-Octadecen-1-ol, (9Z)-			Low systemic toxicity expected	2						
C16	68002-94-8	C16-18 and C18 Unsatured	Rat 4 Wk	Gavage	840 mg/kg [Henkel, 1973]	2						
C16	68155-00-0	Alcohols, C14-18 and C16-18-unsatd			Low systemic toxicity expected	2						
C18	112-92-5	1-Octadecanol Supporting Substance	Rat 4 wk Rat 5 wk	Gavage Diet	>1000 mg/kg [Henkel, 1986a] 2000 mg/kg [Hansen, 1992b]	1 2						
C18	97552-91-5	C18-22 Alcohol			Low systemic toxicity expected	2						
C20	629-96-9	1-Eicosanol			Low systemic toxicity expected	2						
C22	661-19-8	1-Docosanol	Rat 26 wk Dog 26 wk	Gavage Gavage	1000 mg/kg [Iglesias,2002a] 2000 mg/kg [Iglesias,2002a]	1 1						

Linear Alcohols							Essentially Linear Alcohols					
	CAS	CHEMICAL NAME	Species/ Study type/ Duration [1]	Route	NOAEL [Ref]	Rel.	CAS	CHEMICAL NAME	Species/ Study type/ Duration [1]	Route	NOAEL [Ref]	Rel.
C24	123607-66-9	Alcohols, C24-34 Supporting Substance	Dog 52 wk	Gavage	> 250 mg/kg [Aleman, 2001]	2						
			Rat, 2 wk	Gavage	>5000 mg/kg [Rodiero 1998b]	2						
			Rat , 13 wk	Gavage	>625 mg/kg [Rodiero, 1998b]	2						
			Rat, 52 wk	Gavage	1000 mg/kg [Rodiero, 1998b]	2						

Note:

1 Entries in **bold** refer to key studies

3.1.6 Mutagenicity

Data Availability. The results of the available *in vitro* and *in vivo* mutagenicity data for the category of long chained alcohols are summarised in Table 3.8.

Linear Alcohols. Table 3.8 lists the bacterial mutagenicity (Ames test) data for a representative number of linear alcohols covering this sub-category comprehensively. These data show a consistent lack of mutagenic activity across the whole range of linear alcohols. In addition to these *in vitro* results, 1-dodecanol, 1-octadecanol, 1-docosanol and C24-34 alcohols were consistently negative in an *in vivo* mouse bone marrow micronucleus test. Further support for the lack of mutagenicity of the category aliphatic alcohols is provided by 1-butanol, a substance below the minimal chain length considered in this category. The data for n-butanol show no evidence of mutagenic activity in a battery of *in vitro* assays in bacterial cells, absence of clastogenicity in mammalian cell cultures and a mouse micronucleus assay (OECD SIDS n-Butanol, 2004).

Essentially Linear Alcohols. A representative number of essentially linear alcohols of this class showed a consistent negative response in the bacterial reverse gene mutation test (Ames assay). Other available data include negative chromosomal aberration tests in RL1 cells for C10-16 alcohols (Type C, linearity >80%) and in CHO cells for C_{10}-$_{16}$ alcohols (Type B, linearity 50%) (Dean, 1980; Sasol, 1998g).

2-Ethyl hexanol, a substance supporting the category, was negative in a comprehensive data set covering *in vitro* (bacterial and mammalian cell gene mutation assays, a chromosomal aberration and an Unscheduled DNA Synthesis [UDS] assay) and *in vivo* assays (mouse micronucleus and a dominant lethal test) (WHO, 1993).

Further data to support the assessment for the potential genotoxicity of the essentially linear alcohols can be derived from data of a series of Alkyl Acetates including C6-8, C7-9, C8-10, C9-11 and C11-14 branched alkyl esters. These alkyl acetates are manufactured from the corresponding primary, branched alcohols and cover a carbon chain length of C6 to C14. The standard protocol of *in vitro* mutagenicity test routinely applies a mammalian metabolic activation system (S9); the esterases present in this activation system produce acetic acid and the corresponding (branched) alcohol. The mutagenicity tests for these esters have, therefore, included the corresponding alcohols and the mutagenicity data available for these esters can be applied to further assess the mutagenic potential for the sub-category of the essentially linear alcohols (HPV, 2005). A summary of the data for these acetates as shown in Table 3.7 below has shown a clear absence of mutagenic activity for the alkyl acetates and the branched alcohols with a carbon chain length ranging from C6 to C14.

Table 3.7 Summary of the mutagenicity data for branched alkyl acetates

Chain length branched alcohol	C6	C6-C8	C7-C9	C11-14
CAS No.	88230-35-7	90438-79-2	108419-32-5	108419-35-8
In Vitro Assay				
Gene mutation	Negative	Negative	Negative	Negative
Chromosomal Aberration	Negative	Negative		
In vivo Assay				
Mouse Micronucleus			Negative	Negative

On the basis of the available data for the sub-category of the essentially linear aliphatic alcohols together with the data of highly branched materials such as 2-ethyl-hexanol and the highly branched aliphatic alcohols covering a carbon chain length ranging from C6 to C14 it can be concluded that the essentially linear alcohols are without a mutagenic potential.

It is important to note that the category of long chain aliphatic alcohols under consideration does not contain any structural elements that are of concern for potential mutagenic activity (Ashby and Tenant, 1991). Furthermore, primary alcohols (linear and branched) in the range C1 to C5 do not have a mutagenic potential (Bevan, 2001; OECD SIDS butanol, 2001). Furthermore, in a review by WHO-JECFA a series of 22 saturated aliphatic branched-chain primary alcohols and the corresponding aldehydes and acids in the range C4 to C8 showed no activity in a battery of in vitro and in vivo mutagenicity tests (WHO, 1998). On this basis it is concluded that the category of long chained alcohols does not have a mutagenic potential and that read-across within the category of long chained alcohols can be justified.

Conclusion: The category long chained alcohols do not have a genotoxic potential.

Table 3.8 Genetic toxicity

Linear Alcohols					Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	Study Type* Result [Ref]	Rel.	CAS	CHEMICAL NAME	Study Type Result [Ref]	Rel.
C5					123-51-3	Isoamyl alcohol	Supporting substance	
C6	111-27-3	1-Hexanol	Neg; Ames [Henkel, 1990]	1				
C7	111-70-6	1-Heptanol Supporting Substance			68603-15-6	C6-12 Alcohols (Type C) > 80% lin	Neg. Ames. [Shell, 1996]	1
					85566-14-9	Alcohols, C7-11-branched and linear	Supporting substance	
C8	111-87-5	1-Octanol	Neg; Ames [Henkel, 1982a; HLS, 1996k]	2	104-76-7	1-Hexanol, 2-ethyl- Supporting Substance	Neg; Ames, GM, UDS, MN, CA, dom. Leth. [WHO, 1993]	2
C8	68603-15-6	C6-12 Alcohols Type D	Expected to be non-mutagenic	2				
C8	85566-12-7	C8-10 Alcohols	Expected to be non-mutagenic	2				
C8	68551-07-5	C8-18 Alcohols	Expected to be non-mutagenic	2				
C9	143-08-8	1-Nonanol	Supporting substance		66455-17-2	C9-11 Alcohols	Expected to be non-mutagenic	2
C9					68603-15-6	C6-12 Alcohols (type B)	Expected to be non-mutagenic	2
C10	112-30-1	1-Decanol	Neg Ames** [HLS, 1996l]	2				
C10	67762-41-8	C10-16 Alcohols Type A	Expected to be non-mutagenic	2				
C10	85665-26-5	Alcohols, C10-12	Expected to be non-mutagenic	2				
C11					112-42-5	1-Undecanol	Expected to be non-mutagenic	2
C11					68603-15-6	C6-12 Alcohols Type A	Expected to be non-mutagenic	2
C12	112-53-8	1-Dodecanol Supporting Substance	Neg. Ames [Thomson, 1996a] Neg. Ames [Shimizu, 1985; Henkel, 1982b] Neg. MN; [Banduhn, 1992]	1 2	67762-41-8	C10-16 Alcohols	Type B: Neg Ames, CA; 50%Lin [Sasol, 1998f, g] Type C: Neg Ames, CA >80% lin. [Dean, 1980] Type D Expected to be non-mutagenic	1 2 2

Linear Alcohols					Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	Study Type* Result [Ref]	Rel.	CAS	CHEMICAL NAME	Study Type Result [Ref]	Rel.
C12	67762-25-8	C12-18 Alcohols	Type A Non-mutagenic expected Type B Neg Ames [Henkel 1982c]	2 2	63393-82-8	C12-15 Alcohols Type A, B	Expected to be non-mutagenic	2
C12	68855-56-1	C12-16 Alcohols	Type B Neg. Ames** [HLS, 1996m] Type C. Expected to be non mutagenic	2 2	68855-56-1	C12-16 Alcohols Type A >80% lin	Neg Ames [Ballantyne, 1996]	1
C12	80206-82-2	C12-14 Alcohols Type A, B	Expected to be non-mutagenic	2	75782-86-4	C12-13 Alcohols	Expected to be non-mutagenic	2
C12					68333-80-2	C14-16 Alcohols Type B	Expected to be non-mutagenic	2
C13					112-70-9	1-Tridecanol	Expected to be non-mutagenic	2
C13					90583-91-8	Tridecanol, branched and linear	Expected to be non-mutagenic	2
C14	112-72-1	1-Tetradecanol	Neg Ames [Thompson, 1996b]	1	68333-80-2	C14-16 Alcohols	Expected to be non-mutagenic	2
C14	67762-30-5	C14-18 Alcohols Type B	Expected to be non-mutagenic	2	75782-87-5	C14-15 Alcohols	Expected to be non-mutagenic	2
C15					629-76-5	1-Pentadecanol	Expected to be non-mutagenic	2
C16	36653-82-4	1-Hexadecanol	Neg Ames [Thompson, 1996c;] Neg. Ames [Henkel, 1981d]	1 2				
C16	67762-30-5	C14-18 Alcohols Type A	Expected to be non-mutagenic	2				
C16	67762-27-0	C16-18 Alcohols	Expected to be non-mutagenic	2				
C16	143-28-2	9-Octadecen-1-ol, (9Z)-	Expected to be non-mutagenic	2				
C16	68002-94-8	C16-18 and C18 Unsaturated	Neg. Ames [Banduhn, 1989]	1				
C16	68155-00-0	Alcohols, C14-18 and C16-18-unsatd	Expected to be non-mutagenic	2				
C18	112-92-5	1-Octadecanol Supporting Substance	Neg Ames; MN [Thomson, 1996d]	1				

Linear Alcohols					Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	Study Type* Result [Ref]	Rel.	CAS	CHEMICAL NAME	Study Type Result [Ref]	Rel.
			Neg; Ames [Henkel, 1981f] **Neg**. MN [Hachiya, 1982]	2 2				
C18	97552-91-5	C18-22 Alcohol	**Neg**. Ames [Banduhn, 1995]	1				
C20	629-96-9	1-Eicosanol	Expected to be non-mutagenic	2				
C22	661-19-8	1-Docosanol	**Neg** Ames, [Iglesias, 2002a, Thompson, 1997] **Neg** CA [Iglesias, 2002a] **Neg**. GM [Iglesias, 2002a] **Neg**. MN [Iglesias, 2002a]	2 2 2 2				
C24	123607-66-9	Alcohols, C24-34 Supporting Substance	**Neg**. MN, Dom. Leth [Rodiero, 1998a]	2, 2				

* Ames: Bacterial Gene Mutation assay; CA: Chromosomal Aberration Assay; GM: Gene Mutation assay in mammalian cell cultures: MN: Mouse bone marrow micronucleus test; Dom. Leth. Mouse Dominant Lethal test; UDS: Unscheduled DNA Synthesis assay

** Tested in *S. typhimurium* TA 98 and TA100, only.

3.1.7 Carcinogenicity

Studies in animals.

Data availability. There are no data available for the category of the long chained alcohols reporting in detail about carcinogenicity studies according to current testing standards. Several of the linear alcohols have been tested in experimental investigations studying the potential for initiation, promotion or co-carcinogenicity, however as a rule these data have a low reliability and suffer from significant shortcomings regarding the reporting details, the number of animals, the use of non-standardised or unvalidated protocols, and lack of control of confounders (e.g. local irritation). As a whole the information available on carcinogenicity is regarded to have limited reliability.

Hexanol-1, 1-octanol, 1-decanol, 1-dodecanol, 1-tetradecanol, 1-hexadecanol and 1-octadecanol were tested in one or more mouse skin painting studies using applications 2 - 3 times weekly for periods up to 60 -70 weeks. Development of local skin tumours was not reported in any of these assays. All of these experiments were conducted as part of investigative studies into co-carcinogenicity or tumour promotion properties of aliphatic alcohols (Sicé, 1966; Bingham, 1969; Van Duuren, 1976).

The aliphatic alcohols were applied repeatedly over periods up to 60 weeks to the skin of mice that had been initiated or were co-exposed with carcinogens such as 7, 12-dimethylbenz[a]-anthracene or benzo[a]pyrene (B[a]P). In most of the experimental protocols the application of aliphatic alcohols induced significant dermal irritation at the site of treatment and led to formation of local tumours; in some cases a decrease in latency of tumour development or co-carcinogenicity was reported (Sicé, 1966; Van Duuren *et al.*, 1976; Bingham, 1969).

In other assays 1-octanol, 1-dodecanol or 1-octadecanol were repeatedly injected into the peritoneal cavity or implanted in the bladder of mice. No induction of primary lung tumours was recorded, however a low incidence of benign bladder tumours was reported (Stoner, 1973; Bryan *et al*, 1966). Ando (1972) published a study in which small groups of mice (n = 4-6), implanted intra-peritoneally with Ehrlich ascites tumour cells, were exposed i.p. to different doses of 1-decanol, 1-dodecanol, 1-tetradecanol, 1-hexadecanol and 1-octadecanol once daily for 5 consecutive days. Although a prolongation of survival time was observed, no conclusions can be drawn regarding the carcinogenic potential of these alcohols.

Conclusion. Several members of the category of the long chained alcohols have been tested as control substances in skin painting studies. Even taking into account the limitations of these experiments, the data show that none of aliphatic alcohols tested have a potential to induce local skin tumours upon repeated dermal application at or above the maximum tolerated (irritant) dose. However, these data are unsuitable to assess properties such as co-carcinogenicity or tumour promotion for this category of alcohols. Most of the study protocols considered here have almost certainly induced considerable local effects, however details of the irritation responses are limited and were reported only in a few cases. Irrespective of the causative agent, irritation at the site of application is a significant confounder in skin painting studies and its role in the tumour development of non-genotoxic chemicals has been well established (for examples see Nessel *et al*., 1998, 1999; Argyris, 1985).

The genotoxic potential of the long chain alcohols has been well investigated, both *in vitro* and *in vivo* and no concerns were identified for genotoxicity. Furthermore they lack structural elements of concern for interaction with DNA (Ashby and Tenant, 1991). Together with the lack of response upon repeated application the skin painting studies long chained alcohols are regarded to be of little concern regarding carcinogenicty.

3.1.8 Toxicity for Reproduction

Effects on Fertility. Studies in Animals

Data availability. Table 3.9 presents a listing of the data available for the assessment of the fertility including potential effects on reproductive organs. OECD SIDS Guidelines state that developmental toxicology data coupled with repeat dose toxicity information showing no compound related effects on reproductive organs fulfills the requirement for a screening-level reproductive hazard assessment for the purposes of the program. All of these sources of information, as described below, justify the conclusion that this requirement has been met for this category.

Fertility studies

Dodecanol-1 and 1-octadecanol have been tested for potential reproductive toxicity in a combined repeat dose reproductive/developmental toxicity screening study in rats. The materials were administered to male and female rats via the diet at concentrations up to 30,000 ppm during pre-mating, mating and gestation. Pregnancy rates, uterine parameters, time to pregnancy and gestation length indicated that fertility was not affected by exposure to dodecanol or octadecanol. There were no microscopic changes observed in the reproductive organs (Hansen, 1992 a,b). Docosanol (C22) did not affect reproductive parameters when administered orally at levels up to 1000 mg/kg/day to male and female rats during pre-mating (10 weeks for males and 2 weeks for females), mating and gestation (Iglesias *et al*., 2002b).

Absence of toxicity to reproductive organs at significant doses

Linear alcohols.

As noted previously, testicular atrophy observed in dogs following a 13 week repeated dose exposure to 1000 mg/kg/day 1-hexanol administered via gelatin capsule was attributed to the general ill health, including severe gastrointestinal irritation, of the animals likely due to the manner in which the substance was administered. No effects on reproductive organs were observed in dogs that were exposed to the same test substance in the dietary portion of the study at both the 1% and 0.5% level of exposure (Sc. Assoc., 1966b). Similarly, rats receiving 1-hexanol in the diet at concentrations of 1% (with step-wise increases to 6%) showed no testicular weight changes or microscopic changes in the gonads (Sc. Assoc. 1966a). In a separate study the potential for testicular toxicity in rats was investigated for C6-12 alcohol (Type D) by oral administration of 1.0 mM/kg for 14 days (Rhodes *et al*., 1984). Administration of high doses (up to 1000 mg/kg/day) of 1-hexadecanol, 1-octadecanol, 1-docosonol or C24 -34 alcohols to rats and/or dogs for periods up to one year was without adverse effects on the reproductive organs (See Table 3.9). Overall, these data justify the conclusion that linear alcohols have no potential for adverse effects on the reproductive organs.

Essentially Linear Alcohols.

In a dedicated 2-week study it was shown that the essentially linear alcohols C6-12 (type C) (linearity> 60%) and C10-16 alcohols (Type D) and 1-tridecanol (linearity >60%) did not induce adverse testicular effects (Rhodes *et al*., 1984).

Repeated dose toxicity studies with iso-amyl alcohol and 2-ethylhexanol, 100% branched materials, were without effects on the reproductive organs in rats following administration for periods of 13 weeks or more (WHO, 1993; Carpanini, 1973).

Also, the 90-day dietary repeat dose study on C14-16 alcohol (Type A, 70% linearity) showed an absence of effects on reproductive organs (Ito, 1978). In this study relative testes and ovary weights were increased at the 1% and/or 5% incorporation level, but at these levels a considerable reduction in bodyweight gain due to inanition was induced. The effects on relative organ weights were considered to be associated with the effects on body weight rather than a direct toxic effect. More importantly, there was no evidence of microscopic changes in the gonads. The NOAEL of this study [*ca.* 200 mg/kg] corresponding to doses of approximately 140 mg/kg and 60 mg/kg for the linear and mono-branched alkyl components of the mixture, respectively (Ito, 1978).

A similar lack of effect on reproductive organs was observed, as noted previously, in the 28-day repeated dose study of C_{10-16} alcohol (Type B) at the highest dose tested, 1,000 mg/kg/day (Sasol, 1999).

Conclusion: Fertility assays did not reveal any adverse reproductive effects. Furthermore, examination of the reproductive organs in a number of repeated-dose studies did not show evidence indicative of adverse reproductive changes. Overall, there are no concerns that the category of Long Chain Aliphatic Alcohols might adversely affect fertility.

Table 3.9 Fertility

Linear Alcohols						Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	NOAEL** (mg/kg)	Study type* / Species / Effects [Reference]	Rel.	CAS	CHEMICAL NAME	Study type / Species / Effects [Reference]	Rel.
C5						123-51-3	Isoamyl alcohol Supporting Substance	RDT* Rat: None [Carpanini, 1973]	2
C6	111-27-3	1-Hexanol	370 1127	RTD*: Dog: none [Sc. Ass. 1966b] RTD: Rat: none [Sc. Ass. 1966a]	2 2				
C7	111-70-6	1-Heptanol		Supporting substance		68603-15-6	C6-12 Alcohols (Type C)	RTD: Rat None >80%lin [Rhodes 1984]	2
						85566-14-9	Alcohols, C7-11-branched and linear	Supporting Substance	2
C8	111-87-5	1-Octanol		Not expected to impair fertility	2	104-76-7	1-Hexanol, 2-ethyl- Supporting Substance	RDT: Rat: None [WHO, 1993]	2
	68603-15-6	C6-12 Alcohols Type D		RDT Rat: None [Rhodes 1984]	2				
C8	85566-12-7	C8-10 Alcohols		Not expected to impair fertility	2				
C8	68551-07-5	C8-18 Alcohols		Not expected to impair fertility	2				
C9	143-08-8	1-Nonanol		Supporting substance		66455-17-2	C9-11 Alcohols	Not expected to impair fertility	2
C9						68603-15-6	C6-12 Alcohols (type B)	Not expected to impair fertility	2
C10	112-30-1	1-Decanol		Not expected to impair fertility	2				

	Linear Alcohols					Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	NOAEL** (mg/kg)	Study type* / Species / Effects [Reference]	Rel.	CAS	CHEMICAL NAME	Study type / Species / Effects [Reference]	Rel.
C10	67762-41-8	C10-16 Alcohols		Not expected to impair fertility	2				
C10	85665-26-5	Alcohols, C10-12		Not expected to impair fertility	2				
C11						112-42-5	1-Undecanol	Not expected to impair fertility	2
C11						68603-15-6	C6-12 Alcohols Type A	Not expected to affect fertility	2
C12	112-53-8	1-Dodecanol Supporting Substance	2000**	Fert* Rat: None [Hansen,1992a]	2	67762-41-8	C10-16 Alcohols	Type B: RDT Rat: None 50% lin [TNO, 1999] Type C: Not expected to affect fertility Type D: RDT Rat: None [Rhodes, 1984]	1 2 2
C12	67762-25-8	C12-18 Alcohols Type A, B		Not expected to impair fertility	2	63393-82-8	C12-15 Alcohols Type A, B	Not expected to impair fertility	2
C12	68855-56-1	C12-16 Alcohols Type B, C		Not expected to impair fertility	2	68855-56-1	C12-16 Alcohols Type A	Not expected to impair fertility	2
C12	80206-82-2	C12-14 Alcohols Type A, B		Not expected to impair fertility	2	75782-86-4	C12-13 Alcohols	Not expected to impair fertility	2
C12						68333-80-2	C14-16 Alcohols Type B	Not expected to impair fertility	2
C13						112-70-9	1-Tridecanol	RDT Rat: None [Rhodes, 1984]	2
C13						90583-91-8	Tridecanol, branched and linear	Not expected to impair fertility	2
C14	112-72-1	1-Tetradecanol		Not expected to impair fertility	2	68333-80-2	C14-16 Alcohols Type A	RDT Rat: None 70% Lin [Ito, 1978]	2

Linear Alcohols						Essentially Linear Alcohols			
	CAS	CHEMICAL NAME	NOAEL** (mg/kg)	Study type* / Species / Effects [Reference]	Rel.	CAS	CHEMICAL NAME	Study type / Species / Effects [Reference]	Rel.
C14	67762-30-5	C14-18 Alcohols Type B		Not expected to impair fertility	2	75782-87-5	C14-15 Alcohols	Not expected to impair fertility	2
C15						629-76-5	1-Pentadecanol	Not expected to impair fertility	2
C16	36653-82-4	1-Hexadecanol	1054 2000 1000	RDT Dog: None [Sc. Ass. 1966b] RDT Rat: None [Sc. Ass. 1966a] RDT Rat: None [Henkel, 1985a]	2 2 2				
C16	67762-30-5	C14-18 Alcohols Type A		Not expected to impair fertility	2				
C16	67762-27-0	C16-18 Alcohols		Not expected to impair fertility	2				
C16	143-28-2	9-Octadecen-1-ol, (9Z)-		Not expected to impair fertility	2				
C16	68002-94-8	C16-18 and C18 Unsaturated		Not expected to impair fertility	2				
C16	68155-00-0	Alcohols, C14-18 and C16-18-unsatd		Not expected to impair fertility	2				
C18	112-92-5	1-Octadecanol Supporting Substance	**2000** 1000	Fert. Rat: None [Hansen, 1992b], RDT Rat None [Henkel, 1986a]	2 2				
C18	97552-91-5	C18-22 Alcohol		Not expected to affect fertility	2				
C20	629-96-9	1-Eicosanol		Not expected to impair fertility	2				
C22	661-19-8	1-Docosanol	**>1000** >2000	Repro* Rat: None [Iglesias, 2002b] RDT Dog None [Iglesias, 2002a]	2 2				
C24	123607-66-9	Alcohols, C24-34 Supporting Substance	>250 1000	RDT Dog: None [Aleman, 2001] RDT Rat: None [Rodiero, 1998b]	2 2				

*RTD Repeated dose toxicity study: Effects on reproductive organs; Fert.: Fertility screening study: Effects on reproduction; Repro. Reproduction study (1 or 2 generation): Effects on reproduction.

** Bold entries refer to NOAEL for fertility; non-bold entries refer to NOAEL for effects on reproductive organs

Developmental Toxicity

Data Availability. The available developmental toxicity studies for the category of the long chained alcohols are presented in Table 3.10. The data cover a representative group of the category of the linear alcohols, covering the low (C6, C8, C9), intermediate (C10, C12) and high (C18, C22 and C24-34) end of this category. For the essentially linear alcohols, the key data are derived from a study of the supporting substances iso-amyl alcohol and of C_{7-11} alcohol [CAS 85566-14-9] (65% linearity).

Linear Alcohols.
Inhalation of 1-octanol, 1-nonanol or 1-decanol at the maximum achievable vapour concentrations (0.4, 0.14 and 0.10 mg/L, respectively) from days 1-19 did not result in any treatment-related changes on maternal, uterine and foetal parameters. Although these exposure levels are below the concentrations inducing adverse effects, they represent a worst-case scenario for potential human exposure (Nelson, 1990).

Oral - studies in rats

Hexanol-1 was administered orally to rats during day 6-15 of gestation (Rodwell, 1988). At the 1000 mg/kg dose level a decreased maternal body weight gain and a minimal reduction in foetal body weights was recorded. The foetal weights at this treatment level were within the range of the historical data and this finding is not considered to represent an adverse developmental effect. There were no treatment-related changes in the incidence of visceral and skeletal variations and malformations.

Administration of 1-octanol at daily gavage doses of 0, 130, 650, 975 or 1300 mg/kg resulted in significant, dose-related maternal toxicity, including clinical signs (CNS depression, nasal discharge and pneumonia), and slight decreases in body weight gain and food consumption at 650, 975 or 1300 mg/kg/day. No adverse effects were recorded on foetal and developmental parameters (Hellwig and Jaeckh, 1997).

In a screening study for developmental toxicity, dietary administration of 1-dodecanol to pregnant rats throughout the gestation period at nominal concentrations up to 2000 mg/kg/day was without adverse maternal or developmental effects (Hansen, 1992a). Similarly, the longer chain linear alcohols did not show any maternal or developmental toxicity based on a reproductive/developmental toxicity screen with 1-octadecanol (C18), or a developmental toxicity studies with 1-docosanol and C24-C34 alcohols (Iglesias, 2002b; Rodriguez, 1998).

Oral - studies in rabbits

A developmental toxicity studies in rabbits with 1-docosanol and C24-C34 alcohols was without adverse maternal and developmental effects (Iglesias, 2002b, Rodriguez, 1998).

Overall, the category of the linear alcohols has shown a chain length dependant response with maternal toxicity in rats observed only at chain lengths of C6 and C8. No embryotoxicity or foetotoxicity was noted in any of the studies for the linear alcohols. The sub-category of the linear aliphatic alcohols does not have a potential for adverse development effects.

Inhalation - studies in rats

For 1-hexanol, inhalation of 3.5 mg/L (the maximum vapour concentration achievable; 7 hours/day) throughout the gestation period did not result in any adverse effects in maternal animals and foetuses. There was a slight increase of questionable significance in the number of resorptions (1.3/litter; a value at the upper range of the spontaneous incidence, the corresponding control incidence was 0.4/litter, an unexpectedly low value). In another developmental toxicity study using the oral route of exposure (Rodwell, 1988; see below) the number of resorptions was unaffected by treatment even at dose level up to 1000 mg/kg, supporting the conclusion that this finding represents a chance observation.

Essentially Linear Alcohols.

The available information for this sub category is limited to oral studies in rats, conducted with C7-11 alcohols and a surrogate substance, 2-ethylhexanol, and inhalation studies in rats and rabbits with isoamylalcohol.

Oral – studies in rats

The developmental toxicity for the class of the essentially linear alcohols was investigated in C_{7}-$_{11}$ alcohols (linearity *ca*. 65%) [CAS 85566-14-9] by daily oral gavage of rats during days 6-15 of pregnancy at dose levels up to 1440 mg/kg/day. No treatment related adverse effects were noted in maternal, uterine and foetal parameters (Hellwig and Jaeckh, 1997).

2-Ethylhexanol is used as surrogate for the sub-category of the essentially linear alcohols to assess the repeated dose toxicity of 100% branched alcohols (section 3.5.1). While moderate developmental toxicity induced by 2-ethylhexanol (2EH) has been linked with the formation of the corresponding carboxylic acid metabolite. 2-ethylhexanoic acid is considered the proximate developmental toxicant of 2EH, inducing significant maternal toxicity mortality, respiratory and CNS effects; its developmental effects consisting mainly of limb and vertebral malformations and variations.

Discussion of developmental toxicity of the essentially linear sub-category

The available information is limited to a negative oral study in rats with C7-11 material. Additional information is provided from oral study conducted with 2-ethylhexanol in rats which gave positive findings, and negative inhalation studies in rats and rabbits conducted with isoamylalcohol. Therefore there is a concern regarding the developmental toxicity of longer chain category members.

It is likely that the essentially linear alcohols will be metabolised to the corresponding carboxylic acid, as indicated in section 3.1.1. The Structure Activity Relationships for the developmental toxicity of aliphatic carboxylic acids have been well established: Aliphatic carboxylic acids with a single alkyl-branch at the C2 position with the side chain being C2 or higher have a potential for developmental toxicity. Carboxylic acids with a single methyl-branch at the C2 position or acids branched at a position other than C2, irrespective of the length of the side chain or the backbone, lack a potential for developmental toxicity. The foetoxicity appears to be associated in particular with carboxylic acids with a total carbon chain length in the range of C7-C9. (DiCarlo *et al*., 1986; Narotsky *et al.,* 1994; Scott *et al*., 1994; Bojic, *et al*., 1996; Ambroso *et al*., 1999). Therefore, it is likely that the positive findings with 2-ethylhexanol are not relevant for a discussion of the developmental toxicity of the essentially linear sub category, as the branched components of the essentially linear alcohols have a single side chain, predominantly consisting of a methyl group. Furthermore, the (Q)SAR for the carboxylic acids indicates that developmental toxicity is associated with chain lengths of C7-9, for which good quality negative data for the essentially linear sub category exist. For higher chain length category members the (Q)SAR suggests that there is no concern for developmental toxicity (DiCarlo *et al*., 1986; Narotsky *et al*., 1994; Scott *et al*., 1994; Bojic, *et al*., 1996; Ambroso *et al*., 1999)

Overall, it is anticipated that the essentially linear sub-category are not developmental toxicants.

The essentially linear alcohols under consideration in this category typically consist of linear alcohols and branched alcohols. Taking into account the well-established Quantitative Structure Activity Relationship ((Q)SAR) for the developmental toxicity, the sub-category of essentially linear alcohols do not meet the critical structural requirements necessary for a developmental toxicity potential: substitution at the 2-position with a side chain of C2 or higher. On this basis it is concluded that:

- 2-ethylhexanol is an inappropriate surrogate to directly assess the developmental toxicity for the sub-category of essentially linear aliphatic alcohols in this category.
- The well-established (Q)SAR, including the chain-length dependency, for the developmental toxicity of the branched aliphatic carboxylic acid can be extended to the corresponding branched alcohols, suggesting that alcohols with a chain lengths of C10 and above are of lesser concern for developmental toxicity

Inhalation - studies in rats

As discussed in the section on repeated dose toxicity (3.1.5), iso-amyl alcohol (IAA) has been selected as a surrogate for the branched alcohols at the low end of the category of the essentially linear alcohols. A developmental toxicity study for IAA in rats was without any evidence for and developmental effects upon exposure to atmospheres of 10 mg/l [highest dose tested] (6 hours daily) during days 6-15 of gestation. Maternal effects consisted of a slight depression of body weight gain (ca. 75% of the growth in controls) at the highest exposure group during the initial phases (days 6-9) of the exposure period. The maternal NOEC was 2.5 mg/kg (Klimisch *et al*., 1995).

Inhalation - Studies in rabbits

A developmental toxicity study for IAA in rabbits caused depression maternal body weight during days 6-15 of gestation in the group exposed to atmospheres of 10 mg/L without any evidence for developmental effects upon exposure to atmospheres of 10 mg/l [highest dose tested] (6 hours daily) during organogenesis. The maternal NOAEC was 2.5 mg/L based on the reduction in maternal animals; the developmental NOAEC was 10 mg/L (highest dose tested (Klimisch *et al*., 1995).

Conclusion. The available information confirms the absence of a potential for developmental toxicity for the category of the linear and essentially linear alcohols. Furthermore, the available data are considered to cover chain-lengths representative of the whole category and fulfilling the requirement for a screening-level hazard assessment for developmental toxicity potential for the category of the long chained alcohols.

Table 3.10 Developmental toxicity

Linear Alcohols						Essentially Linear Alcohols				
	CAS	CHEMICAL NAME	Study type / Species / Route / Effects	NOAEL [Ref]	Rel.*	CAS	CHEMICAL NAME	Study type / Species Route / Effects	NOAEL [Ref]	Rel.*
C5						123-51-3	Isoamyl alcohol Supporting Substance	Dev.Tox Rat Inhalation: None Dev. Tox Rabbit Inhalation: None	Mat. 2.5 mg/L Dev. 10 mg/L [Klimisch ‘95] Mat. 2.5 mg/L/ Dev. 10 mg/L [Klimisch ‘95]	2 2
C6	111-27-3	1-Hexanol	Dev. Tox Rat Inhalat'n: None Dev. Tox rat oral; None	Mat/Dev. 3.5 mg/L [Nelson, 1989] Dev 1000 mg/kg Mat 200 mg/kg [Rodwell, 1988]	2 4					
C7	111-70-6	1-Heptanol	Supporting substance			68603-15-6	C6-12 Alcohols (Type C)	Not expected to be a developmental toxicant in the absence of maternal toxicity		
						85566-14-9	Alcohols, C7-11-branched and linear Supporting Substance	Dev. Tox. Rat Oral	Mat/Dev >1440 mg/kg [Hellwig, 1997]	2
C8	111-87-5	1-Octanol	Dev Tox Rat Inhalat'n: None Dev. Tox Rat Ora: Nonel	Mat/Dev.> 0.4 mg/L [Nelson, 1990, 1996] Mat 130 mg/kg Dev 1300 mg/kg [Hellwig et al, 1997]	2 2	104-76-7	1-Hexanol, 2-ethyl-	Supporting substance		

Linear Alcohols						Essentially Linear Alcohols				
	CAS	CHEMICAL NAME	Study type / Species / Route / Effects	NOAEL [Ref]	Rel.*	CAS	CHEMICAL NAME	Study type / Species Route / Effects	NOAEL [Ref]	Rel.*
	68603-15-6	C6-12 Alcohols Type D	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C8	68551-07-5	C8-18 Alcohols	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C8	85566-12-7	C8-10 Alcohols	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C9	143-08-8	1-Nonanol Supporting Substance	Dev.Tox Rat Inhalat'n: None	Mat/Dev> 0.15 mg/l [Nelson, 1990, 1996]	2	66455-17-2	C9-11 Alcohols	Not expected to be a developmental toxicant in the absence of maternal toxicity		
C9			Not expected to be a developmental toxicant in the absence of maternal toxicity			68603-15-6	C6-12 Alcohols (type B)	Not expected to be a developmental toxicant in the absence of maternal toxicity		
C10	112-30-1	1-Decanol	Dev.Tox Rat Inhalat'n: None	Mat/Dev >0.1mg/L [Nelson, 1990a, 1996]	2					
C10	67762-41-8	C10-16 Alcohols Type A	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C10	85665-26-5	Alcohols, C10-12	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C11						112-42-5	1-Undecanol	Not expected to be a developmental toxicant in the absence of maternal toxicity		

	Linear Alcohols					Essentially Linear Alcohols				
	CAS	CHEMICAL NAME	Study type / Species / Route / Effects	NOAEL [Ref]	Rel.*	CAS	CHEMICAL NAME	Study type / Species Route / Effects	NOAEL [Ref]	Rel.*
C11						68603-15-6	C6-12 Alcohols	Not expected to be a developmental toxicant in the absence of maternal toxicity		
C12	112-53-8	1-Dodecanol Supporting Substance	Screen Rat Diet: None	Dev/Mat >2000 mg/kg [Hansen, 1992a]	2	67762-41-8	C10-16 Alcohols Type B, C, D	Not expected to be a developmental toxicant in the absence of maternal toxicity		
C12	67762-25-8	C12-18 Alcohols Type A, B	Not expected to be a developmental toxicant in the absence of maternal toxicity			63393-82-8	C12-15 Alcohols Type A, B	Not expected to be a developmental toxicant in the absence of maternal toxicity		
C12	68855-56-1	C12-16 Alcohols Type B, C	Not expected to be a developmental toxicant in the absence of maternal toxicity			68855-56-1	C12-16 Alcohols Type A	Not expected to be a developmental toxicant in the absence of maternal toxicity		
C12	80206-82-2	C12-14 Alcohols Type A, B	Not expected to be a developmental toxicant in the absence of maternal toxicity			75782-86-4	C12-13 Alcohols	Not expected to be a developmental toxicant in the absence of maternal toxicity		
C12						68333-80-2	C14-16 Alcohols	Not expected to be a developmental toxicant in the absence of maternal toxicity		
C13						112-70-9	1-Tridecanol	Not expected to be a developmental toxicant in the absence of maternal toxicity		
C13						90583-91-8	Tridecanol, branched and linear	Not expected to be a developmental toxicant in the absence of maternal toxicity		
C14	112-72-1	1-Tetradecanol	Not expected to be a developmental toxicant in the absence of maternal toxicity			68333-80-2	C14-16 Alcohols Type A	Not expected to be a developmental toxicant in the absence of maternal toxicity		

Linear Alcohols						Essentially Linear Alcohols				
	CAS	CHEMICAL NAME	Study type / Species / Route / Effects	NOAEL [Ref]	Rel.*	CAS	CHEMICAL NAME	Study type / Species Route / Effects	NOAEL [Ref]	Rel.*
C14	67762-30-5	C14-18 Alcohols Type B	Not expected to be a developmental toxicant in the absence of maternal toxicity			75782-87-5	C14-15 Alcohols	Not expected to be a developmental toxicant in the absence of maternal toxicity		
C15						629-76-5	1-Pentadecanol	Not expected to be a developmental toxicant in the absence of maternal toxicity		
C16	36653-82-4	1-Hexadecanol	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C16	67762-30-5	C14-18 Alcohols Type A	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C16	67762-27-0	C16-18 Alcohols	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C16	143-28-2	9-Octadecen-1-ol, (9Z)-	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C16	68002-94-8	C16-18 and C18 Unsaturated	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C16	68155-00-0	Alcohols, C14-18 and C16-18-unsatd	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C18	112-92-5	1-Octadecanol Supporting Substance	Screen Rat Diet: None	Dev/Mat >2000 mg/kg [Hansen, 1992b]	2					

Linear Alcohols						Essentially Linear Alcohols				
	CAS	CHEMICAL NAME	Study type / Species / Route / Effects	NOAEL [Ref]	Rel.*	CAS	CHEMICAL NAME	Study type / Species Route / Effects	NOAEL [Ref]	Rel.*
C18	97552-91-5	C18-22 Alcohol	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C20	629-96-9	1-Eicosanol	Not expected to be a developmental toxicant in the absence of maternal toxicity							
C22	661-19-8	1-Docosanol	Dev.Tox Rat gavage: None Dev. Tox Rabbit Gavage; None	Mat/Dev >1000 [Iglesias, 2002b] Mat/Dev >2000 mg/kg [Iglesias, 2002b]	2 2					
C24	123607-66-9	Alcohols, C24-34; Supporting Substance	Dev. Tox Rat Gavage: None Dev. Tox. Rabbit Gavage: None	Mat/Dev >1000 [Rodriguez 1998 Mat/Dev >1000 mg/kg [Rodriguez 1998]	2 2					

*

3.2 Initial Assessment for human health

A review of the toxicological database for the category of the linear alcohols demonstrates that members of the category of the long chained alcohols are of a low order of toxicity upon single or repeated exposure. Overall, the data show an inverse relationship between chain length and toxicity. The shorter chain linear alcohols tend to induce more pronounced effects when compared to materials with a longer chain length. This is illustrated most clearly by the degree of [local] irritation in studies involving single (acute) or repeat administration. Linear alcohols have no skin sensitisation potential, are not mutagenic and have not shown any adverse effects on fertility, development and reproduction. There is a clear relationship between the chain length and the toxicological properties justifying read-across of potential toxicological properties between members of this category.

For the essentially linear alcohols the toxicological database demonstrates that this class is also of a low order of toxicity following acute and repeated exposures. The overall profile of the toxicity is qualitatively and quantitatively similar to that of the class of the linear alcohols for all of the end points assessed in this comparison. The relationship between chain length and toxicological properties is also present for the class of the essentially linear alcohols and is very similar to that of the linear alcohols.

The key human health hazards for this category are skin and eye irritation. For the aliphatic alcohols in the range C6 – C11 a potential for skin and eye irritation exists, without concerns for tissue destruction or irreversible changes. Aliphatic alcohols in the range C12 – C16 have a low degree of skin irritation potential; alcohols with chain lengths of C18 and above are non-irritant to skin. The eye irritation potential for alcohols with a chain length of C12 and above has been shown to be minimal.

The end points acute toxicity and irritation have been investigated using substances with a linearity of 5 to 100%. Skin sensitisation studies are available for materials with 50-100% linearity showing no sensitising potential. For the assessment of the repeated dose toxicity, reproduction and development test materials with a degree linearity of minimally 50 % were used in key studies. A lack of mutagenic potential was determined for this category, including highly branched substances. Surrogate substances for the sub-category of the essentially linear alcohols include 100% branched aliphatic alcohols thereby extending the toxicological profile of this category and justifying the read-across within the category of the long-chain aliphatic alcohols.

4 HAZARDS TO THE ENVIRONMENT

The long chain alcohols covered by this submission fit into the neutral organics class and would be expected to exert their toxicity predominantly through a narcosis mode of action. The effects data are reviewed, and the understanding of the properties of multi-component substances is set out.

4.1 Aquatic effects

The approach used in this section is to present the best available measured data, and then describe how gaps for end points with no measured value can be filled by estimation. This can be done for both essentially pure substances and for complex reaction products, provided the composition is described sufficiently.

Annex VIII shows that the acute toxicity of essentially pure alcohols to fish and invertebrates may be described by conventional quantitative-structure-activity-relationships ((Q)SARs). The (Q)SARs developed for alcohols may be used either on their own, to predict the toxicity of single carbon number alcohols, or in conjunction with partitioning models to predict the toxicity of multi-component substances. A partitioning model described in Annex IX, which is very similar to others already in the literature, has been developed which allows the composition of a water accommodated fraction to be predicted on the basis of the substance composition and the loading rate. It has been validated against those studies where the composition of test medium has been measured, either for individual homologues or total dissolved material.

4.1.1 Acute toxicity test results

Many acute toxicity tests have been carried out on this family of alcohols, addressing toxicity to all three trophic levels, fish, invertebrates and algae. For studies in which the test substance had a single carbon chain length, a key study has been identified for each taxonomic level. Where there were two or more studies of the same quality but on different species within the same taxonomic group, the lower toxicity value (more severe effect) was chosen. For studies in which the test substance was a multi-component substance (commercial products) and where there was more than one type of the substance a key study was identified for each type.

The results of tests performed on single carbon chain length alcohols are generally reported in terms of the nominal or measured dissolved concentration of the alcohol in the test medium and identified as EC_{50} or LC_{50} values. However there are also instances where the reported effect concentration exceeded the solubility of the alcohol. These instances are distinguished in the results tables either by the result being reported as an LL_{50} or EL_{50}, implying that the test medium was a Water Accommodated Fraction (WAF), or by a note indicating that the test substance loading exceeded the solubility of the alcohol. In the latter case it has had to be assumed (because it is not apparent from the test report) that undissolved alcohol may have been present in the test medium and that there was the potential for physical (rather than toxicity) effects to occur.

For studies using multi-component substances it is not possible to interpret the results on the basis of measured dissolved concentrations of the alcohol components and directly relate these to the concentration of the multi-component substance itself. This is because the test medium does not contain dissolved concentrations of the components in the same ratio as present in the substance itself. The toxicity data for mixed carbon chain length alcohols are therefore also expressed using different conventions. Where the effect concentrations occurred at concentrations below the solubility of a multi-component substance they are reported as nominal or measured concentrations and are again identified as EC_{50} or LC_{50} values. In cases where the test media were WAFs, or where the loading of a multi-component substance exceeded the solubility of one or more of its components, the result is reported either as an LL_{50} or EL_{50}, denoting that the test medium was a Water Accommodated Fraction (WAF), or by a note indicating that the test substance loading exceeded the solubility of the multi-component substance. Once again in the latter case it has had to be assumed (because it is not apparent from the test report) that undissolved alcohol may have been present in the test medium and that there was the potential for physical (rather than toxicity) effects to occur.

In Section 2.2.5 it was highlighted that biodegradation is likely to be a significant loss mechanism for the alcohols under review. If loss of test substance from aquatic test media is significant it will undermine the results of tests where analysis of exposure was not performed. For example, exposure concentrations of 1-octanol (CAS No. 111-87-5) in a 7-day test with the Fathead minnow (*Pimephales promelas*) declined by $\geq$90% in the unspecified period between media renewals (Pickering *et al*., 1996). However the NOEC has been expressed relative to nominal concentrations and must represent a significant overestimate of the true value and therefore an underestimate of the true toxicity. Similarly, the exposure concentration of the same substance that corresponded to the NOEC determined in a 21-day semi-static chronic test with *Daphnia magna*, declined by >35% over the 3-4 day period between media renewals (Kuhn *et al*., 1989). This suggests that exposure concentrations expressed as nominal values would have significantly overestimated the actual concentrations. The above examples highlight that test results expressed only in terms of nominal concentrations must be treated with considerable caution and at may underestimate the toxicity of the substance.

Trends in results, described in this section, are supported by reliable measured data for branched alcohols which are members of the Oxo Alcohols Category. For full details please refer to the Oxo alcohols draft SIAR and SIDS dossiers.

4.1.1.1 Acute toxicity to fish

The best quality test data on single carbon chain lengths are shown in Table 4.1. The results show the toxicity of the single carbon number chain length alcohols increases from an LC_{50} of 97 mg/L for C6 to 1.0 mg/L for C12. At higher carbon numbers there is an absence of acute toxicity (LC_{50} values are reported as being greater than the highest test concentration) and this is explained by the water solubility of an alcohol limiting its bioavailability, such that an acutely toxic concentration is not achieved.

The results of a 7-day, semi-static toxicity test with 1-octanol using *Pimephales promelas* larvae aged 1, 4 and 7 days at the start of the study have been reported by (Pickering *et al*., 1996) but are not included in the table. NOECs based on nominal concentrations were 1.5-11.9 mg/L for survival. Measured concentrations in the test were reduced to non-detectable in most test vessels in the old media. The poor maintenance of exposure concentrations means that the reported NOEC values almost certainly underestimate the true toxicity of the substance. The results of this test are also discussed later with respect to chronic toxicity.

The data for multi-component substances of different carbon chain length alcohols (commercial products) are shown in Table 4.2. The results show the multi-component substances containing alcohols with carbon numbers in the ranges of C8-10 and C6-12 to be acutely toxic at concentrations of between 0.7 and 10 mg/L. At these concentrations all the components are likely to have been fully dissolved. In contrast, C10-16 and C12-16 multi-component substances exhibited effects at loading rates where not all components were fully dissolved. Under such circumstances the presence of retained undissolved test material, such as occurred in the Shell Toxicology

Laboratory (1978a) test, opens up the possibility for physical fouling of the test organism and this needs to be kept in mind when interpreting the result. The C12-14, 14-16 and 16-18 multi-component substances did not exhibit acute effects at loading rates where the solubility of the component alcohols was exceeded.

The results for both the single carbon number alcohols and the multi-component substances indicate that, for fish, there is an acute toxicity cut-off for alcohols with carbon numbers ≥C14.

Table 4.1 Key fish acute toxicity studies on single carbon chain length linear alcohols

CAS	Chemical Name	Comments	Water solubility (mg/L)	Species	Method/ Guideline	Exposure regime	Endpoint	Value (mg/L)[1,2]	Reliability	Reference
111-27-3	1-Hexanol		5900 at 20°C	*Pimephales promelas*	US EPA 1975	Flow-through	96 h LC$_{50}$	97 (m)	2	Veith, Call and Brooke, 1983a,b
111-70-6	1-Heptanol	Supporting	1300 at 20°C	*P. promelas*	ASTM 1980	Flow-through	96 h LC$_{50}$	38 (m)	2	Broderius and Kahl, 1985
111-87-5	1-Octanol		550 at 25°C	*P. promelas*	ASTM 1980	Flow-through	96 h LC$_{50}$	13 (m)	2	Veith, Call and Brooke, 1983a,b; Brooke *et al*., 1984; Broderius and Kahl, 1985
143-08-8	1-Nonanol	Supporting	130 at 20 °C	*P. promelas*	ASTM 1980	Flow-through	96 h LC$_{50}$	5.5 (m)	2	Broderius and Kahl, 1985
112-30-1	1-Decanol		40	*P. promelas*	US EPA 1975	Flow-through	96 h LC$_{50}$	2.3 (m)	2	Veith, Call and Brooke, 1983a,b; Brooke *et al*., 1984
112-42-5	1-Undecanol		8.0 at 20°C	*P. promelas*	US EPA 1975	Flow-through	96 h LC$_{50}$	1.0 (m)	2	Veith, Call and Brooke, 1983a,b
112-53-8	1-Dodecanol	Supporting	1.9 at 20°C	*P. promelas*	US EPA 1975	Flow-through	96 h LC$_{50}$	1.0 (m)	2	Veith, Call and Brooke, 1983a,b
112-70-9	1-Tridecanol		0.38 at 20°C	*P. promelas*	US EPA 1975	Flow-through	96 h LC$_{50}$	>0.33 (m)	2	Veith, Call and Brooke, 1983a,b
112-72-1	1-Tetradecanol		0.19 at 25°C	*Salmo gairdneri*[3]	OECD 203	Semi-static	96 h LC$_{50}$	> 1 (n) (>LoS)	2	Wetton, 1996b
36653-82-4	1-Hexadecanol		0.013 at 25°C	*S. gairdneri*[3]	OECD 203	Semi-static	96 h LC$_{50}$	>0.4 (n) (>LoS)	2	Wetton, 1996c
112-92-5	1-Octadecanol	Supporting	0.0011 at 25°C	*S. gairdneri*[3]	OECD 203	Semi-static	96 h LC$_{50}$	>0.4 (n) (>LoS)	2	Wetton, 1996d
661-19-8	1-Docosanol		0.001	*Oncorhynchus mykiss*	OECD 203	Semi-static	96 h LL$_{50}$	>1000 (n) (>LoS)	2	Wetton, 2000

Notes:

1 >LoS: concentration/Loading rate greater than the limit of water solubility

2 (n) based on nominal concentrations, (m) based on measured concentrations.

3 Now known as *Oncorhyncus mykiss*. The names used in the study reports are given here.

Table 4.2 Fish acute toxicity studies on mixed carbon chain length alcohols

CAS	Chemical name	Comments[1]	Water solubility (mg/L)	Species	Method/ Guideline[2]	Exposure regime	Endpoint	Value (mg/L)[3]	Reliability code	Reference
85566-12-7	Alcohols, C8-10		202 predicted at 1000 mg/L loading rate	*S. gairdneri*[4] and *L. macrochirus*	EPA 1975	Static	96 h LC_{50}	6.5-10 (n)	2	EG&G Bionomics, 1975
68603-15-6	Alcohols, C 6-12	Type B	510 at 20°C at 1000 mg/L loading rate	*S. gairdneri*[4]	Not specified	Static	96 h LC_{50}	6.3-10 (n)	2	Shell Toxicology Laboratory, 1979
68603-15-6	Alcohols, C 6-12	Type B	510 at 20°C at 1000 mg/L loading rate	*Scopthalmus maximus* (marine species)	Not specified	Semi-static	96 h LC_{50}	5.8 (n)	2	Huntingdon Life Sciences Ltd., 1991d
68603-15-6	Alcohols, C 6-12	Type C	510 at 20°C at 1000 mg/L loading rate	*I. idus*[4]	Not specified	Static	96 h LC50	0.7-0.8 (n)	2	Reiff, 1978
67762-41-8	Alcohols, C 10-16	Type B	2.4 at 25°C	*Brachydanio rerio*	OECD 203 WAF	Semi-static	96 h LL_{50}	15 (n) (>LoS)	1	Sasol, Sastech Research and Development, 2000a
67762-41-8	Alcohols, C 10-16	Type C	2.4 at 25°C	*S. gairdneri*[4]	Not specified	Static	96 h LC_{50}	4.0-10 (>LoS)	2	Shell Toxicology Laboratory, 1978a
67762-41-8	Alcohols, C 10-16	Type C	2.4 at 25°C	*Scopthalmus maximus* (marine species)	Not specified	Semi-static	96 h LC_{50}	10 (n) (>LoS)	2	Huntingdon Life Sciences Ltd., 1991c
68855-56-1	Alcohols, C 12-16	Type A	0.80 at 20°C	*Oncorhynchus mykiss*	OECD 203 WAF	Semi-Static	96 h LL50	100-300 (n) (>LoS)	1	Eadsforth, Palmer and Cann, 2000
68855-56-1	Alcohols, C 12-16	Type B	0.80 at 20°C	*O mykiss*	Not specified	Static	96 h LC_{50}	57 (n) (>LoS)	2	Huntingdon Life Sciences 1996i
80206-82-2	Alcohols, C 12-14	not possible to determine compositional type	ca. 4 predicted at 1000 mg/L loading rate	*L. idus*	OECD 203	Static	48 h LC_{50}	>5000 (n) (>LoS)	2	Henkel, 1999m
68333-80-2	Alcohols, C 14-16	Type A	0.70 at 20°C	*S. gairdneri*[4]	Not specified	Static	96 h LC_{50}	>500 (n) (>LoS)	2	Shell Toxicology Lab 1978b

CAS	Chemical name	Comments[1]	Water solubility (mg/L)	Species	Method/ Guideline[2]	Exposure regime	Endpoint	Value (mg/L)[3]	Reliability code	Reference
68002-94-8	Alcohols, C 16-18 and 18 Unsaturated	-	0.0404 predicted at 1000 mg/L loading rate	*L. idus*	OECD 203	Static	48 h LC_{50}	>10000 (>LoS)	2	Henkel, 1999o

Notes:

1 Compositional Types are described in section 1.1.3.
2 WAF denotes test medium was a water-accommodated fraction
3 >LoS: LC_{50} observed was greater than the limit of solubility of at least some components of the substance. (n) based on nominal concentrations, (m) based on measured concentrations.
4 Now known as *Oncorhyncus mykiss*. The names used in the study reports are given here.

The results of applying (Q)SARs and (for the multi-component substances) partition modelling to predict the acute toxicity of single carbon number alcohols and the commercial products (i.e. the multi-component substances) to fish are given in Table 4.3. The results show that the multi-component substances containing alcohols with carbon numbers equal to or less than C14 are generally predicted to be toxic at concentrations in the range 0.48 to 3.8 mg/L, the exact value depending upon their detailed and relative compositions. There are also instances in which multi-component substances containing alcohols with carbon numbers <C14 are predicted to be non-toxic but this only occurs when the multi-component substance also contains alcohols with carbon numbers >C14. Multi-component substances comprising of alcohols with carbon numbers that are all above C14 are predicted to be non-toxic at loading rates that exceed the solubility values of all the component alcohols.

Table 4.3 Estimated acute toxicity to fish for commercial products (using partition model[1])

CAS	Chemical Name	Comment[2]	Predicted 96 h LC/LL$_{50}$ by Partition model (mg/L)[3]
68603-15-6	C6-12 Alcohols	TYPE D	3.8
68551-07-5	C8-18 Alcohols		3.6
66455-17-2	C9-11 Alcohols		2.1
67762-41-8	C10-16 Alcohols	TYPE A	0.52
85665-26-5	C10-12 Alcohols		2.1
68603-15-6	C6-12 Alcohols	TYPE A	1.7
67762-41-8	C10-16 Alcohols	TYPE D	2.6
67762-25-8	C12-18 Alcohols	TYPE A	1.2
67762-25-8	C12-18 Alcohols	TYPE B	Predicted to be non-toxic at the limit of solubility
63393-82-8	C12-15 Alcohols	TYPE A	2.4
63393-82-8	C12-15 Alcohols	TYPE B	2.6
68855-56-1	C12-16 Alcohols	TYPE C	Predicted to be non-toxic at limit of solubility
80206-82-2	C12-14 Alcohols	TYPE A	0.48
80206-82-2	C12-14 Alcohols	TYPE B	0.77
75782-86-4	C12-13 Alcohols		0.58
68333-80-2	C14-16 Alcohols	TYPE B	2.6l
90583-91-8	Tridecanol, branched and linear		Predicted to be non-toxic at the limit of solubility
75782-87-5	C14-15 Alcohols		Predicted to be non-toxic at the limit of solubility
67762-30-5	C14-18 Alcohols	TYPE B	Predicted to be non-toxic at the limit of solubility
629-76-5	1-Pentadecanol		Predicted to be non-toxic at the limit of solubility
67762-30-5	C14-18 Alcohols	TYPE A	Predicted to be non-toxic at the limit of solubility
67762-27-0	C16-18 Alcohols		Predicted to be non-toxic at the limit of solubility
143-28-2	9-Octadecen-1-ol, (9Z)-		Predicted to be non-toxic at the limit of solubility
68155-00-0	Alcohols, C14-18 and C16-18-unsatd.		Predicted to be non-toxic at the limit of solubility
97552-91-5	C18-22 Alcohol		Predicted to be non-toxic at the limit of solubility

CAS	Chemical Name	Comment[2]	Predicted 96 h LC/LL_{50} by Partition model (mg/L)[3]
629-96-9	1-Eicosanol		Predicted to be non-toxic at the limit of solubility

[1]The partition model is described in Annex IX.
[2]Compositional Types are described in section 1.1.3.
[3]A Klimisch reliability score of 2 (valid with restrictions) is assigned to the estimated toxicity values, on the basis that the method used was well validated.

4.1.1.2 Acute toxicity to aquatic invertebrates

The best quality invertebrate acute toxicity data for single carbon chain length linear alcohols are shown in Table 4.4. The results show the toxicity of the alcohols to increase from an EC_{50} of 200 mg/L for C6 to 0.77 mg/L for C12. Effects have also been observed in tests with C13 and C14 alcohols but at concentrations that exceeded the solubility of the alcohols. Although not explicitly identified in the test reports, physical effects (rather than true toxicity) cannot therefore be excluded from the interpretation of the results for these two alcohols.

The data for multi-component substances of carbon chain lengths (commercial products) are shown in Table 4.5. The results show the multi-component substances containing alcohols with carbon numbers in the ranges of C6-12 and C8-10 to be acutely toxic at concentrations of between 4.6 and 30 mg/L. At these concentrations it is likely that all components will have been fully dissolved. For the C12-14 and C12-18 multi-component substances there was evidence of toxic effects in tests conducted on test media prepared as water-accommodated fractions at loading rates that exceeded the solubility of some components. For the C16-18 alcohol multi-component substance there was evidence of effects in test media that could have contained undissolved test material. The possibility of physical effects (rather than true toxicity) contributing to the observed effects were not discussed in the test report but cannot be excluded.

The measured data do not permit a toxicity cut-off to be identified for the single carbon number alcohols or the multi-component substances. This is because the potential for physical effects to contribute to the results obtained for the C13 and 14 single carbon number alcohols, and the multi-component substances containing components with carbon numbers that are all >C12, cannot be excluded.

Table 4.4 Key studies for invertebrate acute toxicity studies on single carbon chain length linear alcohols

CAS #	Chemical name	Comment	Water solubility (mg/L)	Species	Method/ Guideline	Exposure regime	Endpoint	Value (mg/L)[1]	Reliability code	Reference
111-27-3	1-Hexanol		5900 at 20°C	*Daphnia magna*	Not specified	Static	24 h EC_{50}	200 (n)	2	Bringmann and Kuhn, 1982
111-70-6	1-Heptanol	Supporting	1300 at 20°C	*D. magna*	Not specified	Static	24 h EC_{50}	82 (n)	2	Bringmann and Kuhn, 1982
111-87-5	1-Octanol		550 at 25°C	*D. magna*	Not specified	Static	24 h EC_{50}	20 (n)	2	Bringmann and Kuhn, 1982
112-30-1	1-Decanol		40	*D. magna*	OECD 202	Static	48 h EC_{50}	2.9 (n)	2	Henkel, 1999b
68516-18-7	Decene, hydroformylation products	Supporting. hydroformylation product (=C11)	No data	*D. magna*	EPA 1975	Static	48 h LC_{50}	4.2 (n)	2	Burgess and Forbis, 1983b
112-42-5	1-Undecanol		8.0 at 20°C	*Nitocra spinipes*	Not specified	Static	96 h LC_{50}	0.8-1.1 (n)	2	Bengtsson, Renberg, and Tarkpea, 1984
112-53-8	1-Dodecanol	Supporting	1.9 at 20°C	*D. magna*	OECD 202	Static	48 h EC_{50}	0.77(n)	2	Laboratory of Pharmacology and Toxicology, 1997
112-70-9	1-Tridecanol		0.38 at 20°C	*D. magna*	Not specified	Not specified	EC_{50} (duration unknown)	0.51 (>LoS)	4	Unilever, 1995
112-72-1	1-Tetradecanol		0.19 at 25°C	*D. magna*	Not specified	Not specified	EC_{50} (duration unknown)	4.0 (>LoS)	4	Unilever, 1995

[1] >LoS: LC_{50} observed was greater than the limit of solubility (n) based on nominal concentrations, (m) based on measured concentrations.

Table 4.5 Invertebrate acute toxicity studies on mixed carbon chain length alcohols alcohols (species are freshwater unless noted otherwise)

CAS	Chemical name	Comment	Water solubility (mg/L)	Species	Method/ Guideline[2]	Exposure regime	Endpoint	Value (mg/L)[3]	Reliability code	Reference
68603-15-6	Alcohols, C6-12	Type C	510 at 20°C at 1000 mg/L loading rate	*D. magna*	OECD 202	Semi-static	48 h EC_{50}	5.9	1	Wenzel (2005)
Mixture of 68527-05-9 & 70955-11-2-SUPPORTING	Mixture of hexane and octene hydroformylation products	i.e. alcohols, C7-9	No data	*Daphnia magna*	EPA 1975	Static	48 h LC_{50}	30 (n)	2	Burgess and Forbis, 1983c
68603-15-6	Alcohols, C 6-12	Type B	44 at 20°C	*D. magna*	Not specified	Static	48 h EC_{50}	7 (n)	2	Garforth, 1983
68603-15-6	Alcohols, C 6-12	Type B	44 at 20°C (in freshwater)	*Crangon crangon* (marine)	UK MAFF	Semi-static	96 h LC_{50}	4.6 (n)	2	Huntingdon Life Sciences Ltd. 1991a.
Mixture of 68516-18-7, 68527-05-9 & 70955-11-2-SUPPORTING	Mixture of octane and decene hydroformylation products	i.e. alcohols, C9-11	No data	*D. magna*	EPA 1975	Static	48 h LC_{50}	11 (n)	2	Burgess and Forbis, 1983d
67762-41-8	Alcohols, C C10-16	Type B and C	Ca. 2.4 at 25°C	*D. magna*	OECD 202 WAF	Static	48 h EL_{50}	0.23-0.28 (m)	1	Palmer and Cann, 2000a
67762-41-8	Alcohols, C 10-16	Type B	2.9 at 25°C	*D. magna*	OECD 202 WAF	Static	48 h EL_{50}	2.8 (n)	1	Sasol, Sastech Research and Development, 2000b
67762-41-8	Alcohols, C 10-16	Type C	2.4 at 25°C (in freshwater)	*Crangon crangon* (marine)	UK MAFF	Semi-static	96 h LC_{50}	>10 (n) (>LoS)	2	Huntingdon Life Sciences Ltd. 1991b.
67762-25-8	Alcohols, C 12-18	Type A	1.7 predicted at 100 mg/L loading rate	*D. magna*	EU 92/69/EWG	Static	48 h EL_{50}	40 (n) (>LoS)	1	Kirch, 1998a
68855-56-1	Alcohols, C 12-16	Type A	0.80 at 20°C	*D. magna*	OECD 202 WAF	Static	48 h EL_{50}	<1.0	1	Palmer and Sherren, 2001a
80206-82-2	Alcohols, C	Type A	4.6 predicted at	*D. magna*	EU	Static	48 h EL_{50}	63 (n)	1	Kirch, 1998b

CAS	Chemical name	Comment	Water solubility (mg/L)	Species	Method/ Guideline[2]	Exposure regime	Endpoint	Value (mg/L)[3]	Reliability code	Reference
	12-14		1000 mg/L loading rate		92/69/EWG WAF			(>LoS)		
68002-94-8	Alcohols, C 16-18 and 18 Unsaturated		0.044 predicted at 1000 mg/L loading rate	*D. magna*	EU Guideline 92/69/EWG	Static	48 h EC_{50}	70 (n) (>LoS)	2	Henkel KGaA. 1995.

[1] Compositional Types are described in section 1.1.3.

[2] WAF denotes test medium was a water-accommodated fraction

[3] >LoS: EC_{50} observed was greater than the limit of solubility of at least some components of the substance. (n) based on nominal concentrations, (m) based on measured concentrations.

The results of applying (Q)SARs and (for the multi-component substances) partition modelling to predict the acute toxicity of single carbon number alcohols and the commercial products (i.e. the multi-component substances) to invertebrates are given in Table 4.6. The results show that the multi-component substances containing alcohols with carbon numbers equal to or less than C14 are generally predicted to be toxic at concentrations in the range 4.3 to 0.21 mg/L, the exact value depending upon their detailed and relative compositions. There are also instances in which multi-component substances containing alcohols with carbon numbers in the range C14-16 are also predicted to be toxic. Multi-component substances comprising of alcohols with carbon numbers that are all above C14 are predicted to be non-toxic at loading rates that exceed the solubility values of all the component alcohols.

The predicted data therefore suggest a toxicity cut-off for multi-component substances containing components with carbon numbers >C14.

Table 4.6 Estimated acute toxicity to invertebrates (*Daphnia*) for commercial products (using partition model[1])

CAS	Chemical Name	Comments[2]	Predicted 48 h EC/LL$_{50}$ by partition model[1] (mg/L)[3]
68603-15-6	C6-12 Alcohols	Type D	4.3
85566-12-7	C8-10 Alcohols		3.0
68551-07-5	Alcohols, C8-18		1.3
66455-17-2	C9-11 Alcohols		2.3
67762-41-8	C10-16 Alcohols	Type A	0.31
85665-26-5	Alcohols, C10-12		1.1
68603-15-6	C6-12 Alcohols	Type A	1.7
67762-41-8	C10-16 Alcohols	Type D	0.21
67762-25-8	C12-18 Alcohols	Type B	17
63393-82-8	C12-15 Alcohols	Type A	0.21
63393-82-8	C12-15 Alcohols	Type B	0.21
68855-56-1	C12-16 Alcohols	Type B	0.25
68855-56-1	C12-16 Alcohols	Type C	2.2
80206-82-2	C12-14 Alcohols	Type B	0.23
75782-86-4	C12-13 Alcohols		0.49
68333-80-2	C14-16 Alcohols	Type B	0.21
90583-91-8	Tridecanol, branched and linear		Predicted to be non-toxic at limit of solubililty
68333-80-2	C14-16 Alcohols	Type A	0.13
75782-87-5	C14-15 Alcohols		0.29
67762-30-5	C14-18 Alcohols	Type B	Predicted to be non-toxic at the limit of solubility
629-76-5	1-Pentadecanol		Predicted to be non-toxic at the limit of solubility
36653-82-4	1-Hexadecanol		Predicted to be non-toxic at the limit of solubility
67762-30-5	C14-18 Alcohols	Type A	Predicted to be non-toxic at the limit of solubility
67762-27-0 (Also mixture of 36653-82-4 and	C16-18 Alcohols		Predicted to be non-toxic at the limit of solubility

CAS	Chemical Name	Comments[2]	Predicted 48 h EC/LL_{50} by partition model[1] (mg/L)[3]
112-92-5)			
143-28-2	9-Octadecen-1-ol, (9Z)-		Predicted to be non-toxic at the limit of solubility
68155-00-0	Alcohols, C14-18 and C16-18-unsatd.		Predicted to be non-toxic at the limit of solubility
97552-91-5	C18-22 Alcohol		Predicted to be non-toxic at the limit of solubility
629-96-9	1-Eicosanol		Predicted to be non-toxic at the limit of solubility
661-19-8	1-Docosanol		Predicted to be non-toxic at the limit of solubility

[1]The partition model is described in Annex IX.

[2]Compositional Types are described in section 1.1.3.

[3]A Klimisch reliability score of 2 (valid with restrictions) is assigned to the estimated toxicity values, on the basis that the method used was well validated.

4.1.1.3 Toxicity to algae

The best quality data algal toxicity data for single carbon chain lengths are shown in Table 4.7. The data show the toxicity of the alcohols to increase from an E_rC_{50} of 80 mg/L for C6 to 0.62 mg/L for C12. The C14 and C16 alcohols were not toxic to algae. These results indicate a toxicity cut-off at C14 and above.

The data for mixed carbon chain length alcohols (commercial products) are shown in Table 4.8. The data show the multi-component substances containing alcohols with carbon numbers in the ranges of C6-12 to C12-16 to be acutely toxic at concentrations of between 3.1 and 0.03-0.1 mg/L. At these concentrations all all the components are likely to have been fully dissolved. For the C12-18 and C14-16 multi-component substances there was evidence of toxic effects in tests conducted on water-accommodated fractions prepared at loading rates that will have exceeded the solubility of some components.

Table 4.7 Key algal toxicity studies for single carbon chain length linear alcohols

CAS #	Chemical name	Comment	Water solubility (mg/L)	Species	Method/ Guideline	Endpoint	Value (mg/L)[1]	Reliability code	Reference
111-27-3	1-Hexanol		5900 at 20°C	*Pseudokirchneriella subcapitata*	OECD 201	72 h E_rC_{50} NOEC	80 (m) 11 (m)	1	Wenzel, 2005
111-87-5	1-Octanol		550 at 25°C	*Scenedesmus subspicatus*	DIN 38 412 Parts 1 & 9/ OECD 201	48h E_bC_{50} and E_rC_{50}	6.5-14 (n)	4	Kuhn and Pattard, 1990
112-53-8	1-Dodecanol	Supporting	1.9 at 20°C	*S. subspicatus*	OECD 201	72 h E_bC_{50} 72 h E_rC_{50} 72 h E_bC_0	0.62 (n) 2.6 (n) 0.40 (n)	2	Henkel, 1994d
112-72-1	1-Tetradecanol		0.19 at 25°C	*S. subspicatus*	DIN 38 412 Part 9/OECD 201	96 h E_bL_{50} and E_rL_{50}	>10 (n) (>LoS)	2	Guhl, 1992d
36653-82-4	1-Hexadecanol		0.013 at 25°C	*S. subspicatus*	DIN 38 412 Part 9/OECD 201	96 h E_bL_{50} 96 h E_rL_{50}	680 (n) >980 (n) (>LoS)	2	Guhl, 1992c

[1] >LoS: LC_{50} observed was greater than the limit of solubility. (n) based on nominal concentrations, (m) based on measured concentrations.

Table 4.8 Algal studies for mixed carbon chain length alcohols

CAS	Chemical name	Comment	Water solubility (mg/L)	Species	Method/ Guideline[2]	Endpoint	Value (mg/L)[3]	Reliability code	Reference
68603-15-6	Alcohols, C6-12	Type C	10 at 20°C	*S. capricornutum*[4]	Not specified	96 h E_bC_{50}	3.1 (n)	2	Pearson and Eadsforth, 1984
68603-15-6	Alcohols, C 6-12	Type B	10 at 20°C	*Selenastrum capricornutum*[4]	Not specified	96h E_rC_{50} NOEC	2.7 (n) 1.0 (n)	2	Stephenson, 1982a
67762-41-8	Alcohols, C 10-16	Type B and C	2.4 at 25°C	*R. subcapitata*[4]	OECD 201 WAF	72 h E_rL_{50} 72 h E_bL_{50} NOEL	0.1-0.3 (n) 0.1-0.3 (n) 0.1 (n)	1	Palmer and Cann, 2000a
67762-41-8	Alcohols, C 10-16	Type B	2.4 at 25°C	*S. capricornutum*[4]	OECD 201 WAF	72 h E_rL_{50} 72 h E_bL_{50} NOEL	0.44 (n) 0.23 (n) 0.058 (n)	1	Sasol, Sastech Research and Development, 2001
67762-25-8	Alcohols, C 12-18	Type A	0.36 – 1.8 predicted at 1000 mg/L loading rate	*P. subcapitata*	OECD 201 WAF	72 h E_rL_{50} 72 h E_bL_{50} NOEL	7.5 (n) 2.3 (n) 1.2 (n) (>LoS)	1	Wenzel, 2003
68855-56-1	Alcohols, C 12-16	Type A	10 at 20°C	*Raphidocelis subcapitata*[4]	OECD 201 WAF	72 h E_rL_{50} 72 h E_bL_{50} NOEL	0.1-0.3 (n) 0.03-0.1 (n) 0.003 (n)	1	Palmer and Cann, 2000b
68855-56-1	Alcohols, C 12-16	Type A	10 at 20°C	*R. subcapitata*[4]	OECD 201 WAF	72 h E_rL_{50} 72 h E_bL_{50} NOEL	0.46-1.0 (n) 0.46-1.0 (n) 0.46 (n)	1	Eadsforth, Palmer and Cann, 2000
80206-82-2	Alcohols, C 12-14	Type A	3.3 predicted at 1000 mg/L loading rate	*R. subcapitata*[4]	OECD 201 WAF	72 h E_rL_{50} 72 h E_bL_{50} NOEL	0.1-0.3 (n) 0.03-0.3 (n) 0.003 (n)	1	Palmer and Cann, 2000b
68333-80-2	Alcohols, C 14-16	Type A	0.70 at 20°C	*R. subcapitata*[4]	OECD 201 WAF	72 h E_rL_{50} 72 h E_bL_{50} NOEL	22-46 (n) 22-46 (n) 4.6 (n) (>LoS)	1	Whale, Palmer and Cann, 2000

[1] Compositional Types are described in section 1.1.3.

[2] WAF denotes test medium was a water-accommodated fraction

[3] >LoS: EC_{50} observed was greater than the limit of solubility of at least some components of the substance. (n) based on nominal concentrations, (m) based on measured concentrations.

[4] Now known as *Pseudokirchneriella subcapitata*. The names used in the study reports are given here.

To fill gaps in the database for algae, the toxicity of single carbon chain length alcohols and commercial products (multi-component substances) has been estimated by read-across and expert judgement. The relationships between the measured and predicted data for different trophic levels has been used as the basis for the read-across; that is to say that rather than reading across a value from a different substance, expert judgement was applied in assessing the expected level of toxicity of the substance in algae, based on available measured and predicted effect concentrations for the same substance in fish and *Daphnia magna*.

The measured and estimated toxicity values for the single carbon number alcohols are given in Tables 4.9 and for the multi-component substances in Table 4.10. The results of gap filling are not considered further because the derived values cannot be considered to be independent observations.

Table 4.9 Measured and estimated acute toxicity to algae for essentially pure commercial products (using expert judgement[1])

CAS	Chemical name	Comments	Water solubility (mg/L)	Algae EC_{50} (mg/L) [2]
111-27-3	1-Hexanol		5900 at 20°C	80
111-70-6	1-heptanol	Supporting	1313 at 20°C	10-100 (read across)
111-87-5	1-Octanol		551 at 25°C	6.5-14
143-08-8	1-Nonanol	Supporting	128 at 20 °C	1.0-10 (read across)
112-30-1	1-Decanol		39.5	1.0-10 (read across)
68516-18-7	Decene, hydroformylation products	Supporting	-	0.1-1.0 (read across)
112-42-5	1-Undecanol		8.0 at 20°C	0.1-1.0 (read across)
68603-15-6	C 6-12 alcohols	Type A	9.7 mg/L at a loading rate of 1000 mg/L [modelling]	1-10 (read across)
112-53-8	1-Dodecanol	Supporting	1.93 at 20°C	0.62 (biomass) -2.6 (growth) Other result agrees closely (EC_{50} 0.97)
112-70-9	1-Tridecanol		0.38 at 20°C	0.1-1.0 (read across)
90583-91-8	Tridecanol, branched and linear		0.38 mg/L at a loading rate of 1000 mg/L [modelling]	>LOS (read across)
112-72-1	1-Tetradecanol		0.191 at 25°C	Effects seen >LOS
629-76-5	1-Pentadecanol		0.102 at 25°C	No effects expected at LoS (read across)
36653-82-4	1-Hexadecanol		0.013 at 25°C	Effects seen >LOS
143-28-2	9-Octadecen-1-ol, (9Z)-	C18 (unsaturated)	0.042 (prediction)	No effects expected at LoS (read across)

112-92-5	1-Octadecanol	Supporting	0.0011 at 25°C	No effects expected at LoS (read across)
629-96-9	1-Eicosanol		0.0027 mg/L at a loading rate of 1000 mg/L [modelling][1]	No effects expected at LoS (read across)
661-19-8	1-Docosanol		0.0027 mg/L at a loading rate of 1000 mg/L [modelling] [1]	No effects expected at LoS (read across)

[1] Approach to expert judgement for algal toxicity is discussed in Annex VIII

[2] A Klimisch reliability score of 2 (valid with restrictions) is assigned to the estimated algal toxicity values, on the basis that the value was predicted using read across and expert judgement with validation based on measured data across the data set.

Table 4.10. Estimated acute toxicity to algae for complex commercial products (using expert judgement[1])

CAS	Chemical name	Comment[3]	Water solubility (mg/L), sum of all components	Algae E(L)C_{50} (mg/L) [2]
68603-15-6	C6-12 Alcohols	Type C	510 mg/L at a loading rate of 1000 mg/L [modelling]	3.1
68603-15-6	C6-12 Alcohols	Type D	293 mg/L at a loading rate of 1000 mg/L [modelling]	1.0-10 (read across)
85566-12-7	C8-10 Alcohols		202 (predicted, at a loading rate of 1000 mg/L)	1.0-10 (read across)
68551-07-5	C8-18 Alcohols		26.5 (predicted, at a loading rate of 1000 mg/L)	0.1-1.0 (read across)
66455-17-2	C9-11 Alcohols		44.0 (predicted, at a loading rate of 1000 mg/L)	0.1-1.0 (read across)
68603-15-6	C6-12 Alcohols	Type B	43.9 mg/L at a loading rate of 1000 mg/L [modelling]	2.7
67762-41-8	C10-16 Alcohols	Type A	7.1 mg/L at a loading rate of 1000 mg/L[modelling]	0.1-1.0 (read across)
85665-26-5	C10-12 Alcohols		34 (predicted, at a loading rate of 1000 mg/L)	0.1-1.0 (read across)
67762-41-8	C10-16 Alcohols	Type B	2.9	EL_{50} 0.1-0.3 (both biomass and growth) Two other results support
67762-41-8	C10-16 Alcohols	Type C	2.4 at 25°C	E_bL_{50} 0.03-0.3; E_rL_{50} [One other result supports
67762-41-8	C10-16 Alcohols	Type D	0.67 mg/L at a loading rate of 1000 mg/L [modelling]	0.1-1.0 (read across)
67762-25-8	C12-18 Alcohols	Type A	1.7 (predicted, at a loading rate of 100 mg/L)	E_bL_{50} 2.3; E_rL_{50} 7.5 The value is >LOS
67762-25-8	C12-18 Alcohols	Type B	0.35 mg/L at a loading rate of 1000 mg/L [Modelling]	10-100 (read across)
63393-82-8	C12-15 Alcohols	Type A	0.63 (predicted, at a loading rate of 1000 mg/L)	0.1-0.3 (read across)

CAS	Chemical name	Comment[3]	Water solubility (mg/L), sum of all components	Algae $E(L)C_{50}$ (mg/L) [2]
63393-82-8	C12-15 Alcohols	Type B	0.67 mg/L at a loading rate of 1000 mg/L [Modelling]	0.1-0.3 (read across)
68855-56-1	C12-16 Alcohols	Type B	3.2 mg/L at a loading rate of 1000 mg/L [modelling]	0.1-0.3 (read across)
68855-56-1	C12-16 Alcohols	Type C	0.42 mg/L at a loading rate of 1000 mg/L [modelling]	1.0-10 (read across)
68855-56-1	C12-16 Alcohols	Type A	0.80 at 20°C	Results variable, mostly < 1; some valid results loaded 3-9 mg/L. Lowest (critical) result is E_bL_{50} 0.03-0.1; E_rL_{50} = 0.1-0.3. All reported results are EL_{50}s except one 2-day test, EC_{50} 0.4 mg/L.
80206-82-2	C12-14 Alcohols	Type A	4.6 mg/L at a loading rate of 1000 mg/L [modelling]	E_bL_{50} 0.03-0.3 E_rL_{50} = 0.1-0.3 Other results also EL_{50} values >1 mg/L
80206-82-2	C12-14 Alcohols	Type B	2.8 (predicted, at a loading rate of 1000 mg/L)	0.1-1.0 (read across)
75782-86-4	C12-13 Alcohols		1.1 (predicted, at a loading rate of 1000 mg/L)	0.1-1.0 (read across)
68333-80-2	C14-16 Alcohols	Type B	0.64 mg/L at a loading rate of 1000 mg/L [modelling]	0.1-1.0 (read across)
68333-80-2	C14-16 Alcohols	Type A	0.70 at 20°C	Effects seen >LOS. 0.1-1.0 (read across)
75782-87-5	C14-15 Alcohols		0.15 (predicted, at a loading rate of 1000 mg/L)	0.1-1.0 (read across)
67762-30-5	C14-18 Alcohols	Type B	0.12 (predicted, at a loading rate of 1000 mg/L)	>LoS (read across)
67762-30-5	C14-18 Alcohols	Type A	0.035 (predicted, at a loading rate of 1000 mg/L)	>LoS (read across)
67762-27-0	C16-18 Alcohols		0.03 (predicted, at a loading rate of 1000 mg/L)	>LoS (read across)
68002-94-8	C16-18 and 18 Unsaturated alcohols		0.045 (predicted, at a loading rate of 1000 mg/L)	>LoS (read across)
68155-00-0	C14-18 and 16-18-unsaturated alcohols		0.024 (predicted)	>LoS (read across)
97552-91-5	C18-22 Alcohols		0.0056 (predicted, at a loading rate of 1000 mg/L)	>LoS (read across)

[1] Approach to expert judgement for algal toxicity is discussed in Annex IX

[2] A Klimisch reliability score of 2 (valid with restrictions) is assigned to the estimated algal toxicity values, on the basis that the value was predicted using read across and expert judgement with validation based on measured data across the data set.

[3] Compositional Types are described in section 1.1.3.

4.1.2 Chronic toxicity test results

4.1.2.1 Chronic toxicity to fish

Currently, the only data that provides a possible indication of chronic toxicity to fish are for 1-octanol. A NOEC of between 0.75 and 3.0 mg/L has been determined for growth reduction in a 7-day test with larval Fathead minnows (*Pimephales promelas*) (Pickering *et al*., 1996) that has been assigned reliability 2. The result is expressed relative to nominal exposure concentrations and it is significant to note that measured concentrations declined by >90% over the period between media renewals (not specified in the source document). The true toxicity is therefore likely to have been greater than that expressed due to the observed loss of test substance concentration in the old media. The duration of this test is too short for it to be considered a true chronic study.

4.1.2.2 Chronic toxicity to invertebrates

Data of an acceptable quality are available for 21-day reproduction studies with *Daphnia magna* for the single carbon chain length alcohols 1-octanol (Kuhn *et al*., 1989), 1-decanol, 1-dodecanol (supporting), 1-tetradecanol and 1-pentadecanol (Schafers, 2005a-d respectively). The data were obtained generally in accordance with standard test guideline OECD 211. However some modifications to the normal guideline procedures were necessary to reduce losses of test substances due to the extensive and rapid biodegradation of the alcohols. Details of the modifications to the guideline are provided in the SIDS dossiers and in Annex X to the SIAR.

The results of the tests are presented in Table 4.11. The new experimental data are combined with literature data for octanol (C8). In spite of the guideline modifications significant losses of test substance still occurred. It was therefore necessary to report the results both in terms of the mean of the measured concentrations in the fresh media and the mean of the measured concentrations in the fresh and old media. The test substance renewal interval was 24 hours. Survival and reproduction endpoints have been summarized using standard statistical techniques. Conclusions for each test are presented as both NOEC and EC_{10}. The 1-octanol study is reliability 2, valid with restrictions; the other studies are reliability 1.

Table 4.11. Chronic (21-d) aquatic toxicity of long chain alcohols to *Daphnia magna*.

	Survival				Reproduction			
	NOEC		EC10		NOEC		EC10	
	µg/L	µmol	µg/L	µmol	µg/L	µmol	µg/L	µmol
	Exposure based on mean measured concentrations in fresh and old media							
C8	1000	2.34	1000	7.68	1000	7.68	1000	7.68
C10	370	0.08	340	2.15	110	0.69	210	1.33
C12	14	0.06	33	0.18	14	0.08	13	0.07
C14	13	0.28	130	0.61	1.6	0.01	6.3	0.03
C15	>63	>0.28	>63	>0.28	7.8	0.03	12	0.05
	Exposure based on mean measured initial concentration							
C8	1000	7.68	1000	7.68	1000	7.68	1000	7.68
C10	960	6.06	934	5.90	350	2.21	610	3.85
C12	163	0.86	230	1.21	160	0.86	147	0.81
C14	140	0.65	180	0.83	9.8	0.05	70	0.33
C15	240	1.05	>240	>1.01	56	0.25	74	0.32

No measured data are available for multi-component substances of different carbon chain length alcohols.

The effect of long chain alcohols on *Daphnia magna* survival is generally less sensitive than the effect on reproduction. A pattern of increased toxicity with increasing chain length is also apparent. In the octanol study, the most sensitive and only reported effect was on time to first brood release which occurred at 1000 µg/L (nominal concentration). For comparison of results across chain lengths and structure activity models the response for survival and reproduction was assumed to be equal to the effect on time to first brood.

The data indicates that for survival and reproduction, the NOEC and EC_{10} values increase from C14 to C15. This is almost certainly due to exceeding the boundary of water solubility as would be expected from conventional toxicological theory (Rufli *et al*. 1998). Under these circumstances a more accurate interpretation of the results might be obtained by setting the exposure to the solubility of the substance (i.e., 49 µg/L). This has the effect of lowering the toxicity values but they are still higher than those for the C14 substance. This pattern is not in keeping with the trend of reducing acute toxicity values (i.e. higher toxicity) observed between the C8 and C14 alcohols. However it must be appreciated that significant uncertainty exists in identifying the true exposure concentrations in the region of the water solubility of a substance. Rufli *et al*. (1998), in a review of aquatic toxicity testing of sparingly soluble compounds, also point out that interpretation of toxicity responses observed above the solubility limit is aggravated by artefacts and that testing should only occur at or below the limit.

For alcohols with carbon numbers higher than C15 there are significant experimental difficulties in producing, maintaining and quantifying exposures of the test substance. This explains why there are no data for such substances.

A fuller description of the 2005 chronic studies on *Daphnia magna* is given in Annex X. Structure-activity relationships are also developed in this annex to estimate $NOEC_{reproduction}$, as measured data showed this to be the more sensitive endpoint (as indicated earlier). It is possible to apply these structure-activity relationships to estimate chronic toxicity endpoints for other members of the Category.

In Annex X, two (Q)SAR relationships are developed. One equation is based on Total Mean Measured concentrations and the other is based on Initial Mean Measured concentrations. It can be concluded that the NOEC for reproduction would be within the range of the two estimates.

The two (Q)SAR relationships are as follows:

$$\text{Log } NOEC_{reproduction} = -1.03 * \log Kow + 4.28 \qquad \text{(a)}$$

$$\text{Log } NOEC_{reproduction} = -0.70 * \log Kow + 3.31 \qquad \text{(b)}$$

These (Q)SARs have been used to estimate $NOEC_{reproduction}$ for *Daphnia magna* for the other single-component members of the Category. The results are presented in Table 4.12 below.

Table 4.12. Estimated values of NOEC$_{reproduction}$ for other members of the Category

CAS	Chemical Name	Mol Wt.	Log Kow^1	Water solubility (mg/L)	Estimate based on (Q)SAR (a) (µmol/L)	Estimate based on (Q)SAR (b) (µmol/L)	Estimate based on (Q)SAR (a) (mg/L)	Estimate based on (Q)SAR (b) (mg/L)
111-27-3	1-Hexanol	102	2.12	5900	125	67	13	6.8
112-42-5	1-Undecanol	172	4.73	8.0	0.26	1.0	0.044	0.17
112-70-9	1-Tridecanol	200	5.64	0.38	0.030	0.23	0.006	0.046
36653-82-4	1-Hexadecanol	242	6.78	0.013	N/A	N/A	N/A	N/A
143-82-8	9-Octadecen-1-ol, (9Z)-	268	7.07	0.042 (e)	N/A	N/A	N/A	N/A
629-96-9	1-Eicosanol	298	7.62	0.0011 (e)	N/A	N/A	N/A	N/A
661-19-8	1-Docosanol	326	7.75	0.001 (e)	N/A	N/A	N/A	N/A

Note: 1 – (Q)SAR based on estimated log Kow so estimates used as the basis for these estimated NOECs, even where measured values are available.

For substances of chain length greater than C15, no chronic effects would be expected.

Estimation of NOEC for members of the Category comprising a range of chain lengths would be subject to significant uncertainty and is not attempted here.

4.1.2.3 Chronic toxicity to algae

Two algal toxicity studies on single carbon chain length alcohols were identified as being suitable for assessing chronic toxicity. Other algal studies used a WAF methodology and/or used test concentrations greater than the limit of water solubility and/or did not report a NOEC or equivalent statistic.

The most reliable data were obtained in a test with hexanol reported by Wenzel (2005). A 72-h ErC$_{50}$ value of 80 mg/L and a NOEC of 11 mg/L were reported for hexanol based on measured exposure concentrations.

A test with dodecanol resulted in 72-h EC$_{50}$ and EC$_0$ (equivalent to a NOEC) values, expressed relative to nominal exposure concentrations, of 0.62 and 0.40 mg/L respectively.

4.1.3 Acute to chronic toxicity ratios and (Q)SAR toxicity predictions for aquatic organisms

The ratio of an acute EC$_{50}$ or LC$_{50}$ value determined for a substance to a chronic NOEC or EC$_x$ determined for the same substance (or the equivalent test statistics expressed as loading rates) is termed an acute:chronic ratio (ACR). ACRs for non-polar narcotics are typically in the range 3-10 (van Leeuwen *et al.*, 1992).

4.1.3.1 Fish

There are insufficient test data to derive acute to chronic ratios for fish.

4.1.3.2 Invertebrates

The data set that was used to determine ACRs for long chain aliphatic alcohols and the resulting values are presented and discussed fully in Annex X. The data set is limited, and restricted to only one species, *Daphnia magna.* The resulting ACR values for all the alcohols tested (up to C15) are <100, suggesting that they have a non-specific narcotic mode of action.

4.1.3.3 Algae

Two algal toxicity studies on single carbon chain length alcohols can be used to estimate an acute:chronic ratio.

The most reliable data were obtained in a test with hexanol reported by Wenzel (2005). A 72-h ErC_{50} value of 80 mg/L and a NOEC of 11 mg/L were reported for hexanol based on measured exposure concentrations. These values give an acute to chronic ratio of 7.3.

A test with dodecanol resulted in 72-h EC_{50} and EC_0 (equivalent to a NOEC) values, expressed relative to nominal exposure concentrations, of 0.62 and 0.40 mg/L respectively. These values give an acute to chronic ratio of 1.6.

The results of the tests on the mixed carbon chain length alcohols are generally expressed relative to loading rates. The ratios of acute to chronic toxicity that are obtained from the results expressed in this way are generally in the range of 2 to 10. There are two exceptional values: acute:chronic ratios of 100 were obtained for CAS Numbers 68855-56-1 (compositional type A) and 80206-82-2 (compositional type A). However, in a second test with 68855-56-1 type A and in two further tests with 80206-82-2 (compositional type A), ratios of approximately 2 and 2.5 and 6 were obtained.

4.1.4 Toxicity to micro-organisms

There are several studies testing the toxicity of alcohols to single species of micro-organisms. Given the range of endpoints and species tested, and since this is not a SIDS endpoint, no attempt has been made to identify key studies. The range of results is shown in Table 4.13, for test species relevant to WWTP (studies on various other types of organisms are reported in the substance dossiers). In general, micro-organism studies showed less toxicity than studies with aquatic organisms.

Table 4.13. Micro-organism toxicity for species of potential relevance to WWTP systems

CAS	Chemical Name	Comment	Species	Endpoint	Result (mg/L)	Reliability	Reference
111-27-3	1-Hexanol		*Pseudomonas putida*	16-hr Toxicity Threshold (TT)	62	2	Bringmann and Kuhn, 1980
111-27-3	1-Hexanol		*Uronema parduczi*	EC_0	93	4	Verschueren, 1996
111-27-3	1-Hexanol		*P. putida*	30 min EC_{10}	3000	4	Henkel unpublished
111-27-3	1-Hexanol		*P. putida*	16-hr EC_{10}	10,000	4	unreferenced; IUCLID 2000 CD-ROM
111-70-6	1-heptanol	Supporting	*P. putida*	16-hr Toxicity Threshold (TT)	67	2	Bringmann and Kuhn, 1980
111-70-6	1-heptanol	Supporting	*U. parduczi*	EC_0	17	4	Verschueren, 1996

CAS	Chemical Name	Comment	Species	Endpoint	Result (mg/L)	Reliability	Reference
111-87-5	1-Octanol		*P. putida*	16-hr Toxicity Threshold (TT)	>50	4	Bringmann and Kuhn, 1980
111-87-5	1-Octanol		*Chilomonas paramecium*	48 h EC_{5}	>20	4	Verschueren, 1996
111-87-5	1-Octanol		*U. parduczi*	20 h TGK 5%	23	4	Bringmann and Kuhn, 1980
111-87-5	1-Octanol		*Clostridium acetobutylicum* (anaerobic)	6-h EC_{50}	130.3	4	Izard *et al*., 1989
111-87-5	1-Octanol		Activated sludge	3 h EC_{50}	350	4	Tang *et al*., 1990
111-87-5	1-Octanol		Activated sludge	EC_{50}	325.6	4	Beaubien *et al*., 1985
111-87-5	1-Octanol		Activated sludge	24h EC_{50}	200	4	Tang *et al*., 1990
111-87-5	1-Octanol		*P. putida*	30 min EC_{10}	10,000	4	Bringmann and Kuhn, 1980
111-87-5	1-Octanol		Mixed culture	75 min EC_{50}	625	4	Vaishnav *et al*., 1986
112-30-1	1-Decanol		*P. putida*	30-min. EC_{0}	10,000	2	Henkel, 1999a
112-30-1	1-Decanol		Mixed microbial culture	75 min EC_{50}	443	4	Vaishnav *et al*., 1985
112-30-1	1-Decanol		*P. putida*	30 min EC_{0}	10,000	4	Henkel, unpublished
112-53-8	1-Dodecanol	Supporting	*P. putida*	30-min. EC_{0}	>10,000	1	Henkel, 1994b
80206-82-2	C12-14 Alcohols		*P. putida*	30 min EC_{0}	>10,000	4	Henkel unpublished
80206-82-2	C12-14 Alcohols		*P. putida*	30 min EC_{0}	10,000	4	Henkel unpublished
112-72-1	1-Tetradecanol		*P. putida*	30 min EC_{50}	>10,000	4	Henkel unpublished
68002-94-8	C16-18 and C18 Unsturated		*P. putida*	30-min. EC_{10}	> 10,000	2	Henkel, 1988a
			P. putida	30 min EC_{10}	1000	4	Henkel, unpublished
112-92-5	1-Octadecanol	Supporting	*P. putida*	30-min. EC_{0}	> 10,000	1	Henkel, 1994c

4.2 Terrestrial effects

There are no data on the toxicity of alcohols to soil dwelling organisms. The significance of this lack of data may need to be considered in future, since Level III results indicate that if released to air, or directly to soil, e.g. via spreading of WWTP sludge, a significant proportion of longer chain alcohols would be expected to arise in the terrestrial compartment. However, the absolute quantity is expected to be small, and rapid degradation is anticipated, particularly in view of the rapid degradation seen in studies using soils.

4.3 Other environmental effects

There are no data on the toxicity of alcohols to sediment dwelling organisms.

4.4 Development of PNECs

4.4.1 PNECaquatic values

The database for chronic aquatic effects of single carbon number alcohols consists primarily of results from *Daphnia magna* reproduction tests. Available data suggest that the three taxonomic groups - fish, inverts and algae - are of comparitive susceptibility to the long chain aliphatic alcohols. It is therefore prudent to use the data from the taxonomic group with the largest number of measured results and the most reliable estimated values.

Data for C8, C10, C14 and C15 substances within the category are available. For other substances within the category and up to a carbon number of 14 it is possible to calculate *Daphnia magna* chronic values using the (Q)SAR described in Annex X. Above C15 it has been argued that no chronic effects would be expected at concentrations below the solubility of the substance.

The following logic could be applied when deriving PNECaquatic values for members of the category strictly in accordance with EU Technical Guidance (TGD, 2002):

- For substances with carbon numbers <C15 and with measured chronic data the PNECaquatic could be derived by dividing the NOEC value for *Daphnia magna* reproduction by an Assessment Factor of 100.
- For the C15 alcohol, chronic effects appear to have occurred at a concentration close to the limit of solubility of the substance. However, the lower limit of NOEC (based on mean measured concentration in fresh and old media) is well below the measured or predicted solubility limit. The PNEC might therefore be given as a range based on the measured NOECs, as for other measured results.
- For substances with carbon numbers <C15 but with no measured chronic data the PNECaquatic could be derived by dividing the NOEC value for *Daphnia magna* reproduction predicted by (Q)SAR by an Assessment Factor of 100.
- For substances with carbon numbers >C15 it can be assumed that there will be no chronic effects and therefore it is inappropriate to derive a PNECaquatic.

Some consideration might be given to reducing the size of the Assessment Factor based upon a detailed evaluation of the relative susceptability of the key taxonomic groups.

4.4.2 PNECsediment values

There are no toxicity data for sediment-dwelling organisms. For carbon chain lengths greater than C15, chronic toxicity is expected to be greater than the limit of solubility and therefore a sediment PNEC cannot be determined.

PNECsediment values for alcohols with carbon chain lengths $\leq$C15 could be calculated from the aquatic values by equilibrium partitioning according to the EU Technical Guidance Document (TGD, 2002). An organic carbon fraction of 0.05, a solid:water ratio of 1:4, a solid bulk density of

2500 kg.m^{-3} and a bulk density of wet suspended matter of 1150 kg.m^{-3} would be used in the calculation.

For substances with log K_{ow} >5, it is normal practice to consider the possibility of additional exposure via feeding and this would need to be taken into account in any risk assessment. This is relevant to chain lengths C12 and above.

4.4.3 Secondary poisoning

The possibility of secondary poisoning via the food chain is considered to be minimal. Although the maximum bioconcentration factors are high for some members of the category, these are unlikely to be found in any studies due to the rapid metabolism *in vivo*; furthermore, exposure would be low due to degradation and in all environmental compartments.

4.5 Initial assessment for the environment

The category of long chain aliphatic alcohols consists of essentially pure and mixed reaction product substances. A substantial amount of physicochemical property data and aquatic ecotoxicology data are available. Where there are gaps, (Q)SAR or read-across data have been used to fill them.

Long chain aliphatic alcohols are characterised by being very susceptible to biodegradation.

Long chain aliphatic alcohols with carbon numbers ≤C15 have been shown to have measurable invertebrate chronic toxicity in laboratory tests but only under conditions where extreme measures were taken to maintain exposure concentrations. It is highly unlikely that chronically toxic concentrations of alcohols with carbon numbers ≤C15 would be maintained in the environment.

5 RECOMMENDATIONS

Human Health:

The chemicals of the category of the long chain aliphatic alcohols are of low priority for further work. The members of this category are of a low order of toxicity by all common routes of exposure upon acute or repeated exposure. Overall, the toxicology database for this category shows an inverse relationship between chain length and toxicity. The key human health hazards identified for this category are the irritative properties for skin and eye of aliphatic alcohols with chain lengths of C11 or below. These hazards are well characterized and do not to lead tissue destruction or irreversible changes. They should nevertheless be noted by chemical safety professionals and users.

Environment:

The category comprises a homologous series of linear and essentially linear C6 - 22 alcohols. Increasing carbon chain length leads to a predictable pattern in physico-chemical properties; this drives a distinct range of fate behaviours in the environment. Category members all have the same mode of ecotoxicological action. In addition, all of the category members are rapidly biodegradable especially at environmentally relevant concentrations. Alcohols are metabolised/biotransformed in living organisms; this biotransformation suggests that bioaccumulation potentials based on octanol-water partition coefficients may be overestimates. Measured BCF data on a related alcohols Category supports the concept that the bioaccumulation potential of these substances will be lower than estimated from log Kow.

Many of the substances in the category do not present a hazard for the environment (acute aquatic toxicity >100 mg/l, or above water solubility with no effects exhibited) and are of low priority for further work. These category members are CAS Numbers: 36653-82-4, 629-96-9, 661-19-8, 143-28-2, 67762-27-0, 67762-30-5, 97552-91-5, 68155-00-0.

Some of the substances in this category present a hazard for the environment (acute toxicity to fish, daphnids and algae in the range 1 - 100 mg/l). However all of these substances are readily biodegradable. Therefore these subgroup members are of low priority for further work. These subgroup members are CAS Numbers: 111-27-3, 111-87-5, 85566-12-7, 67762-25-8, 68002-94-8.

The remaining substances in the category present a greater hazard for the environment (high acute toxicity to fish, daphnids and algae, in the range 0.1 - 1 mg/l, and/or high chronic toxicity). The substances in this subgroup biodegrade rapidly and environmental monitoring data from seven countries indicates exposures to the environment is anticipated to be low and are included in an Annex to the SIAR. The chemicals in this subgroup that should be candidates for further work by member countries, who are invited to perform an exposure assessment and, if necessary, a risk assessment, are CAS Numbers: 112-30-1, 112-42-5, 90583-91-8, 112-70-9, 112-72-1, 629-76-5, 68603-15-6, 67762-41-8, 68855-56-1, 63393-82-8, 66455-17-2, 68333-80-2, 75782-86-4, 75782-87-5, 80206-82-2, 68551-07-5, 85665-26-5.

6 REFERENCES

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7 DATA SEARCH STRATEGY

Consortium member companies contributed in-house studies of physical-chemical properties, environmental fate and transport, ecotoxicity, and animal toxicity for the chemicals and multi-component substances in the category. To supplement the industry data, literature searches were conducted of the following databases

- Hazardous Substances Database (HSDB)
- Registry of Toxic Effects of Chemical Substances (RTECS)
- Aquatic Toxicity Information Retrieval (AQUIRE)
- Sax's Dangerous Properties of Industrial Materials
- Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profiles
- International Uniform Chemical Information Database (IUCLID)
- Environmental Chemical Data Information Network (ECDIN)
- TOXLINE
- www.chemfinder.com
- ECOSAR v0.99h (part of the EPIWIN suite v3.12)

as well as standard scientific data compendia such as Verschueren (1996), CRC Handbook of Chemistry and Physics and The Merck Index.

The open literature was searched in Chemical Abstracts as follows.

Date of last literature search: 13th January 2006

**represents any string of characters*

```
Jun 01 2004 at 10:10:11
Search:  QSAR OR structure-activity OR ecotox* OR ecolog* OR biodegrad* OR
physicochem* OR physico-chem* OR partition coefficient OR Kow OR bioaccumulat*
NOT  doctype: p

Search:  QSAR OR structure-activity OR ecotox* OR ecolog* OR biodegrad* OR
physicochem* OR physico-chem* OR partition coefficient OR Kow OR bioaccumulat*
NOT  doctype: p  AND  alcohol*

5280 hits

Identical search 13th Jan 2006:  2763 hits since 2004

Search:  QSAR OR structure-activity OR ecotox* OR ecolog* OR biodegrad* OR
physicochem* OR physico-chem* OR partition coefficient OR Kow OR bioaccumulat*
NOT  doctype: p  AND  alcohol*  AND  language: english
```

Search: QSAR OR structure-activity OR ecotox* OR ecolog* OR biodegrad* OR physicochem* OR physico-chem* OR partition coefficient OR Kow OR bioaccumulat* NOT doctype: p AND alcohol* AND language: english AND doctype: gr (general review)

97 hits

Identical search 13th Jan 2006: 75 hits since 2004

Search: QSAR OR structure-activity OR ecotox* OR ecolog* OR biodegrad* OR physicochem* OR physico-chem* OR partition coefficient OR Kow OR bioaccumulat* NOT doctype: p AND alcohol* AND language: english AND adsor*

13th Jan 2006: 115 hits since 2004

Search: QSAR OR structure-activity OR ecotox* OR ecolog* OR biodegrad* OR physicochem* OR physico-chem* OR partition coefficient OR Kow OR bioaccumulat* NOT doctype: p AND alcohol* AND language: english AND 111-27-3 or 111-70-6 or 111-87-5 or 112-30-1 or 112-42-5 or 112-70-9 or 112-72-1 or 143-08-8 or 143-28-2 or 629-76-5 or 629-96-9 or 661-19-8 or 1454-85-9 or 36653-82-4 or 63393-82-8 or 64365-05-5 or 66455-17-2 or 6762-25-8 or 67762-27-0 or 67762-30-5 or 67762-41-8 or 68002-94-8 or 68155-00-0 or 68333-80-2 or 68425-38-7 or 68551-07-5 or 68603-15-6 or 68855-56-1 or 75782-86-4 or 75782-87-5 or 80206-82-2 or 85566-12-7 or 85665-26-5 or 97552-91-5 or 97659-45-5 or 104-67-7 or 112-53-8 or 112-92-5 or 123-51-3 or 85566-14-9 or 123-96-6

660 hits

Identical search 13th Jan 2006: 107 hits since 2004

Revised search using only those CAS still sponsored/supporting as part of the Category, in January 2006 (111-27-3 or 111-87-5 or 112-30-1 or 112-42-5 or 112-70-9 or 112-72-1 or 629-76-5 or 36653-82-4 or 143-28-2 or 629-96-9 or 661-19-8 or 63393-82-8 or 66455-17-2 or 67762-25-8 or 67762-27-0 or 67762-30-5 or 67762-41-8 or 68551-07-5 or 68002-94-8 or 68155-00-0 or 68333-80-2 or 68603-15-6 or 68855-56-1 or 75782-86-4 or 75782-87-5 or 80206-82-2 or 85566-12-7 or 85665-26-5 or 97552-91-5 or 90583-91-8 or 111-70-6 or 112-53-8 or 112-92-5 or 143-08-8 or 104-76-7 or 123-51-3 or 85566-14-9 or 123607-66-9 or 68516-18-7 or 68527-05-9 or 70955-11-2): 107 hits since 2004

Jun 01 2004 at 12:59:55
Search: 111-27-3 or 111-70-6 or 111-87-5 or 112-30-1 or 112-42-5 or 112-70-9 or 112-72-1 or 143-08-8 or 143-28-2 or 629-76-5 or 629-96-9 or 661-19-8 or 1454-85-9 or 36653-82-4 or 63393-82-8 or 64365-05-5 or 66455-17-2 or 67762-25-8 or 67762-27-0 or 67762-30-5 or 67762-41-8 or 68002-94-8 or 68155-00-0 or 68333-80-2 or 68425-38-7 or 68551-07-5 or 68603-15-6 or 68855-56-1 or 75782-86-4 or 75782-87-5 or 80206-82-2 or 85566-12-7 or 85665-26-5 or 97552-91-5 or 97659-45-5 or 104-67-7 or 112-53-8 or 112-92-5 or 123-51-3 or 85566-14-9 or 123-96-6 NOT doctype: p

Revised search using only those CAS still sponsored/supporting as part of the Category, in January 2006 (see above for list): 40789 hits in total

Search: 111-27-3 or 111-70-6 or 111-87-5 or 112-30-1 or 112-42-5 or 112-70-9 or 112-72-1 or 143-08-8 or 143-28-2 or 629-76-5 or 629-96-9 or 661-19-8 or 1454-85-9 or 36653-82-4 or 63393-82-8 or 64365-05-5 or 66455-17-2 or 67762-25-8 or 67762-27-0 or 67762-30-5 or 67762-41-8 or 68002-94-8 or 68155-00-0 or 68333-80-2 or 68425-38-7 or 68551-07-5 or 68603-15-6 or 68855-56-1 or 75782-86-4 or 75782-87-5 or 80206-82-2 or 85566-12-7 or 85665-26-5 or 97552-91-5 or 97659-45-5 or 104-67-7 or 112-53-8 or 112-92-5 or 123-51-3 or 85566-14-9 or 123-96-6 NOT doctype: p AND language: english

22780 hits

Revised search using only those CAS still sponsored/supporting as part of the Category, in January 2006 (see above for list): 2430 hits since 2004

Search: 111-27-3 or 111-70-6 or 111-87-5 or 112-30-1 or 112-42-5 or 112-70-9 or 112-72-1 or 143-08-8 or 143-28-2 or 629-76-5 or 629-96-9 or 661-19-8 or 1454-85-9 or 36653-82-4 or 63393-82-8 or 64365-05-5 or 66455-17-2 or 67762-25-8 or 67762-27-0 or 67762-30-5 or 67762-41-8 or 68002-94-8 or 68155-00-0 or 68333-80-2 or 68425-38-7 or 68551-07-5 or 68603-15-6 or 68855-56-1 or 75782-86-4 or 75782-87-5 or 80206-82-2 or 85566-12-7 or 85665-26-5 or 97552-91-5 or 97659-45-5 or 104-67-7 or 112-53-8 or 112-92-5 or 123-51-3 or 85566-14-9 or 123-96-6 NOT doctype: p AND language: english AND ecotoxic* or fish or daphni* or alga*

Search: 111-27-3 or 111-70-6 or 111-87-5 or 112-30-1 or 112-42-5 or 112-70-9 or 112-72-1 or 143-08-8 or 143-28-2 or 629-76-5 or 629-96-9 or 661-19-8 or 1454-85-9 or 36653-82-4 or 63393-82-8 or 64365-05-5 or 66455-17-2 or 67762-25-8 or 67762-27-0 or 67762-30-5 or 67762-41-8 or 68002-94-8 or 68155-00-0 or 68333-80-2 or 68425-38-7 or 68551-07-5 or 68603-15-6 or 68855-56-1 or 75782-86-4 or 75782-87-5 or 80206-82-2 or 85566-12-7 or 85665-26-5 or 97552-91-5 or 97659-45-5 or 104-67-7 or 112-53-8 or 112-92-5 or 123-51-3 or 85566-14-9 or 123-96-6 NOT doctype: p AND language: english AND ecotoxic* or fish or daphni* or alga* NOT sauce

216 hits

Revised search using only those CAS still sponsored/supporting as part of the Category, in January 2006 (see above for list): 30 hits since 2004

Search: 111-27-3 or 111-70-6 or 111-87-5 or 112-30-1 or 112-42-5 or 112-70-9 or 112-72-1 or 143-08-8 or 143-28-2 or 629-76-5 or 629-96-9 or 661-19-8 or 1454-85-9 or 36653-82-4 or 63393-82-8 or 64365-05-5 or 66455-17-2 or 67762-25-8 or 67762-27-0 or 67762-30-5 or 67762-41-8 or 68002-94-8 or 68155-00-0 or 68333-80-2 or 68425-38-7 or 68551-07-5 or 68603-15-6 or 68855-56-1 or 75782-86-4 or 75782-87-5 or 80206-82-2 or 85566-12-7 or 85665-26-5 or 97552-91-5 or 97659-45-5 or 104-67-7 or 112-53-8 or 112-92-5 or 123-51-3 or 85566-14-9 or 123-96-6 NOT doctype: p AND language: english AND biodegrada*

86 hits

Revised search using only those CAS still sponsored/supporting as part of the Category, in January 2006 (see above for list): 13 hits since 2004

Search: 111-27-3 or 111-70-6 or 111-87-5 or 112-30-1 or 112-42-5 or 112-70-9 or 112-72-1 or 143-08-8 or 143-28-2 or 629-76-5 or 629-96-9 or 661-19-8 or 1454-85-9 or 36653-82-4 or 63393-82-8 or 64365-05-5 or 66455-17-2 or 67762-25-8 or 67762-27-0 or 67762-30-5 or 67762-41-8 or 68002-94-8 or 68155-00-0 or 68333-80-2 or 68425-38-7 or 68551-07-5 or 68603-15-6 or 68855-56-1 or 75782-86-4 or 75782-87-5 or 80206-82-2 or 85566-12-7 or 85665-26-5 or 97552-91-5 or 97659-45-5 or 104-67-7 or 112-53-8 or 112-92-5 or 123-51-3 or 85566-14-9 or 123-96-6 NOT doctype: p AND language: english AND pubyear: 1993-current

Search: 111-27-3 or 111-70-6 or 111-87-5 or 112-30-1 or 112-42-5 or 112-70-9 or 112-72-1 or 143-08-8 or 143-28-2 or 629-76-5 or 629-96-9 or 661-19-8 or 1454-85-9 or 36653-82-4 or 63393-82-8 or 64365-05-5 or 66455-17-2 or 67762-25-8 or 67762-27-0 or 67762-30-5 or 67762-41-8 or 68002-94-8 or 68155-00-0 or 68333-80-2 or 68425-38-7 or 68551-07-5 or 68603-15-6 or 68855-56-1 or 75782-86-4 or 75782-87-5 or 80206-82-2 or 85566-12-7 or 85665-26-5 or 97552-91-5 or 97659-45-5 or

104-67-7 or 112-53-8 or 112-92-5 or 123-51-3 or 85566-14-9 or 123-96-6 NOT doctype: p AND language: english AND pubyear: 1993-current AND (vapor pressure) or (vapour pressure)

132 hits

Revised search using only those CAS still sponsored/supporting as part of the Category, in January 2006 (see above for list): 55 hits since 2004

Search: 111-27-3 or 111-70-6 or 111-87-5 or 112-30-1 or 112-42-5 or 112-70-9 or 112-72-1 or 143-08-8 or 143-28-2 or 629-76-5 or 629-96-9 or 661-19-8 or 1454-85-9 or 36653-82-4 or 63393-82-8 or 64365-05-5 or 66455-17-2 or 67762-25-8 or 67762-27-0 or 67762-30-5 or 67762-41-8 or 68002-94-8 or 68155-00-0 or 68333-80-2 or 68425-38-7 or 68551-07-5 or 68603-15-6 or 68855-56-1 or 75782-86-4 or 75782-87-5 or 80206-82-2 or 85566-12-7 or 85665-26-5 or 97552-91-5 or 97659-45-5 or 104-67-7 or 112-53-8 or 112-92-5 or 123-51-3 or 85566-14-9 or 123-96-6 NOT doctype: p AND language: english AND pubyear: 1993-current AND partition coefficient

37 hits

Revised search using only those CAS still sponsored/supporting as part of the Category, in January 2006 (see above for list): 98 hits since 2004

Search: 111-27-3 or 111-70-6 or 111-87-5 or 112-30-1 or 112-42-5 or 112-70-9 or 112-72-1 or 143-08-8 or 143-28-2 or 629-76-5 or 629-96-9 or 661-19-8 or 1454-85-9 or 36653-82-4 or 63393-82-8 or 64365-05-5 or 66455-17-2 or 67762-25-8 or 67762-27-0 or 67762-30-5 or 67762-41-8 or 68002-94-8 or 68155-00-0 or 68333-80-2 or 68425-38-7 or 68551-07-5 or 68603-15-6 or 68855-56-1 or 75782-86-4 or 75782-87-5 or 80206-82-2 or 85566-12-7 or 85665-26-5 or 97552-91-5 or 97659-45-5 or 104-67-7 or 112-53-8 or 112-92-5 or 123-51-3 or 85566-14-9 or 123-96-6 NOT doctype: p AND language: english AND pubyear: 1993-current AND bioaccumulat* or bioconcentrat*

12 hits

Revised search using only those CAS still sponsored/supporting as part of the Category, in January 2006 (see above for list): 2 hits since 2004

Annexes

Contents

ANNEX I PHYSICO-CHEMICAL PROPERTIES: MEASURED VALUES AND (Q)SAR PREDICTIONS

Structure-activity relationships (SARs) whether they are qualitative or quantitative are used in the SIAR to show the coherence of the data set and to fill data gaps. They are collectively referred to as (Q)SARs. The approach used in this Annex is to compare the measured values given in the main part of the SIAR with predictions from various methods, then to recommend and apply a preferred technique to filling data gaps. In some cases published methods are used as they stand, in other cases it has been necessary to adapt or develop them.

For each property that is a SIDS element, it is necessary to fill data gaps as necessary across the category. For some properties, a range of options exist: different methods are available, as computer software or otherwise. As a general rule, one method may perform better than another for a particular type of chemical, or a method may require slight adjustment for the chemical type of interest. For both reasons, validation using measured data may be important to help achieve the best prediction.

Measured data for branched long-chain alcohol structures in particular were in short supply. Data reported in the open literature and collated in relation to the USA submission of C6-13 iso-alkyl alcohols for the US Chemicals HPV Challenge initiative have been referred to, together with measured data for the long chain alcohols category. Measured data for long chain linear and branched alkanes have also been used.

COMPARISON OF DIFFERENT (Q)SAR METHODS

In respect of physicochemical properties, extensive use of the Syracuse Research Corporation methods is made. It is reasonable to consider whether other methods might provide substantially better results. For example, in the model used to predict log K_{ow}, the KOWWIN output has been modified by a term in the carbon number. It could be that another method might not need such a modification. Annex II provides a comparison of the performance of several other computer programs and the SRC package (EPI Suite v. 3.12).

GENERAL TRENDS IN THE DATA

The general trends in the data show properties that vary with the carbon chain length in accordance with normal expectations: as it increases, then the following applies –

- Melting point, boiling point increase and vapour pressure decreases, because molecular weight is higher and intermolecular forces in the substance are all higher; one consequence of this is that flash points decrease at higher molecular weight.
- Water solubility decreases because the free energy required for a molecule to dissolve becomes less favourable for larger molecules;
- Similarly, the octanol-water partition coefficient increases with molecular weight, since each additional CH_2 group makes the octanol phase more preferable in terms of relative solvation energy.

MELTING POINT

The data set was complete for single component sponsored substances in respect of melting points.

The SRC MPBPVP program was used (EPI Suite v. 3.12). This program gives melting point via two methods (adapted Joback method; Gold and Ogle method) and, for these substances, derives a recommended value as the mean of these. For these substances the set of measured data are close to complete for the 'pure' alcohols and these data suggest that the predictions are overestimates, with the level of overestimation increasing as carbon chain length increases.

The data are presented in Table A. I.1 and plotted in Figure A.I.1. Where there is a range in the measured value the mid-point is used.

Table A.I.1. Predicted and measured values of melting point for linear alcohols

Carbon number	Chemical Name	Measured Melting Point (°C)	Predicted value (MPBPVP)
6	1-Hexanol	-44 to -51	-37.86
7	1-Heptanol	-34	-26.03
8	1-Octanol	-15.5 to -17	-14.46
9	1-Nonanol	-5	-3.15
10	1-Decanol	6.4	7.89
11	1-Undecanol	11 to 19	18.67
12	1-Dodecanol	22.6 to 24	29.19
13	1-Tridecanol (linear) (branched)	30.6 to 33	31.69 29.19
14	1-Tetradecanol	35 to 40	49.43
15	1-Pentadecanol	45 to 46	59.15
16	1-Hexadecanol	50	68.61
17	1-Heptadecanol	53.8	77.81
18	1-Octadecanol	58	86.85
19	1-Nonadecanol	63.3	95.88
20	1-Eicosanol	64 to 68	104.9
21	1-Heneicosanol	Estimated ca. 70 [1]	113.92
22	1-Docosanol	72.5	122.94
18-unsat.	9-Octadecen-1-ol, (9Z)-	13 to 19[2]	85.36

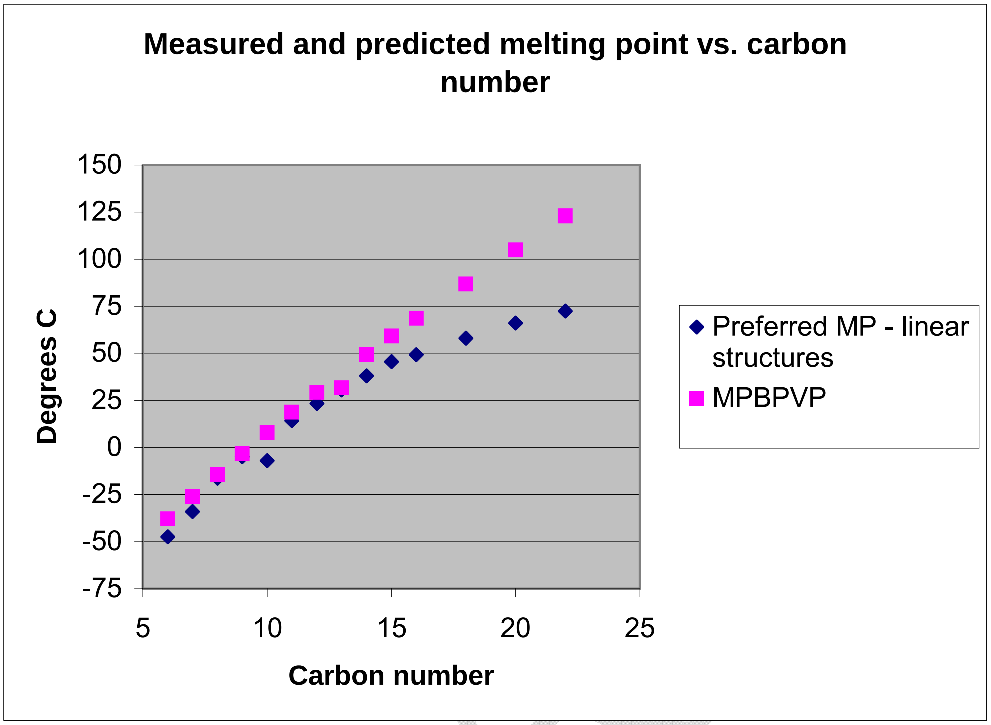
Note:

1 - Based on the relationship between measured and predicted values, approximate melting points can be estimated for those chain lengths where a measured value is unavailable.

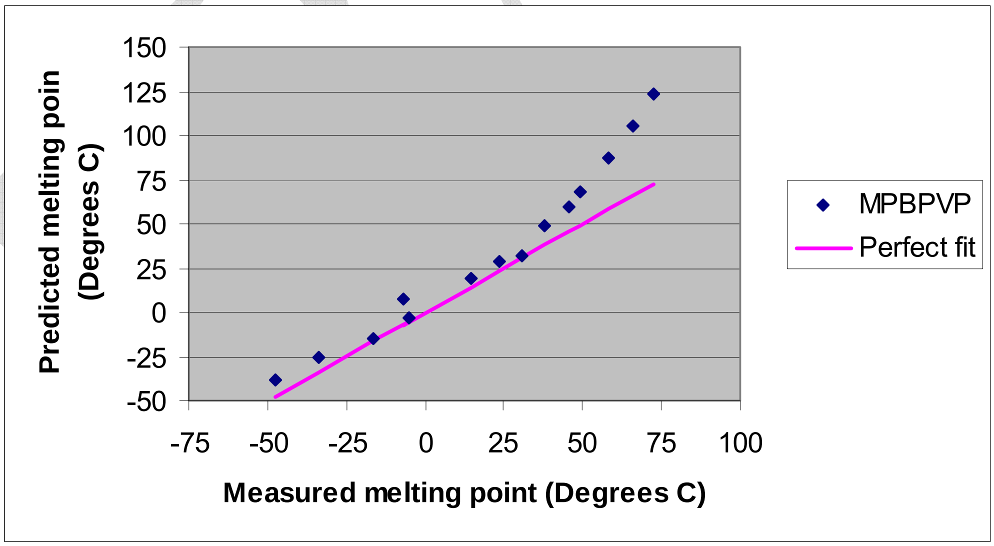
2 – for clarity this is excluded from the graph since this property would be affected by the presence of a double bond.

Figure A.I.1. Measured vs. predicted values of melting point for linear alcohols

a)



b)



The melting points of branched isomers are of a similar value to (slightly lower than) the linear alcohol of corresponding carbon number. The presence of branched isomers in commercial n-alcohols is expected to lower the melting point of those substances slightly, though it is not possible to predict values precisely.

The melting point of an impure sample is reduced. Some substances in the long chain alcohols category are complex reaction products containing a range of chain-length components, and for these, it is expected that this effect would have a significant influence on the value of melting point.

It is not possible to estimate with confidence what the melting range might be, by any available method.

BOILING POINT

The SRC MPBPVP program was used (EPI Suite v. 3.12). This program estimates boiling point using a method adapted from the Stein and Brown method. For these substances the set of measured data are close to complete for the 'pure' alcohols and most of these data suggest that the predictions are highly accurate. At the highest chain lengths data are scarcer and the single value available is much lower than the prediction. It is uncertain whether this is due to a poor measurement or a poor estimate.

The data are presented in Table A.I.2 and plotted in Figure A.I.2.

Table A.I.2. Predicted and measured values of boiling point for linear alcohols

Carbon number	Chemical Name	Measured Boiling Point (°C)	Predicted value (MPBPVP)
6	1-Hexanol	158	159.09
7	1-Heptanol	176	180.33
8	1-Octanol	194 to 195	200.67
9	1-Nonanol	194 to 213 [1]	220.09
10	1-Decanol	229	238.62
11	1-Undecanol	245	256.24
12	1-Dodecanol	259	272.96
13	1-Tridecanol	276	288.77
14	1-Tetradecanol	289	303.68
15	1-Pentadecanol	-	317.69
16	1-Hexadecanol	334 to 344 [1]	330.79
17	1-Heptadecanol	333	342.98
18	1-Octadecanol	210 at 15 mm Hg [1]	354.66
19	1-Nonadecanol	-	366.27
20	1-Eicosanol	309	377.87
21	1-Heneicosanol	-	389.48
22	1-Docosanol	-	401.08
18-unsat.	9-Octadecen-1-ol, (9Z)-	334	358.24

Note

1 - Unreliable data (non-standard pressure; variable result indicates impure sample)

In the absence of reliable measured data, it is considered acceptable to use the value estimated by MPBPVP. The regression statistics below tend to confirm this view, although they could be used to adjust the prediction if necessary:

Regression Statistics	
Multiple R	0.998195
R Square	0.996393
Adjusted R Square	0.995992
Standard Error	4.360243
Observations	11

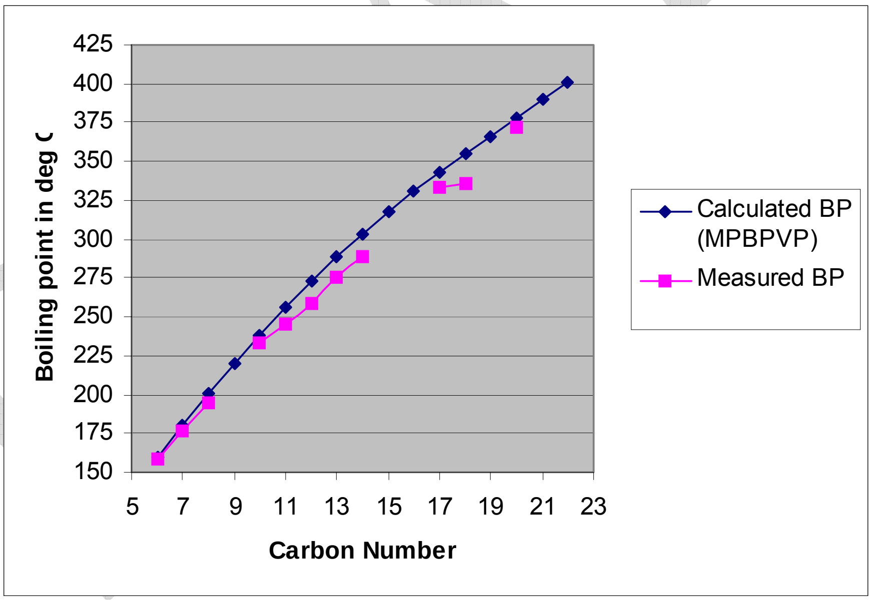
ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1	47268.12	47268.12	2486.262	2.63324E-12
Residual	9	171.1055	19.01172		
Total	10	47439.23			

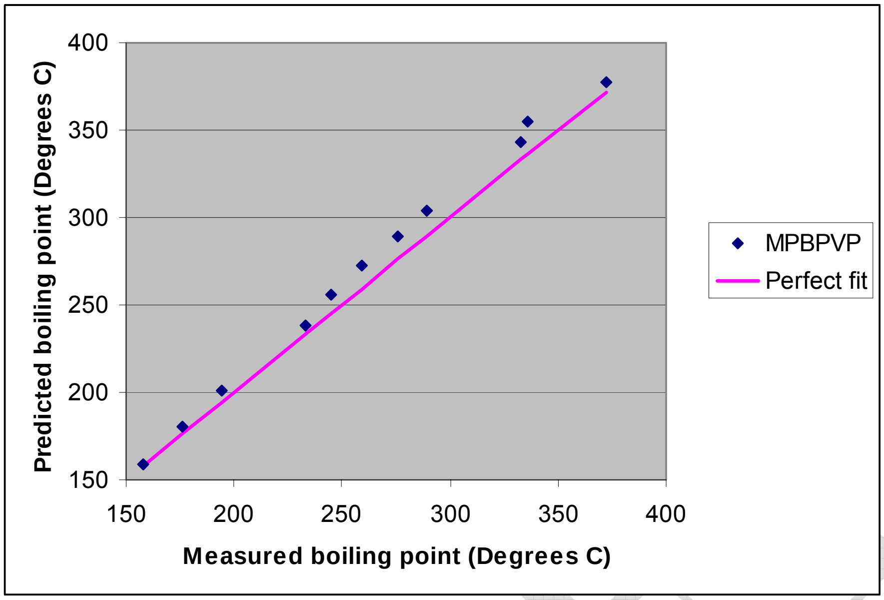
	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	2.975433	5.339999	0.557197	0.590978	-9.104485367	15.05535043
MPBPVP	0.95393	0.019131	49.86243	2.63E-12	0.910651677	0.997207364

Figure A.I.2. Measured vs. predicted values of boiling point for linear alcohols

a)



b)



The boiling points of branched isomers are slightly lower than the linear alcohol of corresponding carbon number. The presence of branched isomers in commercial n-alcohols is expected to raise the boiling point of those substances slightly, though it is not possible to predict values precisely. Some substances in the long chain alcohols category are complex reaction products containing a range of chain-length components. It is not possible to estimate what the boiling range of such substances might be with any useful level of reliability, from the available data set. However, an indication can be gained from the boiling points of the components present.

VAPOUR PRESSURE

The SRC MPBPVP program was used (EPI Suite v. 3.12). The outputs of this program are considered to give a good prediction of the value for linear alcohols, on the basis of a strong correlation between the predicted and measured values. The data are presented in Table A.I.3 and plotted in Figure A.I.3.

Table A.I.3. Predicted and measured values of vapour pressure for linear alcohols

Chemical name	Carbon Number	MPBPVP Predicted VP in Pa	Measured VP in Pa	Log predicted value	Log measured value
1-Hexanol	C6	117.17	122	2.069	2.086
1-Heptanol	C7	39.77	28	1.600	1.447
1-Octanol	C8	13.17	10	1.119	1
1-Nonanol	C9	4.36	3	0.640	0.477
1-Decanol	C10	1.45	1.13	0.161	0.0414
1-Undecanol	C11	0.678	0.39	-0.169	-0.403
1-Dodecanol	C12	0.241	0.11	-0.618	-0.959
1-Tridecanol	C13	0.0315	0.057	-1.501	-1.244

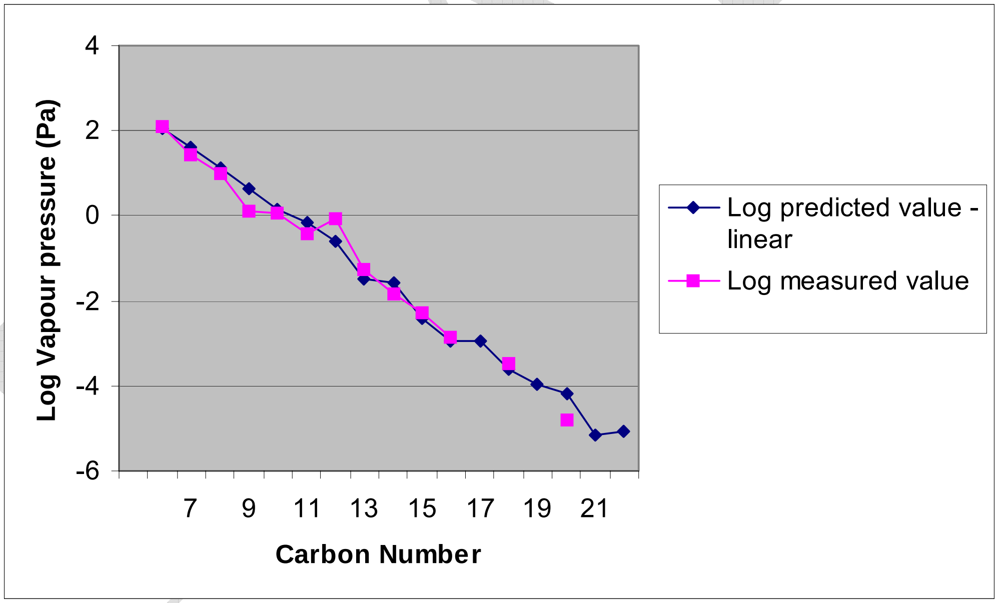
Chemical name	Carbon Number	MPBPVP Predicted VP in Pa	Measured VP in Pa	Log predicted value	Log measured value
1-Tetradecanol	C14	0.0267	0.014	-1.573	-1.835
1-Pentadecanol	C15	0.00378	0.00512	-2.423	-2.291
1-Hexadecanol	C16	0.00119	0.0014	-2.925	-2.854
1-Heptadecanol	C17	0.00115	-	-2.940	-
1-Octadecanol	C18	0.000243	0.00033	-3.614	-3.481
1-Nonadecanol	C19	0.000103	-	-3.984	-
1-Eicosanol	C20	0.0000665	0.000015	-4.177	-4.824
1-Unicosanol	C21	6.637E-06	-	-5.178	-
1-Docosanol	C22	8.153E-06	-	-5.0887	-
9-Octadecen-1-ol, (9Z)- [1]	18-unsat.	0.00198	-		

Note:

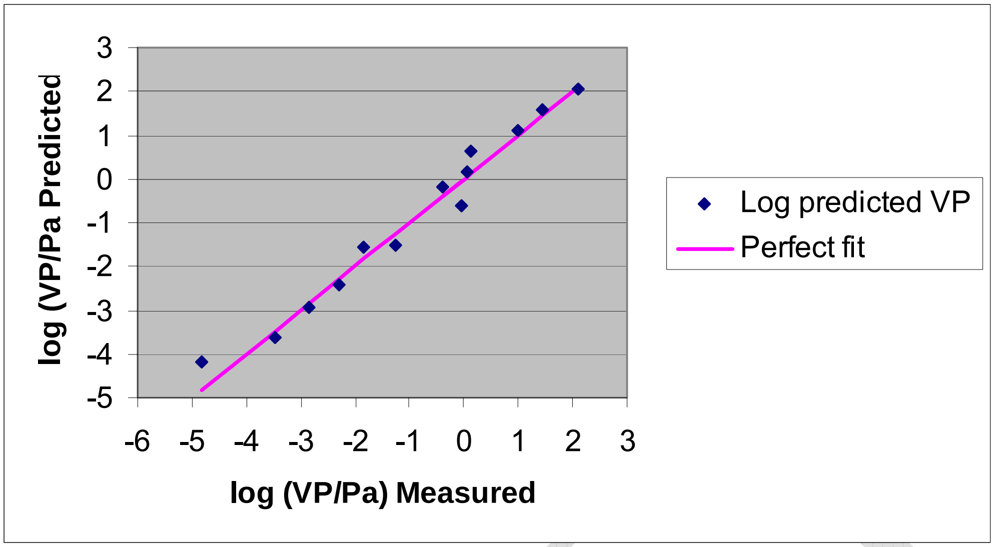
[1] Excluded from the validation due to being the only unsaturated structure, and therefore not directly comparable with the linear saturated alcohols.

Figure A.I.3. log Predicted and measured values of vapour pressure for linear alcohols, plotted against carbon number

a)



b)



The excellence of the prediction can be seen in the following regressions statistics below, showing zero intercept and unit gradient.

Regression Statistics	
Multiple R	0.987672
R Square	0.975496
Adjusted R Square	0.9732684
Standard Error	0.3327402
Observations	13

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1	48.483335	48.483335	437.90693	3.28654E-10
Residual	11	1.2178768	0.1107161		
Total	12	49.701212			

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	-0.0687875	0.1013538	- 0.6786868	0.5113625	-0.29186578	0.154290762
Log predicted VP	0.9989612	0.0477373	20.926226	3.287E-10	0.893892177	1.104030294

Validation data for methyl-branched alcohols and alkanes indicate that MPBPVP performs acceptably for branched structures too, up to a chain length C11. Data for branched structures of longer chain length were not available. Branching positions and number of methyl substituents varies. The data are presented in Table A.I.4 and plotted in Figure A.I.4.

Figure A.I.4. log Predicted and measured values of vapour pressure for branched alcohols and alkanes, plotted against carbon number

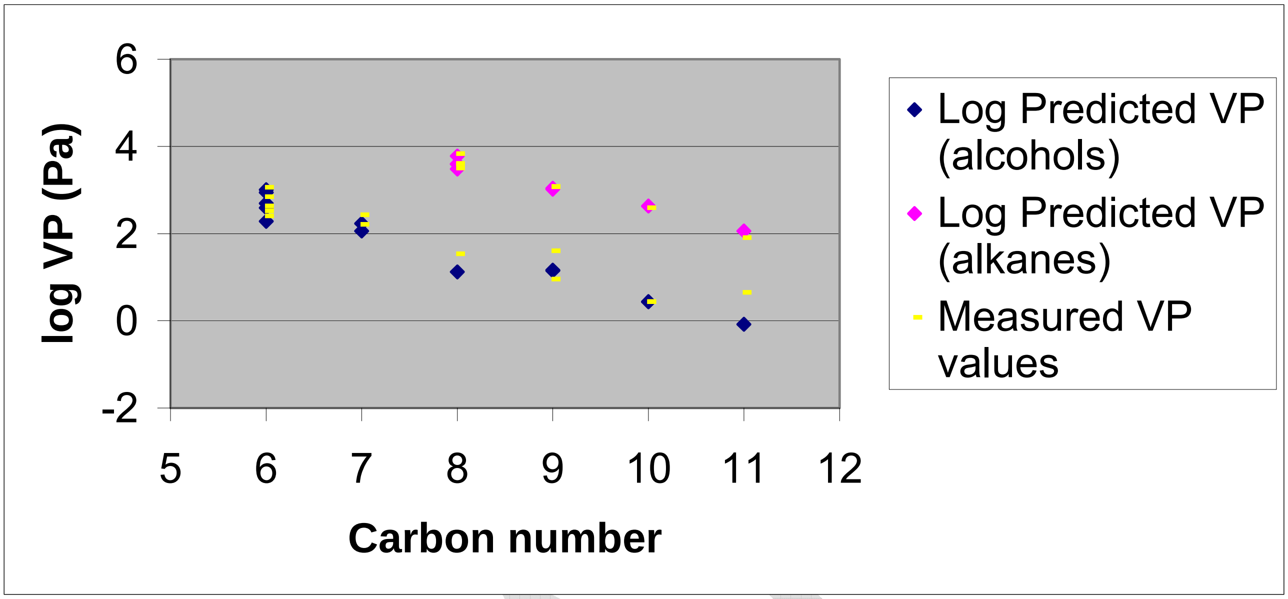


Table A.I.4. Predicted and measured values of vapour pressure for branched alcohols and alkanes

	Carbon Number	MPBPVP Predicted VP in Pa	Measured VP in Pa	Log predicted value		Log measured value
				alcohols	alkanes	
2-Methyl-1-pentanol	6	190.19	255	2.279188		2.407153
2-Hexanol	6	391.02	331	2.592199		2.519702
2,3-Dimethyl-2-butanol	6	1013.46	426	3.005807		2.629002
4-Methyl-2-pentanol	6	497.42	705	2.696723		2.848128
2-Methyl-2-pentanol	6	876.47	1140	2.942737		3.05835
2-Heptanol	7	114.513	164	2.058855		2.213757
5-Methyl-2-hexanol	7	170.24	270	2.231062		2.431134
2-Methyl-3-ethylpentane	8	3005.8	3190		3.47796	3.504063
2,5-Dimethylhexane	8	3950.1	4030		3.596608	3.605294
2,4-Dimethylhexane	8	3883.6	4040		3.589234	3.606725
Isooctane	8	5985	6850		3.777064	3.835827
3-Octanol	8	13.2468	34	1.122111		1.532092
3,3,4-Trimethylhexane	9	1036.07	1180		3.015389	3.071873

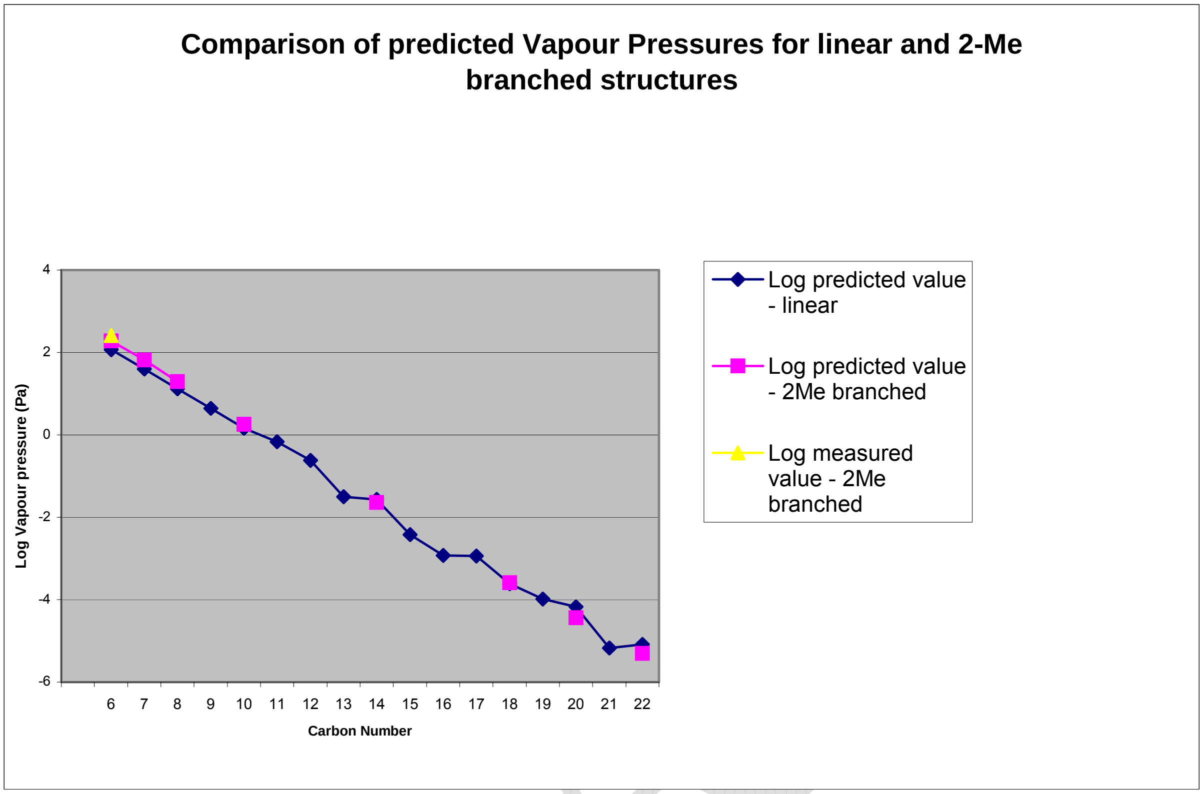
2,3,4-Trimethylhexane	9	1101.24	1200		3.041882	3.079058
2-Nonanol	9	14.497	8.98	1.161278		0.953477
Isononyl alcohol	9	14.098	39.9	1.149158		1.600973
2,6-Dimethyloctane	10	429.59	392		2.633054	2.593084
8-Methyl-1-nonanol	10	2.7132	2.75	0.433482		0.439192
Isodecanol	10	2.7132	2.75	0.433482		0.439402
2-Methyldecane	11	114.114	80.1		2.057339	1.903448
2-Undecanol	11	0.8246	4.44	-0.08376		0.647598

The good correlation between the predicted value of vapour pressure for linear and 2-methyl branched structures demonstrates that it is unlikely that branched components will exhibit different behaviour in terms of environmental fate, and also that such components, present in commercial linear alcohols as by-products, would be unlikely to affect test results. The predictions are presented in Table A.I.5 and plotted in Figure A.I.5.

Table A.I.5. Predicted values of vapour pressure for linear and 2-methyl branched alcohols

Carbon Number	Equivalent linear structure	Equivalent branched structure	MPBPVP Predicted VP in Pa - LINEAR	MPBPVP Predicted VP in Pa - BRANCHED	Log predicted value - LINEAR	Log predicted value - BRANCHED
C6	1-Hexanol	2-Methyl-1-pentanol	117.17	190	2.07	2.28
C7	1-Heptanol	2-Methyl-1-hexanol	39.77	66	1.60	1.82
C8	1-Octanol	2-Methyl-1-heptanol	13.17	19.6	1.12	1.29
C10	1-Decanol	2-Methyl-1-nonanol	1.45	1.81	0.16	0.26
C14	1-Tetradecanol	2-Methyl-1-tridecanol	0.027	0.0227	-1.57	-1.64
C18	1-Octadecanol	2-Methyl-1-heptadecanol	2.43E-04	2.58E-04	-3.61	-3.59
C20	1-Eicosanol	2-Methyl-1-nonadecanol	6.65E-05	3.62E-05	-4.18	-4.44
C22	1-Docosanol	2-Methyl-1-heneicosanol	8.15E-06	4.93E-06	-5.09	-5.31

Figure A.I.5. Predicted values of vapour pressure for linear and 2-methyl branched alcohols



Multi-component substances

Vapour pressures for multi-component substances have been calculated, where necessary, from the compositional data and the pure substance data. This has been done in accordance with basic physicochemical principles by calculation of the partial vapour pressure of each component and then summing the partial vapour pressures. Since it requires access to the confidential compositional data, the full results are not included here.

OCTANOL-WATER PARTITION COEFFICIENT

Reliable measured log K_{ow} values were available for most of the single-component alcohols. These were used to validate the SRC KOWWIN program (EPI Suite v. 3.12). Plotting measured vs predicted log K_{ow}, as shown in Figure A.I.6, trends are evident. The data are summarised in Table A.I.6.

Figure A.I.6 a). Plot of measured log K_{ow} for single component alcohols vs. carbon number

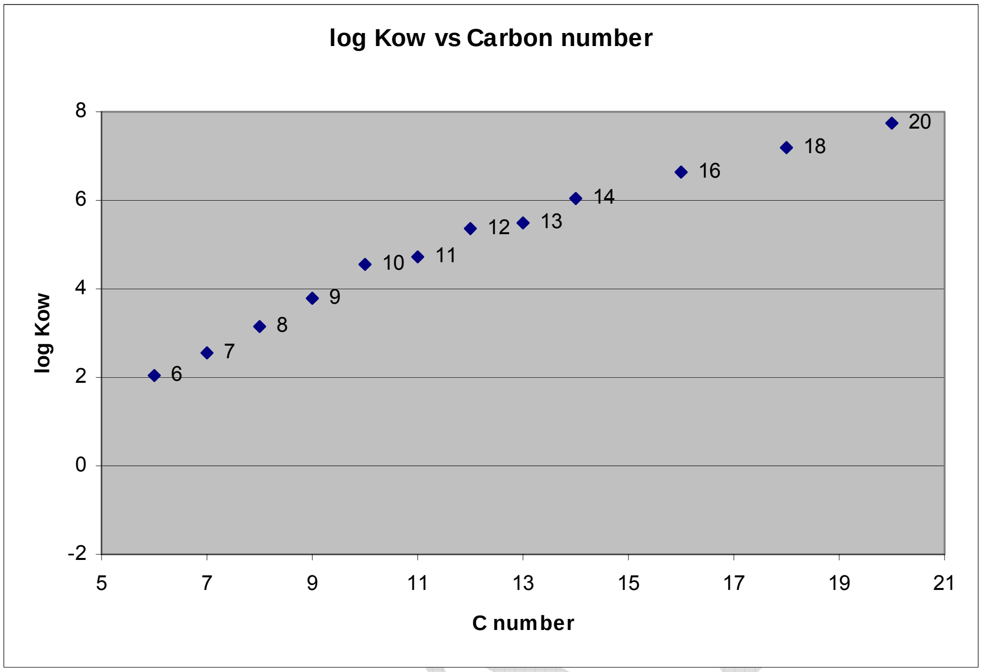
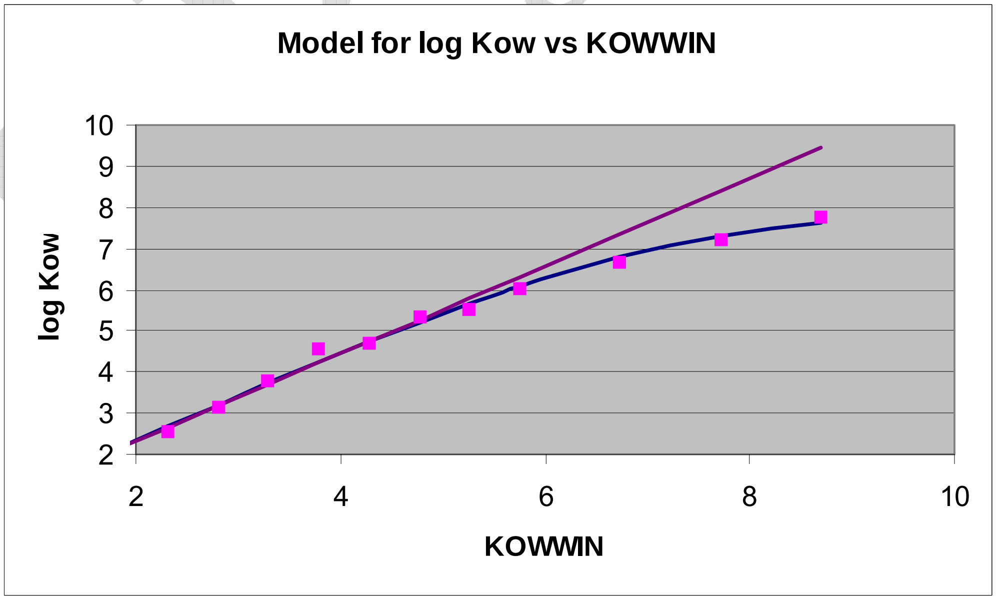


Figure A.I.6 b). Plot of measured vs. predicted log K_{ow} for single component alcohols



By relating the data to carbon number, regression of the data allowed a simple formula to be developed to describe the measured log K_{ow} values (the curved blue line shown in Figure A.I.6). The equation is

$\log K_{ow} = 0.0584 + (1.1421 \text{ x } \log \text{KOWWIN}) - (1.482\text{E-}05 \text{ x carbon-number}^{4})$

The straight purple line in the figure represents the expected linear correlation, found for the lower Carbon numbers. Such in a non-linear trend is found irrespective of the modelling program used. Thus, to fill data gaps, log K_{ow} is estimated by using the SRC KOWWIN program and applying this amendment to the result. The multiple regressions statistics show a very good fit:

Regression Statistics	
Multiple R	0.996876777
R Square	0.993763309
Adjusted R Square	0.992377378
Standard Error	0.158854015
Observations	12

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	2	36.18825528	18.09412764	717.0364898	1.1948E-10
Residual	9	0.227111383	0.025234598		
Total	11	36.41536667			

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	0.058400953	0.193447509	0.301895607	0.769591419	-0.379208048	0.496009954
KOWWIN	1.142144226	0.05701567	20.03211089	8.95195E-09	1.013165722	1.271122731
c4	-1.48165E-05	2.49985E-06	-5.926959417	0.000221553	-2.04716E-05	-9.16145E-06

Table A.I.6. Measured and predicted log K_{ow} for single component substances

Carbon Number	SRC KOWWIN	Predicted Log K_{ow} from amended KOWWIN	Measured value
C6	1.82	2.12	2.03
C7	2.31	2.67	2.57
C8	2.81	3.20	3.15
C9	3.30	3.73	3.77
C10	3.79	4.24	4.57
C11	4.28	4.73	4.72
C12	4.77	5.20	5.36
C13 (linear) (branched)	5.26 5.19	5.64 5.56	5.51
C14	5.75	6.06	6.03
C15	6.24	6.43	-
C16	6.73	6.78	6.65
C17	7.23	7. 08	-
C18	7.72	7.32	7.19
C18 unsat.	7.50	7.07	-

Carbon Number	SRC KOWWIN	Predicted Log K_{ow} from amended KOWWIN	Measured value
C19	8.21	7.50	-
C20	8.70	7.62	7.75
C21	9.19	7.75	-
C22	9.68	7.75	-

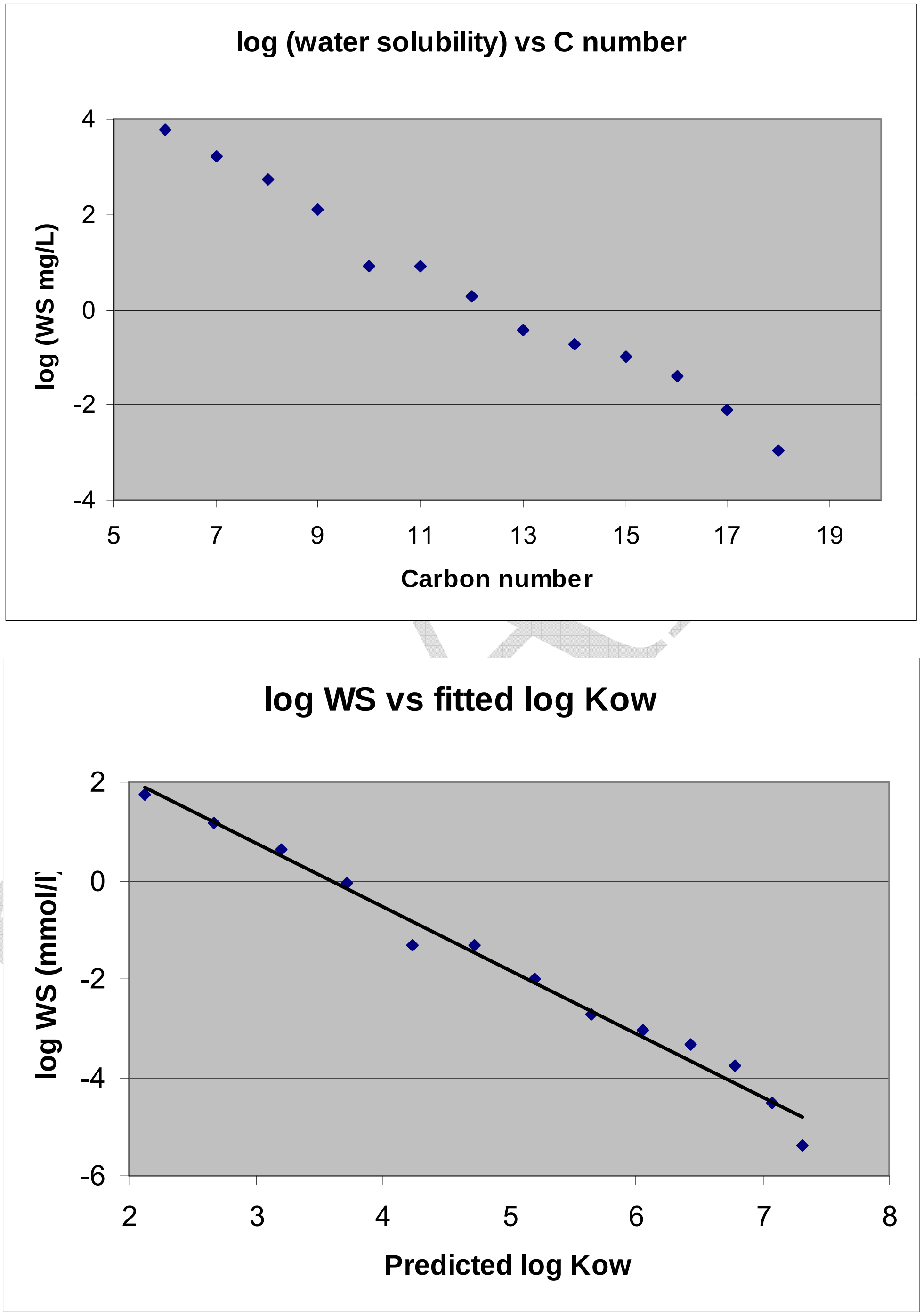
The value of log K_{ow} derived by the equation reaches a peak at around C20 and then begins to drop again. It would be expected that, experimentally, values of log K_{ow} reach a plateau and that the values would not drop again. Therefore for C21 and C22, the same value is read-across from C20. For the multi-component sponsored substances, there cannot be a single value of log K_{ow}. However, the values for the components present are relevant. The presence of branched components is not expected to significantly affect the predicted value.

SOLUBILITY IN WATER

Many established (Q)SARs derive WS based on a correlation with log K_{ow}. Reliable measured water solubility values were available for most of the single-component alcohols. Plotting the values against log K_{ow}, as shown in Figure A.I.7, showed a clear correlation. The data are shown in Table A.I.7

Figure A.I.7. Plot of measured or predicted log K_{ow} vs. water solubility for single-component alcohols

a) Carbon number dependence



b) log K_{ow} dependence

Regression analysis gave the following equation:

$$\text{Log WS (mmol/l)} = -1.284 \times \text{Log } K_{ow} + 4.600$$

Regression Statistics	
Multiple R	0.992639
R Square	0.985332
Adjusted R Square	0.983998
Standard Error	0.282339
Observations	13

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1	58.90287	58.90287	738.9143	1.95E-11
Residual	11	0.87687	0.079715		
Total	12	59.77974			

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	4.599957	0.249511	18.43587	1.28E-09	4.050787	5.149128
log Kow fitted	-1.28422	0.047243	-27.183	1.95E-11	-1.3882	-1.18023

The value is converted into the standard units of mg/L by multiplying by the molecular weight of the substance. It must be noted that the (Q)SAR is not strictly valid outside the range of carbon numbers it was based on.

Table A.I.7. Measured and predicted water solubility for single component substances

Carbon Number	Predicted Water Solubility mg/L [1]	Measured value used in regression mg/L	Other values mg/L
C6	7671.3	5900	6270
C7	1743.6	1670	1600, 1313, 900
C8	400.7	551	495-596, 587, 540, 500
C9	94.2	128	100, 140, 158
C10	22.9	39.5	7.97, 34, 37, 40
C11	5.8	8	8.5
C12	1.6	1.93	1.9, 4.0
C13	4.51E-01	0.38	0.33
C14	1.41E-01	0.191	
C15	4.90E-02	0.102	
C16	1.90E-02	0.013	
C17	8.42E-03	0.008	
C18	4.33E-03	0.0011	
C20	1.93E-03	-	
C22	1.98E-03	-	

Note: 1 Calculated for a 100% pure ideal substance, not necessarily a commercial grade;

Multi-component substances, such as several of the sponsored substances in the long chain alcohols category, have a more complex behaviour in water due to the role of partitioning effects. However, a model of such effects, developed primarily for use in predicting ecotoxicity, also allows the prediction of solubility of the mixture. By manipulation of various factors, it is possible to determine the loading rate at which ~100% is dissolved, and this is effectively the solubility of the mixture. The model itself is described in more detail in Annex IX, but the water solubilities of the various sponsored Category-member mixtures are given in Table A.I.8 below.

Table A.I.8. Predicted water solubilities of multi-component alcohols

CAS	Chemical Name	Comment [1]	Predicted Solubility in water	Solubility predicted at a loading rate of:
85566-12-7	C8-10 Alcohols		202 mg/L.	1000 mg/L
68603-15-6	C6-12 Alcohols	Type A	9.7 mg/L	1000 mg/L
		Type B	43.9 mg/L	1000 mg/L
		Type C	510 mg/L	1000 mg/L
		Type D	293 mg/L	1000 mg/L
66455-17-2	C9-11 Alcohols		44 mg/L.	1000 mg/L
75782-86-4	C12-13 Alcohols		1.1 mg/L.	1000 mg/L
67762-41-8	C10-16 Alcohols	Type A	7.1 mg/L	1000 mg/L
		Type B	1.1 mg/L [2]	1000 mg/L
		Type C	0.67 mg/L	1000 mg/L
		Type D	0.67 mg/L	1000 mg/L
80206-82-2	C12-14 Alcohols	Type A	4.6 mg/L	1000 mg/L
		Type B	2.8 mg/L	1000 mg/L
68855-56-1	C12-16 Alcohols	Type A	0.69 mg/L	1000 mg/L
		Type B	3.2 mg/L	1000 mg/L
		Type C	0.42 mg/L	1000 mg/L
63393-82-8	C12-15 Alcohols	Type A	0.63 mg/L	1000 mg/L
		Type B	0.67 mg/L	1000 mg/L
67762-25-8	C12-18 Alcohols	Type A	1.7 mg/L	100 mg/L
		Type B	0.35 mg/L	1000 mg/L
75782-87-5	C14-15 Alcohols		0.15 mg/L.	1000 mg/L
68333-80-2	C14-16 Alcohols	Type A	0.15 mg/L	1000 mg/L
		Type B	0.64 mg/L	1000 mg/L
67762-30-5	C14-18 Alcohols	Type A	0.04 mg/L	1000 mg/L
		Type B	0.12 mg/L	1000 mg/L
67762-27-0	C16-18 Alcohols		0.030 mg/L	1000 mg/L
68002-94-8	C16-18 and C18 Unsaturated		0.045 mg/L	1000 mg/L
97552-91-5	C18-22 Alcohol		0.0056 mg/L.	1000 mg/L
68155-00-0	Alcohols, C14-18 and C16-18-unsatd.		0.024 mg/L	1000 mg/L
85665-26-5	Alcohols, C10-12		34 mg/L.	1000 mg/L
68551-07-5	Alcohols, C8-18		26.52 mg/L	1000 mg/L

Notes

1 – Compositional 'types' are discussed in section 1.3 of the SIAR.

2 –A measured value of 2.9 mg/L is available (see IUCLID dossier).

ANNEX II: COMPARISON OF DIFFERENT (Q)SAR METHODS FOR PROPERTY PREDICTION FOR THE ALCOHOLS CATEGORY

Introduction

In the category justification, significant use of quantitative structure-activity relationships is made, particularly in respect of physicochemical properties and ecotoxicity. Due to the high abundance of measured data for single components, relatively little data gap filling by (Q)SAR is needed. The general principle that has been adopted is to validate (Q)SARs where they are needed, and to use measured physicochemical properties as inputs if possible.

An important example is provided by the treatment of aquatic ecotoxicity. Regression of measured log EC50 values against log K_{ow} has been performed, and the results are considered to be more useful than more general (Q)SARs available from the literature, such as ECOSAR from the EPI Suite package. However, the findings are in line with expectations for narcotic substances.

In respect of physicochemical properties, extensive use of the validated Syracuse Research Corporation methods in the EPI Suite package is made. It is reasonable to consider whether other methods might provide substantially better results. For example, in the model used to predict log K_{ow}, the KOWWIN output has been modified by a term in the carbon number. It could be that another method might not need such a modification. This Annex compares the performance of several other computer programs and the SRC package.

Programs that have been examined and the criteria used

The programs evaluated were:

KOWWIN
Pallas
MMP
SPARC
Interactive Analysis
CLOGP
ADME Boxes

Some of these programs can only be used for certain end points.

References and a brief summary are given at the end of this document.

The extent of review has, in general, been only as detailed as appeared to be necessary from a qualitative evaluation.

Individual properties

Melting point has not been considered since it is not of significance for this category.

Log K_{ow}

All the methods (Table A.II.1) show a linear increase in the predicted value for each successive carbon added. In general it might be argued that the model MMP-2 predicts the order of magnitude better than the other models. In practice this is not important for the present work because the approach used in the SIAR has been to model measured log K_{ow} as a function of the KOWWIN prediction and carbon number.

Solubility in water

Visual inspection of Table A.II.2 suggests that either WSKOWWIN or SPARC predict water solubility well, and probably SPARC is the most effective. In practice this is not important for the present work because the approach used in the SIAR has been to model measured water solubility as a function of the WSKOWWIN prediction, which provides very good predictions.

Table A.II.1. log K_{ow}: measured vs EPISUITE vs other methods

CAS No	C	Chemical Name	MW	log Kow	KOWWIN	Pallas-1	Pallas-2	Pallas-3	Pallas-com	MMP-1	MMP-2	MMP-3	MMP-4	SPARC	IA	CLOG P	ADME Boxes
111-27-3	6	1-Hexanol	102.2	2.03	2.31	1.91	2.10	1.80	1.94	1.88	1.74	1.79	1.59	2.03	1.83	1.88	1.87
111-70-6	7	1-Heptanol	116.23	2.57	2.81	2.38	2.42	2.43	2.38	2.44	2.31	2.39		2.52			
111-87-5	8	1-Octanol	130.26	3.15	3.30	2.84	2.92	2.95	2.86	2.94	2.53	2.75	2.27	3.01		2.94	
143-08-8	9	1-Nonanol	144.29	3.77	3.79	3.31	3.43	3.47	3.33	3.50	3.10	3.34		3.51			
112-30-1	10	1-Decanol	158.32	4.57	4.28	3.78	3.94	3.99	3.80	4.00	3.32	3.70	2.89	4.02	4.07	4	3.82
112-42-5	11	1-Undecanol	172.35	4.72	4.77	4.24	4.44	4.51	4.27	4.56	3.89	4.30		4.54			
112-53-8	12	1-Dodecanol	186.38	5.36	5.26	4.71	4.95	5.03	4.75	5.08	4.29	4.78		5.03		5.06	
112-70-9	13	1-Tridecanol	200.41	5.51	5.75	5.18	5.46	5.55	5.22	5.61	4.68	5.25		5.59			
112-72-1	14	1-Tetradecanol	214.44	6.03	6.24	5.65	5.97	6.07	5.69	6.11	4.91	5.61	4.00	6.10	6.38	6.11	5.76
36653-82-4	16	1-Hexadecanol	242.5	6.65	7.23	6.58	6.98	7.10	6.64	7.20	5.87	6.69		7.12			
112-92-5	18	1-Octadecanol	270.56	7.19	8.21	7.51	7.99	8.14	7.58	8.23	6.49	7.52	4.99	8.14	8.35	8.23	7.7
629-96-9	20	1-Eicosanol	298.62	7.75	9.19	8.45	9.01	9.18	8.53	9.32	7.46	8.60		9.16			
661-19-8	22	1-Docasonal	326.61		9.68	9.38	10.21	10.11	9.50	10.35	8.08	9.44	5.89	10.20	8.26	10.34	9.64

Table A.II.2. Solubility in water: measured vs. EPISUITE vs. SPARC

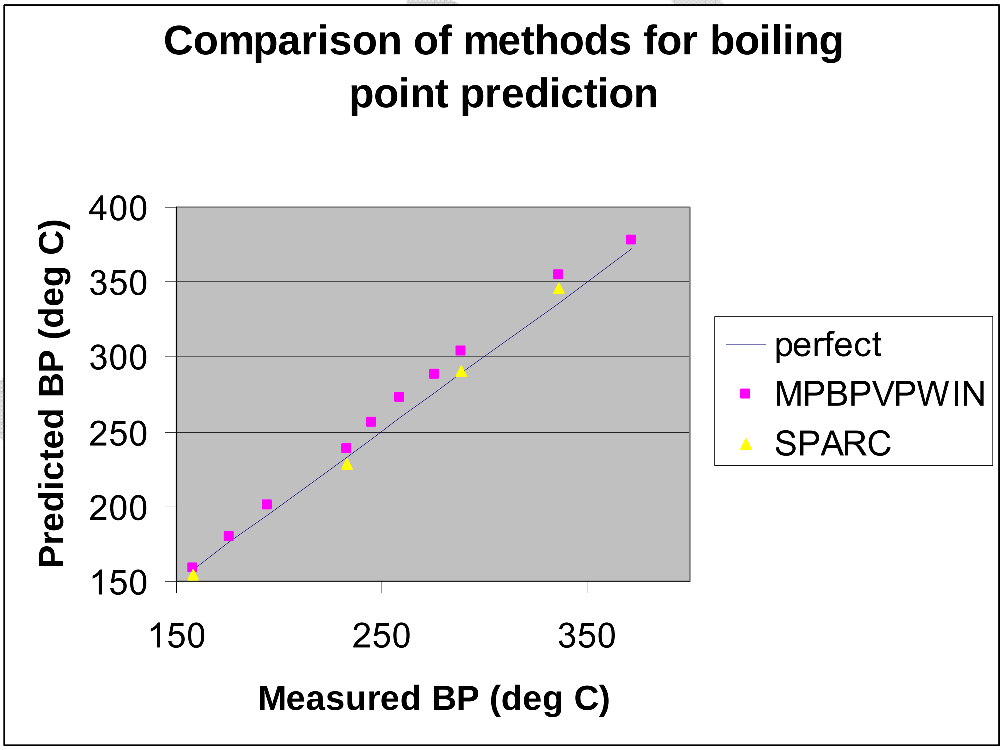
CAS No	C	Chemical Name	MW	Water Solubility (mg/L)	MMP WS-1	WSKOW-WIN NO MP	WSKOWWIN WITH MP	SPARC – with PREDICTED MP	IA	ADME Boxes	WATERNT (EPISUITE)
111-27-3	6	1-Hexanol	102.2	5900	6445	6884		5375	16228	8610	7136
111-70-6	7	1-Heptanol	116.23	1313		2140		1577	3748	3940	2357
111-87-5	8	1-Octanol	130.26	550	750	814		466	757	161	767
143-08-8	9	1-Nonanol	144.29	128		157		131	148	176	247
112-30-1	10	1-Decanol	158.32	39.5	83.1	81.5		37.3	30	31.2	78.6
112-42-5	11	1-Undecanol	172.35	8		18.1		10.2	7.21	22.3	24.8
112-53-8	12	1-Dodecanol	186.38	1.93		4.4		3	2.13	11.1	7.8
112-70-9	13	1-Tridecanol	200.41	0.38			2.81	0.74	0.808	0.41	2.43
112-72-1	14	1-Tetradecanol	214.44	0.19	0.94		0.74	0.2	0.382	0.18	0.76
36653-82-4	16	1-Hexadecanol	242.5	0.013			0.14	0.01	0.158	0.46	0.072
112-92-5	18	1-Octadecanol	270.56	0.0011	0.01		0.031	1.03E-03	0.117	0.04	0.0068
629-96-9	20	1-Eicosanol	298.62				0.007	0.0002	0.118	0.00002	0.00063
661-19-8	22	1-Docasonal	326.61		0.0001			6.89E-05	0.276	0.01	

Boiling point

Inspection of Table A.II.3 and the graph shows that both the readily available methods are effective.

Table A.II.3. Boiling points: measured vs. EPISUITE vs. SPARC

CAS No	C	Chemical Name	MW	BP (°C)	MPBPVPWIN	SPARC
111-27-3	6	1-Hexanol	102.2	158	159.09	154
111-70-6	7	1-Heptanol	116.23	176	180.33	
111-87-5	8	1-Octanol	130.26	194.5	200.67	
1430-8-8	9	1-Nonanol	144.29		220.09	
112-30-1	10	1-Decanol	158.32	233	238.62	228
1124-2-5	11	1-Undecanol	172.35	245	256.24	
112-53-8	12	1-Dodecanol	186.38	259	272.96	
1127-0-9	13	1-Tridecanol	200.41	276	288.77	
112-72-1	14	1-Tetradecanol	214.44	289	303.68	291
36653-82-4	16	1-Hexadecanol	242.5		330.79	
112-92-5	18	1-Octadecanol	270.56	336	354.66	346
629-96-9	20	1-Eicosanol	298.62	372	377.87	

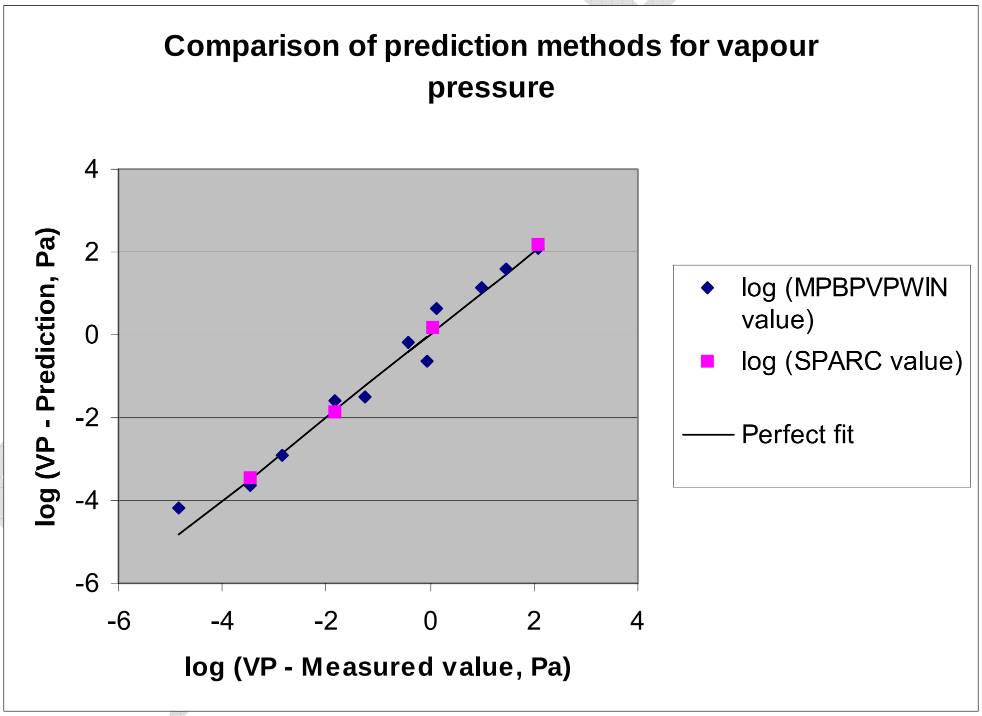


Vapour pressure

Inspection of Table A.II.4 shows that both the readily available methods are effective.

Table A.II.4. Vapour pressure: measured vs. EPISUITE vs. SPARC

CAS No	C	Chemical Name	MW	VP (Pa)	MPBPVPWIN	SPARC (predicted MP)
111-27-3	6	1-Hexanol	102.2	122	117.173	151.3
111-70-6	7	1-Heptanol	116.23	28	39.767	
111-87-5	8	1-Octanol	130.26	10	13.167	
143-08-8	9	1-Nonanol	144.29	1.33	4.3624	
112-30-1	10	1-Decanol	158.32	1.1	1.4497	1.45
112-42-5	11	1-Undecanol	172.35	0.39501	0.6783	
112-53-8	12	1-Dodecanol	186.38	0.87	0.24073	
112-70-9	13	1-Tridecanol	200.41	0.057	0.031521	
112-72-1	14	1-Tetradecanol	214.44	0.01463	0.026733	0.014
36653-82-4	16	1-Hexadecanol	242.5	0.0014	0.00118769	
112-92-5	18	1-Octadecanol	270.56	0.00033	0.00024339	3.50E-04
629-96-9	20	1-Eicosanol	298.62	0.000015	0.0000665	



Further information about the programs examined:

EPISUITE [http://www.syrres.com]
Includes several programs named above:
KOWWIN: a fragment based method
WSKOWWIN: based on the correlation with log K_{ow}, melting point and molecular weight.
MPBPVPWIN: the boiling point is derived from a fragment method. Vapour pressure and melting point are derived from the boiling point by calculation.

Pallas

The Pallas suite of programs contains three methods and then produces a weighted average of them. Pallas–1 is a group-based fragment method, Pallas-2 is an atom-based fragment method, and Pallas-3 is the Rekker method

MMP [http://www.chemistry-software.com/pdf/molecular%20modeling%20pro.pdf]

MMP-1 is an unspecified fragment method based on group fragments.
MMP-2 is an unspecified fragment method based on atom fragments.
MMP-3 is is the method of N. Bodor and P. Buchwald (J. Phys. Chem. B, 1997, 101:3404-3412).
The water solubility method is based on the S. Yalkowsky equation (J. Pharm. Sci, 70: 971) which is a correlation with log K_{ow}.

SPARC [http://ibmlc2.chem.uga.edu/sparc/]

It is not clear from the site how the properties are calculated. It is clear from the output that the water solubility is calculated from a set of basic properties rather than from log K_{ow}.

Interactive Analysis [http://www.logp.com/]

It is not clear from the site how the properties are calculated.

CLOGP[http://www.biobyte.com/]

This is a group based fragment method.

ADME Boxes [http://ap-algorithms.com/predictors.htm]

It is not clear from the site how the properties are calculated.

ANNEX III: NON-CONFIDENTIAL PRODUCT REGISTER AND SPIN DATA BASE DERIVED DATA

Data from the Nordic countries product registers, obtained via the SPIN database, suggests that long chain alcohols are used in a wide range of applications. The data are set out below.

The data presented (Tables A.III.1 to 3) are for the year 2002 (or an earlier year, depending on the available data for the specific substance), and represent the most recent data available at the time of searching. These results are supported by data for earlier years, which are not reproduced here.

TABLE A.III.1 TOTAL USE TONNAGES

Country	Year	# preparations	Tonnes	Consumer preparations	Confidential
CAS no: 111-27-3	Name:	1-Hexanol			
S	2002	9	96.0		
N	2002	17	1.7	X	
DK	2002	44	0.3		
FIN	2002				Yes
CAS no: 111-87-5	Name:	1-Octanol			
DK	2002	38	4.5		
S	2002	16	3.0	Yes	
N	2002	17	0.8	X	
FIN	2002				Yes
CAS no: 112-30-1	Name:	1-Decanol			
S	2002	24	53.0	Yes	
DK	2002	158	1.4		
N	2002	34	0.6	X	
CAS no: 112-42-5	Name:	1-Undecanol			
DK	2002	7	0.0		
S	2002				Yes
CAS no: 112-70-9	Name:	1-Tridecanol			
S	2002	9	0.0	Yes	
N	2002				Yes
DK	2002				Yes
CAS no: 112-72-1	Name:	1-Tetradecanol			
S	2002	42	100.0	Yes	
DK	2002	8	17.9		
N	2002	6	0.1		
CAS no: 143-08-8	Name:	1-Nonanol			
DK	2002	40	0.0		
N	2002	5	0.0		
CAS no: 143-28-2	Name:	9-Octadecen-1-ol, (Z)-			
DK	2002	12	1.0		
N	2002	6	0.0	X	
S	2002	6	0.0		
FIN	2002				Yes
CAS no: 629-76-5	Name:	1-Pentadecanol			
DK	2002				Yes
CAS no: 629-96-9	Name:	1-Eicosanol			
S	2002				Yes
CAS no: 661-19-8	Name:	1-Docosanol			
S	2002				Yes
CAS no: 36653-82-4	Name:	1-Hexadecanol			
S	2002	65	51.0	Yes	

Country	Year	# preparations	Tonnes	Consumer preparations	Confidential
N	2002	30	4.6	X	
DK	2002	69	1.6		
FIN	2002				Yes
CAS no: 63393-82-8	Name:	Alcohols, C12-15			
DK	2002				Yes
S	2002				Yes
CAS no: 66455-17-2	Name:	Alcohols, C9-11			
S	2002				Yes
CAS no: 67762-25-8	Name:	Alcohols, C12-18			
DK	2002	6	34.5		
S	2002	7	5.0		
N	2002				Yes
FIN	2002				Yes
CAS no: 67762-27-0	Name:	Alcohols, C16-18			
S	2002	65	332.0	Yes	
DK	2002	17	31.4		
N	2002				Yes
FIN	2002				Yes
CAS no: 67762-30-5	Name:	Alcohols, C14-18			
S	2002	4	9.0	Yes	
N	2002				Yes
DK	2002				Yes
CAS no: 67762-41-8	Name:	Alcohols, C10-16			
DK	2002	14	8.0		
S	2002	13	2.0	Yes	
N	2002	9	0.2	X	
FIN	2002				Yes
CAS no: 68002-94-8	Name:	Alcohols, C16-18 and C18-unsatd.			
S	2002	25	91.0		
DK	2002	25	0.7		
N	2002				Yes
CAS no: 68155-00-0	Name:	Alcohols, C14-18 and C16-18-unsatd.			
S	2002				Yes
CAS no: 68333-80-2	Name:	Alcohols, C14-16			
S	2002				Yes
CAS no: 68551-07-5	Name:	Alcohols, C8-18			
DK	2002	5	8.1		
N	2002				Yes
S	2002				Yes
CAS no: 68603-15-6	Name:	Alcohols, C6-12			
DK	2002	47	273.2		
N	2002	8	16.7		
S	2002	14	0.0		
CAS no: 68855-56-1	Name:	Alcohols, C12-16			
S	2002	14	148.0	Yes	
DK	2002	8	11.8		
N	2002			X	Yes
CAS no: 75782-86-4	Name:	Alcohols, C12-13			
DK	2002				Yes
S	2002				Yes
CAS no: 80206-82-2	Name:	Alcohols, C12-14			
DK	2002	32	3.2		
N	2002	5	0.3		
S	2002			Yes	Yes

Country	Year	# preparations	Tonnes	Consumer preparations	Confidential
FIN	2002				Yes
CAS no: 85566-12-7	Name:	Alcohols, C8-10			
DK	2002				Yes
S	2002				Yes
CAS no: 85665-26-5	Name:	Alcohols, C10-12			
DK	2002				Yes
CAS no: 97552-91-5	Name:	Alcohols, C18-22			
S	2002				Yes
CAS no: 97659-45-5	Name:	Alcohols, C18-20			
S	2002				Yes
CAS no: 112-53-8	Name:	1-Dodecanol			
S	2002	35	103.0	Yes	
DK	2002	116	18.8		
N	2002	17	7.0	X	
CAS no: 112-92-5	Name:	1-Octadecanol			
S	2002	34	39.0	Yes	
DK	2002	19	1.6		
N	2002	4	0.1		
FIN	2002				Yes
CAS no: 123-51-3	Name:	1-Butanol, 3-methyl-			
DK	2002	16	3.1		
S	2002	6	1.0	Yes	
FIN	2002				Yes
CAS no: 68516-18-7	Name:				
DK	2002				Yes

TABLE A.III.2: INDUSTRIAL USES

Country	Year	Code		# prep	Tonnes
CAS no: 111-27-3	Name:	1-Hexanol			
S	2002	24	Manufacture of chemicals and chemical products	3	96.0
DK	2002	15	Manufacture of food products and beverages	5	0.3
DK	2002	45	Construction	17	0.0
DK	2002	95	Private households with employed persons	11	0.0
DK	2002	74	Other business activities	11	0.0
N	2002	45	Construction	4	0.0
FIN	2002	1	Agriculture and horticulture		
FIN	2002	24	Manufacture of chemicals and chemical products		
CAS no: 111-87-5	Name:	1-Octanol			
S	2002	24	Manufacture of chemicals and chemical products	6	2.0
DK	2002	15	Manufacture of food products and beverages	9	0.2
N	2002	15	Manufacture of food products and beverages	7	0.1
DK	2002	28	Manufacture of fabricated metal products, except machinery and equipment	5	0.0
N	2002	50	Sale, maintenance and repair of motor vehicles and motorcycles; retail sale of automotive fuel	8	0.0
FIN	2002	1	Agriculture and horticulture		
CAS no: 112-30-1	Name:	1-Decanol			
S	2002	24	Manufacture of chemicals and chemical products	6	52.0
DK	2002	24	Manufacture of chemicals and chemical products	17	2.3
DK	2002	15	Manufacture of food products and beverages	14	0.8
N	2002	24	Manufacture of chemicals and chemical products	4	0.3
DK	2002	50	Sale, maintenance and repair of motor vehicles and motorcycles; retail sale of automotive fuel	19	0.2
DK	2002	85	Health and social work	8	0.2
DK	2002	93	Other service activities	9	0.1
DK	2002	45	Construction	10	0.1
N	2002	15	Manufacture of food products and beverages	6	0.1
DK	2002	28	Manufacture of fabricated metal products, except machinery and equipment	5	0.0
DK	2002	55	Hotels and restaurants	7	0.0
DK	2002	74	Other business activities	14	0.0
DK	2002	95	Private households with employed persons	6	0.0
DK	2002	35	Manufacture of other transport equipment n.e.c.	7	0.0
N	2002	50	Sale, maintenance and repair of motor vehicles and motorcycles; retail sale of automotive fuel	7	0.0
N	2002	74	Other business activities	8	0.0

Country	Year	Code		# prep	Tonnes
CAS no: 112-70-9	Name:	1-Tridecanol			
S	2000	22	Publishing, printing and reproduction of recorded media	3	0.0
CAS no: 112-72-1	Name:	1-Tetradecanol			
S	2002	24	Manufacture of chemicals and chemical products	9	91.0
N	2002	85	Health and social work	6	0.0
CAS no: 143-08-8	Name:	1-Nonanol			
DK	2002	74	Other business activities	4	0.0
DK	2002	95	Private households with employed persons	4	0.0
N	2002	55	Hotels and restaurants	5	0.0
CAS no: 143-28-2	Name:	9-Octadecen-1-ol, (Z)-			
DK	2002	28	Manufacture of fabricated metal products, except machinery and equipment	7	0.6
DK	2002	50	Sale, maintenance and repair of motor vehicles and motorcycles; retail sale of automotive fuel	4	0.0
FIN	2002	1	Agriculture and horticulture		
CAS no: 36653-82-4	Name:	1-Hexadecanol			
S	2002	24	Manufacture of chemicals and chemical products	20	47.0
N	2002	24	Manufacture of chemicals and chemical products	4	4.5
S	2002	51	Wholesale trade and commission trade, except of motor vehicles and motorcycles	28	1.0
DK	2002	95	Private households with employed persons	6	0.5
DK	2002	50	Sale, maintenance and repair of motor vehicles and motorcycles; retail sale of automotive fuel	11	0.4
DK	2002	28	Manufacture of fabricated metal products, except machinery and equipment	19	0.4
DK	2002	45	Construction	30	0.3
N	2002	45	Construction	5	0.1
N	2002	35	Manufacture of other transport equipment n.e.c.	16	0.0
N	2002	25	Manufacture of rubber and plastic products	12	0.0
FIN	2002	24	Manufacture of chemicals and chemical products		
CAS no: 67762-25-8	Name:	Alcohols, C12-18			
FIN	2002	24	Manufacture of chemicals and chemical products		
CAS no: 67762-27-0	Name:	Alcohols, C16-18			
S	2002	24	Manufacture of chemicals and chemical products	36	316.0
S	2002	51	Wholesale trade and commission trade, except of motor vehicles and motorcycles	10	10.0
S	2002	25	Manufacture of rubber and plastic products	3	1.0
S	2002	1	Agriculture and horticulture	3	0.0

Country	Year	Code		# prep	Tonnes
S	2002	50	Sale, maintenance and repair of motor vehicles and motorcycles; retail sale of automotive fuel	4	0.0
FIN	2002	24	Manufacture of chemicals and chemical products		
CAS no: 67762-41-8	Name:	Alcohols, C10-16			
S	2002	24	Manufacture of chemicals and chemical products	5	2.0
DK	2002	50	Sale, maintenance and repair of motor vehicles and motorcycles; retail sale of automotive fuel	4	0.1
N	2002	50	Sale, maintenance and repair of motor vehicles and motorcycles; retail sale of automotive fuel	6	0.0
CAS no: 68002-94-8	Name:	Alcohols, C16-18 and C18-unsatd.			
S	2002	28	Manufacture of fabricated metal products, except machinery and equipment	15	2.0
DK	2002	28	Manufacture of fabricated metal products, except machinery and equipment	6	0.4
CAS no: 68603-15-6	Name:	Alcohols, C6-12			
DK	2002	50	Sale, maintenance and repair of motor vehicles and motorcycles; retail sale of automotive fuel	7	0.1
DK	2002	74	Other business activities	16	0.0
N	2002	60	Land transport; transport via pipelines	5	0.0
DK	2002	60	Land transport; transport via pipelines	4	0.0
DK	2002	45	Construction	5	0.0
DK	2002	85	Health and social work	4	0.0
DK	2002	15	Manufacture of food products and beverages	4	0.0
CAS no: 68855-56-1	Name:	Alcohols, C12-16			
S	2002	24	Manufacture of chemicals and chemical products	5	76.0
CAS no: 80206-82-2	Name:	Alcohols, C12-14			
FIN	2002	24	Manufacture of chemicals and chemical products		
CAS no: 112-53-8	Name:	1-Dodecanol			
S	2002	24	Manufacture of chemicals and chemical products	9	91.0
DK	2002	24	Manufacture of chemicals and chemical products	33	10.1
DK	2002	15	Manufacture of food products and beverages	13	0.4
DK	2002	28	Manufacture of fabricated metal products, except machinery and equipment	6	0.3
DK	2002	45	Construction	19	0.1
DK	2002	74	Other business activities	11	0.0
N	2002	15	Manufacture of food products and beverages	7	0.0
DK	2002	29	Manufacture of machinery and equipment	4	0.0
DK	2002	50	Sale, maintenance and repair of motor vehicles and motorcycles; retail sale of automotive fuel	8	0.0

Country	Year	Code		# prep	Tonnes
DK	2002	95	Private households with employed persons	5	0.0
S	2002	50	Sale, maintenance and repair of motor vehicles and motorcycles; retail sale of automotive fuel	9	0.0
S	2002	51	Wholesale trade and commission trade, except of motor vehicles and motorcycles	10	0.0
S	2002	52	Retail trade, except of motor vehicles and motorcycles; repair of personal and household goods	11	0.0
CAS no: 112-92-5	Name:	1-Octadecanol			
S	2002	24	Manufacture of chemicals and chemical products	21	21.0
DK	2002	45	Construction	6	0.0
FIN	2002	24	Manufacture of chemicals and chemical products		
CAS no: 123-51-3	Name:	1-Butanol, 3-methyl-			
FIN	2002	85	Health and social work		

TABLE A.III.3: USE CATEGORIES

Country	Year	Code		# prep	Tonnes
CAS no: 111-27-3	Name:	1-Hexanol			
DK	2002	26	Food/feedstuff flavourings and nutrients	4	0.1
DK	2002	59	Paints, laquers and varnishes	21	0.0
DK	2002	9	Cleaning/washing agents	5	0.0
N	2002	59	Paints, laquers and varnishes	8	0.0
FIN	2002	38	Pesticides, agricultural		
FIN	2002	55	Others		
CAS no: 111-87-5	Name:	1-Octanol			
DK	2002	50	Surface-active agents	4	3.8
DK	2002	9	Cleaning/washing agents	16	0.6
N	2002	9	Cleaning/washing agents	16	0.5
DK	2002	61	Surface treatment	4	0.0
FIN	2002	2	Adhesives, binding agents		
FIN	2002	38	Pesticides, agricultural		
CAS no: 112-30-1	Name:	1-Decanol			
DK	2002	50	Surface-active agents	4	0.8
DK	2002	9	Cleaning/washing agents	67	0.4
N	2002	9	Cleaning/washing agents	27	0.2
DK	2002	2	Adhesives, binding agents	5	0.1
DK	2002	61	Surface treatment	6	0.1
DK	2002	59	Paints, laquers and varnishes	15	0.0
S	2002	9	Cleaning/washing agents	6	0.0
S	2002	50	Surface-active agents	4	0.0
CAS no: 112-70-9	Name:	1-Tridecanol			
S	2000	59	Paints, laquers and varnishes	3	1.0
CAS no: 112-72-1	Name:	1-Tetradecanol			
S	2002	55	Others	5	88.0
S	2002	35	Lubricants and additives	10	8.0
CAS no: 143-08-8	Name:	1-Nonanol			
DK	2002	9	Cleaning/washing agents	9	0.0
N	2002	9	Cleaning/washing agents	5	0.0
CAS no: 143-28-2	Name:	9-Octadecen-1-ol, (Z)-			
DK	2002	5	Anti-freezing agents	4	0.0
FIN	2002	38	Pesticides, agricultural		
CAS no: 629-96-9	Name:	1-Eicosanol			
S	2000	55	Others	8	29.0
CAS no: 661-19-8	Name:	1-Docosanol			
S	2000	55	Others	4	15.0
CAS no: 36653-82-4	Name:	1-Hexadecanol			
S	2002	55	Others	15	46.0
S	2002	50	Surface-active agents	18	5.0
DK	2002	15	Cosmetics	10	0.7
DK	2002	14	Corrosion inhibitors	5	0.6
DK	2002	59	Paints, laquers and varnishes	8	0.4
N	2002	13	Construction materials	19	0.1
DK	2002	9	Cleaning/washing agents	5	0.0
S	2002	9	Cleaning/washing agents	4	0.0
FIN	2002	41	Pharmaceuticals		
FIN	2002	55	Others		
CAS no: 67762-25-8	Name:	Alcohols, C12-18			

Country	Year	Code		# prep	Tonnes
FIN	2002	9	Cleaning/washing agents		
CAS no: 67762-27-0	Name:	Alcohols, C16-18			
S	2002	55	Others	29	316.0
S	2002	50	Surface-active agents	9	13.0
DK	2002	15	Cosmetics	5	0.4
S	2002	41	Pharmaceuticals	8	0.0
FIN	2002	55	Others		
CAS no: 67762-41-8	Name:	Alcohols, C10-16			
DK	2002	9	Cleaning/washing agents	6	0.9
FIN	2002	48	Solvents	4	0.2
N	2002	9	Cleaning/washing agents	15	0.0
S	2002	9	Cleaning/washing agents	6	0.0
FIN	2002	35	Lubricants and additives		
CAS no: 68603-15-6	Name:	Alcohols, C6-12			
DK	2002	9	Cleaning/washing agents	42	0.2
N	2002	61	Surface treatment	9	0.0
CAS no: 68855-56-1	Name:	Alcohols, C12-16			
S	2002	55	Others	4	59.0
S	2002	35	Lubricants and additives	3	0.0
N	2000	59	Paints, laquers and varnishes	8	0.0
CAS no: 80206-82-2	Name:	Alcohols, C12-14			
N	2002	9	Cleaning/washing agents	4	0.1
DK	2002	9	Cleaning/washing agents	13	0.1
FIN	2002	9	Cleaning/washing agents		
CAS no: 112-53-8	Name:	1-Dodecanol			
S	2002	35	Lubricants and additives	10	18.0
S	2002	50	Surface-active agents	6	1.0
DK	2002	9	Cleaning/washing agents	40	0.9
DK	2002	59	Paints, laquers and varnishes	22	0.3
N	2002	9	Cleaning/washing agents	13	0.1
DK	2002	36	Odour agents	33	0.0
CAS no: 112-92-5	Name:	1-Octadecanol			
S	2002	50	Surface-active agents	8	15.0
S	2002	55	Others	14	13.0
DK	2002	15	Cosmetics	4	0.0
FIN	2002	41	Pharmaceuticals		
CAS no: 123-51-3	Name:	1-Butanol, 3-methyl-			
FIN	2002	34	Laboratory chemicals		

ANNEX IV: PRODUCTION, USE AND HUMAN EXPOSURE INFORMATION

Purpose

To provide high end to bounding estimates of the potential human exposure to Long chain aliphatic alcohols (C6-C22) (LCAA) to complement the OECD SIDS Programme review of this category. For this purpose the following categories will be assessed:

- Manufacture,
- Use in industry,
- Commercial or professional applications and
- Use in consumer products.

Coverage

The report covers exposure from manufacturing, industrial use, commercial or professional applications and consumer use for LCAA volumes produced and used in North America, Europe and Asia.

Modelling of potential LCAA exposures to the consumer from the use products containing long chain aliphatic alcohols are presented in this Annex IV. Sources and routes of environmental exposures and potential indirect human exposures are also presented, and discussed in the SIAR in respect of the interpretation of measured environmental concentrations.

Identity of Organization Long Chain Aliphatic Alcohols Consortium
The Soap and Detergent Association,
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1500 K St. NW, Suite 300, Washington, DC 20005

General Information

I. Substance information

(1) Category name

Long Chain Aliphatic Alcohols (C6-C22)

(2) Substance Name(s) and CAS RN

CAS no.	Chemical name
111-27-3	1-Hexanol
111-87-5	1-Octanol
112-30-1	1-Decanol
112-42-5	1-Undecanol
112-70-9	1-Tridecanol
112-72-1	1-Tetradecanol
629-76-5	1-Pentadecanol
36653-82-4	1-Hexadecanol
143-28-2	9-Octadecen-1-ol, (9Z)-
629-96-9	1-Eicosanol
661-19-8	1-Docosanol
63393-82-8	Alcohols, C12-15
66455-17-2	Alcohols, C9-11
67762-25-8	Alcohols, C12-18
67762-27-0	Alcohols, C16-18
67762-30-5	Alcohols, C14-18
67762-41-8	Alcohols, C10-16
68551-07-5	Alcohols, C8-18
68002-94-8	Alcohols, C16-18 and C18 Unsaturated
68155-00-0	Alcohols, C14-18 and C16-18-unsatd.
68333-80-2	Alcohols, C14-16
68603-15-6	Alcohols, C6-12
68855-56-1	Alcohols, C12-16
75782-86-4	Alcohols, C12-13
75782-87-5	Alcohols, C14-15
80206-82-2	Alcohols, C12-14
85566-12-7	Alcohols, C8-10
85665-26-5	Alcohols, C10-12
97552-91-5	Alcohols, C18-22
90583-91-8	Tridecanol, branched and linear

(3) Molecular Formula $C_xH_{(2x+1)}OH$ where x = 6 to 22

Molecular weight 102 to 326

(4) Physical Form

Members of the category of long chain aliphatic alcohols (C6 – C22) are liquid, waxy or solid

II. Summary

(1) Data Collection Efforts
Information in this assessment was assembled from a number of sources:

1) Member company surveys of the Long Chain Aliphatic Alcohols Consortium were used to collect data on production volumes, uses, releases, and potential exposures. To protect proprietary information, an independent third party compiled the resulting data (SDA, 2002)

2) Potential LCAA exposures to the consumer from the use products containing long chain aliphatic alcohols are estimated via modelling and summarized in Section V of this Annex.

(2) Discussion of Key Uncertainties, Limitations, Data Gaps

a) Manufacturers representing a significant majority of the Long Chain Aliphatic Alcohols (C6-22) production volume were involved in the industry survey. Thus, it is possible that there may be production volumes, minor uses and potential exposures beyond those addressed here. The exposure assessments in this annex address primarily the occupational exposure during manufacture, commercial use and consumer product use categories. Information regarding the potential occupational exposure during the use of certain products, in particular use conditions for certain industrial and professional applications is limited and these scenarios will therefore not be addressed in this exposure assessment.

b) This exposure assessment takes a conservative (protective) approach to modelling, selecting inputs based on conservative values for each parameter; thus modelled estimates are likely to significantly exceed actual exposures. For consumer exposure, The exposure scenarios encompass conservative, screening-level inputs (*ca.* 90th percentile) including: the high-end frequency of product use, the high-end amount of product per use, the high-end percent of product retained on skin or clothes following use. All modelled exposures include a default assumption of 100% dermal absorption and bioavailability. Thus, the use of multiple conservative input parameters results in modelled exposure estimates that are at least 1 – 2 orders of magnitude above the true exposure of a typical consumer.

c) Minor application or use of products with a low concentration of long chain aliphatic alcohols (<1%) have not been taken into account. Exposures from these scenarios are not significant compared to those that are discussed in detail. Also, uses of LCAA in applications that are regulated through national and international legislation (e.g. use of LCAA in some emulsifiers, pharmaceuticals, OTC's and agrochemical formulations) have not been included here.

(3) Exposure Results
Table A.IV.1 shows the estimated human exposures for the scenarios assessed.

Table A.IV.1: Summary of Consumer Exposure Scenarios and Estimated Exposures

Exposure Scenario	Estimated Exposure (mg/kg/day)
Indirect Exposure	
Drinking Water Consumption	Negligible (see SIAR section 2.2)
Fish Consumption	Negligible (see SIAR section 2.2)
Dermal Modelling	
Cleaning Products	
Laundry pre-treatment (undiluted)	5.5E-4 to 2.8E-3
Hand-wash of laundry (diluted)	4.3E-5 to 2.2E-4
Hard surface cleaner (diluted)	1.3E-4 to 6.5E-4
Hard surface cleaner (undiluted)	9.2E-4 to 4.6E-3
Laundry product residual on clothing	
Liquid detergent	1.9E-3 to 9.2E-3

Fabric Conditioner	1.7E-3 to 8.6E-3
Personal Care product residual after use	
Antiperspirants	3.7E-0 to 9.2E-0
Body moisturiser	2.8E-0 to 2.8E 1
Cleansing products	2.6E-3 to 2.6E-2
Face/Eye cosmetics	8.1E-1 to 4.1E-0
Hair conditioner	9.7E-3 to 9.7E-2
Hair styling tonic/gel	2.1E-1 to 2.1E-0
Inhalation Modelling	
Spray cleaner	3.6E-6 to 1.8E-5

III. Production, Import and Use

(1) Estimated Volume

N. America - ca. 600,000* tonnes/yr (SDA, 2002)
Europe - ca. 700,000* tonnes/yr (SDA, 2002)
Asia/Pacific - ca. 250,000* tonnes/yr (SDA, 2002)
* Volume rounded to nearest 50 or 100 kT

(2) Function/ Product Use Categories

Long Chain Aliphatic Alcohols (C6 – C22) are used in the manufacture of some major classes of ionic and anionic surfactants (ca. 50% of the manufactured volume). The remainder of the volume of the Long Chain Aliphatic Alcohols finds a wide range of application involving their lubricating, emollient, solubilising or emulsifying properties.

They are widely applied in industrial applications and can found many in products for professional use based on their lubricating, solubilising or emulsifying properties. Long Chain Aliphatic Alcohols (C6 – C22) find use in certain paints, lubricants, emulsifiers, flotation agents rolling and formwork oils. They are used as an additive in certain plastics, paper products and plaster and used in processing of textiles, leather and plastics. Long Chain Aliphatic Alcohols are present in some pharmaceutical products and agrochemical formulations.

Long Chain Aliphatic Alcohols are used in a wide range products intended for consumer products use:

- house hold cleaning products: Example laundry powder, general/hard surface cleaners, fabric conditioners),
- personal care products: Examples shampoo, hair conditioners, styling gel and mousse, cleaners, body washes, skin lotions and creams, antiperspirants, face and eye cosmetics, make up remover and hair dyes)
- fragrances and fragrance ingredients.

IV. Activities, Releases and Exposures — Factors that Mitigate or Exacerbate Exposures

Manufacture

(1) Process Description

1. **Production processes based on oleochemical feedstocks**

There are two major commercial processes for converting oleochemicals to alcohols :

Methyl Ester Hydrogenation – coconut and palm kernel oils and tallow fat are the major feedstocks for this route to alcohols. The triglycerides that compose the major raw materials are first subject to transesterification with excess methanol using an alkaline catalyst. The resulting fatty acid methyl esters are subject to distillation and then may be converted to alcohols by hydrogenation.

Fatty Acid Hydrogenation – this process involves the hydrolysis of fats and oils to the corresponding fatty acids followed by the direct catalytic hydrogenation to alcohols.

Alcohols manufactured by oleochemical processes have a linear structure and an even-numbered carbon chain usually in the range C6 to C22.

2. Production processes based on petrochemical feedstocks

The commercial processes generally used for converting petrochemical feedstocks to alcohols are:

From ethylene via the Ziegler process – like the alcohols manufactured by oleochemical processes those derived from ethylene via Ziegler chemistry have a linear structure and an even-numbered carbon chain usually in the range C6 to C22.

From olefins via OXO and modified-OXO synthesis - the olefin precursors may be linear alpha-olefins (1-alkenes), or linear internal olefins, or mixtures of the two and are reacted with mixture of carbon monoxide and hydrogen. The alcohols produced have one more carbon than the olefin feed and consist of linear alcohols and their corresponding mono C2-alkyl isomers (predominantly methyl) and may fall in the range C7 – C17, contain even and odd numbered carbon chains. The proportion of linear alcohols ranges from approximately 90 to 50% depending on the feed selection and type of OXO process.

In some cases the ca. 50% linear alcohols are further processed by physical separation techniques to obtain:

c. alcohols of approximately 95% mono-branched at the 2-position, predominantly 2-methyl;

d. alcohols of approximately 95% linearity

From olefins derived from the Fischer-Tropsch process – the resulting C12-C13 alcohol consists of approximately 50% linear, 30% mono-methyl branched and 20% other unintended components.

(2) General Description of Potential Releases and Exposures

Manufacture of aliphatic alcohols occurs in established chemical manufacturing facilities that have standard engineering controls and procedures in place to ensure safe handling and use of chemicals. All manufacturers of Long Chain Aliphatic Alcohols that participated in the survey apply process conditions requiring a closed reactor design; long chain aliphatic alcohols are manufactured in a continuous operation at elevated temperature and pressure. On-site they are transported via pipelines and stored predominantly in fixed roof storage tanks with a nitrogen blanket. Purging is controlled and usually restricted by local permits. As rule aliphatic alcohols are transported in bulk by truck, barge or rail; loading systems may include vapour recovery techniques.

The number of workers potentially exposed to LCAA in manufacturing facilities are shown below:

Table A.IV.2 Number of workers potentially exposed to LCAA in manufacturing facilities

	On-site workers potentially exposed			
	Routinely exposed		**Non-routinely exposed**	
	Number of Persons	**Person-hours***	**Number of Persons**	**Person-hours**
North America	89	185,000	38	69,000
Europe	663	137,000	225	45,000

Asia/Pacific	186	39,000	30	11,000

*Rounded to the nearest kPerson-hour

(3) Discussion of Factors that Mitigate or Exacerbate Releases and Exposures

Occupational exposure: All production facilities use standard personal protective equipment to prevent direct skin and eye contact with long chain aliphatic alcohols: for routine operations, including those involving a breach of the closed system goggles or safety glasses, gloves, safety boots and helmets are worn. LCAA are have a low volatility and as a rule engineering controls are available that prevent the need for respiratory protection. For non-routine operations involving a break in the closed system a higher level of protection is applied and usually extra measures are taken to prevent breathing of vapours, if (local) ventilation is inadequate. Operations with a potential for significant exposure require a permit to work system and a case-by-case assessment is made for appropriate protective measures.

Industrial Use

(4) Function/Product Use Description:

a) Long Chain Aliphatic Alcohols are major intermediates in the manufacture of major anionic and ionic surfactants.

b) Long Chain Aliphatic Alcohols are components in a wide range of industrial, commercial and consumer products.

(5) General description of Potential Releases and Exposure

Use of Long Chain Aliphatic Alcohols in the processing of major anionic and ionic surfactants takes place in established chemical manufacturing facilities that have standard engineering controls and procedures in place to ensure safe handling and use of chemicals. The manufacture of these surfactants involves the use of reactive chemicals (e.g. ethylene oxide, sulphuric acid) that are of a higher order of acute, local and repeated dose toxicity than long chain aliphatic alcohols. Detergents based on long chain aliphatic alcohols are manufactured in a totally enclosed system in a batch process. On such sites LCAA are stored predominantly in fixed roof storage tanks with a nitrogen blanket are transported via pipelines. As rule, supply of aliphatic alcohols the producers of Long Chain Aliphatic Alcohols to is via bulk transport by truck, barge or rail.

The number of workers potentially exposed to LCAA in processing facilities are shown below:

In the formulation of products for industrial, commercial or consumer use Long Chain Aliphatic Alcohols are typically formulated in established chemical manufacturing facilities that have standard engineering controls and procedures in place to ensure safe handling and use of a wide variety chemicals, including chemicals that are of a higher order of acute, local and repeated dose toxicity than long chain aliphatic alcohols. The members of Long Chain Aliphatic Alcohols that participated in the survey use continuous process with a closed system for formulating large volumes of product. For formulating smaller volumes, a batch process is typically used. Closed Reactors and/or mixing tank with closed charging systems are typically used for the formulation of LCAA. Products containing LCAA are typically packaged and transported in drums and bags, whereas products produced in higher volumes are stored in tanks and transported in bulk by truck, barge or rail.

The number of workers potentially exposed to LCAA in formulation facilities are shown below:

Table A.IV.3. Number of workers potentially exposed to LCAA in processing facilities

	On-site workers potentially exposed			
	Routinely exposed		**Non-routinely exposed**	
	Number of Persons	**Person-hours***	**Number of Persons**	**Person-hours**
North America	132	283,000	47	76,000
Europe	472	376,000	130	135,000
Asia/Pacific	172	259,000	47	70,000

* Rounded to the nearest kPerson-hour

Table A.IV.4. Number of workers potentially exposed to LCAA in formulation facilities

	On-site workers potentially exposed			
	Routinely exposed		**Non-routinely exposed**	
	Number of Persons	**Person-hours***	**Number of Persons**	**Person-hours**
North America	623	1,224,000	308	613,000
Europe	356	435,000	46	69,000
Asia/Pacific	214	425,000	72	142,000

* Rounded to the nearest kPerson-hour

(6) Discussion of Factors that Mitigate or Exacerbate Releases and Exposures

Occupational exposure: Facilities using of Long Chain Aliphatic Alcohols in the manufacture of major anionic and ionic surfactants or facilities involved in the formulation of products for industrial, commercial or consumer use standard personal protective equipment to prevent direct skin and eye contact with chemicals handled during for routine operations; as a rule goggles or safety glasses, gloves, safety boots and helmets are worn. Activities involving a breach of the closed system also rely on similar standard protective equipment provided no reactive/corrosive substances are being handled. LCAA are of a low volatility and as a rule engineering controls are available preventing the need for respiratory protection. For non-routine operations involving a break in the enclosed system a higher level of protection is applied and sometimes measures are taken to prevent breathing of vapours, if (local) ventilation is inadequate. Operations with a potential for significant exposure require a permit to work system and a case-by-case assessment is made for appropriate protective measures.

Commercial Use

(7) Function/Product Use Description: Long Chain Aliphatic Alcohols have widespread and dispersive use in several industrial sectors and find many commercial uses for mainly for its lubricant and emulsifying properties.

Examples of -formulated- industrial products include:
- Flotation agents
- Lubricants
- Emulsifiers
- Formwork oils
- Rolling oils
- Oilfield chemicals
- Defoamers

Examples of commercial uses include:
- Processing Aid in paper, plastics, textile and leather industry
- Formulation Aid in agrochemicals, pharmaceuticals and OTC's
- Additive in plastics, plaster, paper products

Typical levels of Long Chain Aliphatic Alcohols in products used in industry and commerce are shown in Table AIV.5. The levels as shown in Table AIV.5 represent long chain aliphatic alcohol concentrations in the formulated product and do not take into account any dilution prior to or during use. Ranges are provided for the level in product as reported in a survey conducted by the SDA for the Long Chain Alcohols in 2002 (SDA, 2002). It should be pointed out that many marketed products in these categories may not contain long chain aliphatic alcohols. Applications where the maximum concentration is 1% or below have been omitted from this table.

Table AIV.5: Summary of typical levels of aliphatic alcohols in use in industry and commerce.

Product Category	**Product Formulations (%)**					
	USA		EU		AP	
	Mean	Range	Mean	Range	Mean	Range
Paints	3	1 - 5	3	1 - 5	3	1 - 5
Lubricants			87.5	75-100		
Paper products and processing	37.5	25–50	37.5	25-50	37.5	25-50
Plastic processing			62.5	25-100		
Textile processing			87.5	75-100		
Leather Processing			87.5	75-100		
Plaster Additives			27.5	10 -50		
Formwork Oils			17.5	10 - 25		
Other - Pharmaceuticals	3	1 - 5	3	1 - 5	3	1 - 5

(8) General description of Potential Releases and Exposures

The survey did not provide detailed information regarding potential releases and exposures during use and handling of products intended for industrial and commercial applications.

(9) Discussion of Factors that Mitigate or Exacerbate Releases and Exposures

Occupational exposure: Exposure to long chain aliphatic alcohols through the use of products in industry and commerce is mitigated by following the recommended use and precaution instructions detailed in the material safety data sheet (MSDS). MSDS' reflect the hazard potential of the chemical ingredients in the product and provide details on the precautions necessary when handling these products and the instructions for first aid in case of an accidental exposure.

Consumer Use

(10) Function/ Product Use Description

The main uses of long chain aliphatic alcohols in consumer products include the product categories as shown in the Table A.IV.6.

The level in products shown in Table A.IV.6 indicates long chain aliphatic alcohol concentration in the formulated product and does not take into account any dilution prior to or during use. Ranges are provided for the level in product as reported in a survey conducted by the SDA for the Long Chain Alcohols in 2002 (SDA, 2002). It should be pointed out that many products on the market in these categories do not contain long chain aliphatic alcohols. Applications where the maximum concentration is 1% or below have been omitted from this table.

Table A.IV.6: Summary of typical levels of aliphatic alcohols in use in consumer products

Product Category	**Product Formulations (%)**					
	USA		EU		AP	
	Mean	Range	Mean	Range	Mean	Range
House Hold Products						
Laundry detergents: Powder	3	1 - 5	3	1 - 5	3	1 - 5
Fabric softener	3	1 - 5	3	1 - 5	0.75	0.5 - 1
General and Hard Surface Cleaners	3	1 - 5	-	-	3	1 - 5
Personal Care and Cosmetic products						
Hair						
conditioners gel,	3	1-5	3	1-5	1.88	0.5 – 5
mousse					3	1 - 5
dye					7.5	5-10
Skin lotions, creams, cleaners	3	1 - 5	3	1 - 5	1.88	0.5 - 5
Antiperspirants (solid)	17.5	10-25	17.5	10-25	17.5	10-25
Face/Eye Cosmetics						
Liquid	3	1 – 5	3	1 - 5	3	1 - 5
Powder	3	1 – 5			0.75	
Mascara					3	1 - 5

(11) General Description of Direct Exposures to Consumer Products and of Potential Releases to the Environment Leading to Environmental Exposures and Indirect Human Exposures

Environmental Releases and Indirect human exposures: The fate of environmental releases and potential indirect exposures from down-the-drain discharges following product use are discussed in the SIAR, section 2.2 and corresponding Annexes.

Direct Exposures to Consumer Products**:** Laundry, cleaning and personal care products may be used as is, or diluted prior to or during use. Dermal contact will occur with the use of these products; the exposures resulting from the use of consumer products have been modelled and shown in this Annex.
There is some potential for incidental or accidental ingestion of, inhalation of, and/or eye contact with products during handling and use.

(12) Discussion of Factors that Mitigate or Exacerbate Releases and Exposures

Consumer Exposure: Exposure to long chain aliphatic alcohols in formulated consumer laundry, cleaning and personal care products is mitigated by following the recommended use and precaution instructions on product labels. Product labels reflect the hazard potential of the chemical ingredients in the product. These product labels also include first aid instructions to accompany each hazard warning.

V. Modelling Evaluation: Exposures from Consumer Uses of Products

(1) Activities associated with Modelling Information

The use of consumer laundry detergents, fabric conditioners and personal care products have been modelled using screening level inputs. The skin is the predominant route of exposure associated with the use of these products, but a scenario addressing potential inhalational exposure through the use of sprays is included in this assessment.

(2) Description of Modelled Scenarios

Based on the information presented above the following activities and uses are modelled:

Exposure during the activity/use of products --

Laundry detergent: pre-treatment
Laundry detergent: hand washing laundry
General and hard surface cleaners (diluted and undiluted)

Indirect Exposure from residual on clothing--

Laundry detergents and fabric conditioners on clothing following washing

Exposure from residuals after using products --

Antiperspirants
Cleansing products
Face/Eye cosmetics
Hair conditioner
Hair styling tonic/gel
Skin lotions and creams, including body moisturizer

The exposure during application and use of these products is not modelled due to the short use period (minutes); the resulting exposures are very small in comparison to the exposures associated with the residual amounts that remain on the skin until the next use. The exposure modelling examples shown below include the use of Long Chain Aliphatic Alcohols in body moisturizers; this use is considered to be representative of all skin lotions and creams applications. In fact, the exposure potential associated with the use of body moisturizers represents the worst-case exposure within the category of skin lotions and creams.

(3) Tool or Model

The modelling presented here uses simple, first principle equations, which, when combined with conservative (protective) input values, err on the side of being protective.

GENERAL EXPOSURE MODEL

Potential Chemical Exposure (PE) = Exposure to Product (EXP) x Chemical Concentration in Product Formulation (PF)

DERMAL EXPOSURE MODELS

1. **Exposure during the activity/use of diluted and undiluted laundry and diluted or undiluted hard surface cleaning products:**

$$\frac{[FQ \times CA \times PC \times FT \times CF \times TF \times DA] \times PF}{BW}$$

2. **Exposure to laundry product and fabric conditioner residual on clothing:**

$$\frac{[FQ \times A \times PR \times PT \times DA \times CF] \times PF}{BW}$$

3. **Exposure to residual after using personal care products:**

$$\frac{[FQ \times A \times PR \times DA \times CF] \times PF}{BW}$$

Where:

FQ: Frequency of use (use/day)
CA: Body surface contact area (cm^2)
PC: Product concentration (g/cm^3)
FT: Film thickness on skin (cm)
TF: Time scaling factor (unit less)
DA: Dermal absorption (%)
BW: Body weight (kg)
PF: LCA concentration in product formulation (%)
A: Amount per use (g/day or g/wash)
PR: Percent retained on clothing or on skin (%)
PT: Percent transferred from clothing to skin (%)
CF: Conversion factor (g -> mg)

INHALATION EXPOSURE

4. Inhalation exposure (non-volatile components) to spray cleaning products during use

$$\frac{FQ \times RPC \times IR \times ED \times BA}{BW} \times PF$$

Where:

FQ	Frequency of Use (use/day)
RPC	Respirable Product Concentration in breathing zone (mg/m3)
IR:	Inhalation rate (m^3/hr)
ED:	Exposure duration (hr/day)
BA	Weight fraction absorbed or bioavailable (%)
BW:	Body weight (kg)
PF	Concentration in product formulation (%)

(4) Validation

These exposure calculations use first principle equations and are mathematically consistent with the Exposure Guidelines of the U.S. EPA (1992) with regard to modelling dermal and inhaled doses.

(5) Availability and Documentation

Guidelines for Exposure Assessment. U.S. EPA. 1992. [FRL-4129-5]

(7) Media Modelled

The exposure media are the products containing Long Chain Aliphatic Alcohol (LCAA) used by consumers. The SDA Long Chain Aliphatic Alcohol Consortium fielded surveys among producers and formulators to establish the range of LCAA concentrations in each of a number product forms (SDA, 2002). For each product category containing LCAA, the minimum and maximum of the range(s) were utilised as inputs for the dermal exposure models.

(8 Inputs

The exposure scenarios encompass conservative, screening-level inputs including: the high-end frequency of product use, the high-end amount of product per use, the high-end percent of product retained on skin or clothes following use; typically the 90th percentile is used as a high end value. All modelled exposures include a default assumption of 100% dermal absorption and bioavailability. The use multiple conservative input parameters results in modelled exposure estimates that are at least 1 – 2 orders of magnitude above the true exposure of a typical consumer.

All scenario's, input parameters, their source and justification used in this Annex have been evaluated by the Soap and Detergent Association; they are presented in: Exposure and risks screening methods for consumer product ingredients, issued by The Soap and Detergent Association, Washington, DC., April 2005.

The range of concentrations of the Long Chain Aliphatic Alcohols in specified product types used in these assessments are based on Survey of use and exposure information provided by the member companies of the Long Chain Aliphatic Alcohols Consortium (SDA, 2002).

1. Exposure during the activity/use of diluted and undiluted laundry and diluted and undiluted hard surface cleaning products

$$\frac{[FQ \times CA \times PC \times FT \times CF \times TF \times DA]}{BW} \times PF$$

	Laundry Pre-treatment (undiluted)	**Hand-wash of Laundry (diluted)**	**Hard Surface Cleaners (diluted)**	**Hard Surface Cleaners (undiluted)**
Frequency (FQ) (use/day)*	1	1	1	1
Contact Area (CA) (cm^2)*	360	1680	1680	180
Product Concentration (PC) (g/cm^3)*	0.6	0.01	0.015	1
Film Thickness (FT) (cm)*	0.0024	0.0024	0.0024	0.0024
Conversion Factor (CF) (g -> mg)*	1000	1000	1000	1000
Time Scaling Factor (TF) (unitless)	0.007	0.007	0.014	0.014
Dermal Absorption (DA) (%)*	100	100	100	100
Female body weight (BW) (kg)*	65.4	65.4	65.4	65.4
LCA concentration in product formulation (PF) (%)**	1-5%	1-5%	1-5%	1-5%

* Exposure and Risk Screening methods for consumer product ingredients (N. American data) (SDA, 2005)
** LCAA Consortium survey; Min-Max values (SDA, 2002)

2. Exposure to laundry product residual on clothing

$$\frac{[FQ \times A \times PR \times PT \times DA \times CF]}{BW} \times PF$$

	Laundry Detergent	**Fabric Conditioner**
Amount Per Use (A) (g/day or g/wash)*	121	112
Use Frequency (FQ) (use/day)*	1	1
Percent Retained on Clothing (PR) (%)*	1	1
Percent Transferred from Clothing to Skin (PT) (%)*	1	1
Dermal Absorption (DA) (%)*	100	100
Conversion Factor (CF) (g -> mg)	1000	1000
Female body weight (BW) (kg)*	65.4	65.4
LCAA concentration in product (PF)**	1-5%	1-5%

* Exposure and Risk Screening methods for consumer product ingredients (N. American data) (SDA, 2005)
** LCAA Consortium survey; Min-Max values (SDA, 2002)

3. Exposure to personal care products residual after use

$$\frac{[FQ \times A \times PR \times DA \times CF]}{BW} \times PF$$

	Hair conditioner	**Hair styling tonic/gel****	**Anti perspirants**	**Face/Eye cosmetics**	**Body Moisturiser**	**Cleansing products**
Frequency of Use (FQ) (use/day)*	1	1	2	2	1	2
Amount Per Use (A) (g/use)*	12.7	5.6	1.2	2.65	36.3	1.7
Percent Retained on Skin (PR) (%)*	1	5	100	100	100	1

Dermal Absorption (DA) (%)*	100	100	100	100	100	100
Conversion Factor (CF) (g -> mg)	1000	1000	1000	1000	1000	1000
Body weight (BW) (kg)*	65.4	65.4	65.4	65.4	65.4[c]	65.4
LCAA concentration in product (PF) (%)**	0.5 – 5%	0.5 - 5%	10-25%	1 – 5%	0.5-5%	0.5 - 5%

* Exposure and Risk Screening methods for consumer product ingredients (N. American data) (SDA, 2005)

** LCAA Consortium survey; Min-Max values (SDA, 2002)

4. Inhalation exposure (non volatile components) to spray cleaning products during use.

$$\frac{FQ \times RPC \times IR \times ED \times BA}{BW} \times PF$$

	Spray Cleaner
Frequency of Use (FQ) (uses/day)*	1
Respirable Product Concentration in air (RPC) (mg/m^3)*	0.72
Inhalation Rate (IR) (m^3/hr)*	1.0
Exposure Duration (ED) (hr)*	0.33
Weight fraction absorbed or bioavailable (BA)*	100
Female body weight (BW) (kg)*	65.4
LCA concentration in product formulation (PF) (%)**	0.1-5%

* Exposure and Risk Screening methods for consumer product ingredients (N. American data) (SDA, 2005)

** LCAA Consortium survey; Min-Max values (SDA, 2002)

(9) Model Outputs

1. Exposure during the activity/use of diluted and undiluted laundry and diluted and undiluted hard surface cleaning products

	Potential Dermal Exposure (mg/kg/day) [a]
Laundry Pre-Treatment (undiluted)	5.5E-4 to 2.8E-3
Hand-wash of Laundry (diluted)	4.3E-5 to 2.2E-4
Hard Surface Cleaners (diluted)	1.3E-4 to 6.5E-4
Hard Surface Cleaners (undiluted)	9.2E-4 to 4.6E-3

[a] Range based on minimum and maximum product concentration values (SDA, 2002)

2. Exposure to laundry product and fabric conditioner residual on clothing

	Potential Dermal Exposure (mg/kg/day) [a]
Laundry Detergent	1.9E-3 to 9.2E-3
Fabric conditioner	1.7E-3 to 8.6E-3

[a] Range based on minimum and maximum product concentration values (SDA, 2002)

3. Exposure to personal care product residual after use

	Potential Dermal Exposure (mg/kg/day) [a]
Antiperspirants	3.7E-0 to 9.2E-0
Body moisturiser	2.8E-0 to 2.8E 1
Cleansing products	2.6E-3 to 2.6E-2
Face/Eye cosmetics	8.1E-1 to 4.1E-0
Hair conditioner	9.7E-3 to 9.7E-2
Hair styling tonic/gel	2.1E-1 to 2.1E-0

[a] Range based on minimum and maximum product concentration values (SDA, 2002)

4. Inhalation exposure to spray cleaning products

	Potential Inhalation Exposure (mg/kg/day) [a]
Spray Cleaning Products	3.6E-6 to 1.8E-5

[a] Range based on minimum and maximum product concentration values (SDA, 2002)

(10) Reliability Score: 1 (Reliable without restrictions). The models used are first principle equations, which are sufficiently conservative, have undergone peer review and are generally accepted by authorities. Appropriate inputs have been used, reflecting best available information and conservative estimates where applicable.

(11) Remark. Within the category of Long Chain Aliphatic Alcohols with a chain lengths of C12 and above are typically used in personal care applications as modelled in this section generally

V. References

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ANNEX V: ENVIRONMENTAL FATE PROPERTIES: (Q)SAR PREDICTIONS AND COMPARISON WITH MEASURED VALUES

ATMOSPHERIC DEGRADATION RATE

In the atmosphere, all C-H containing organics are expected to react with photochemically generated hydroxyl radicals. Only three relevant measurements of atmospheric degradation rate are available, all for shorter chain lengths. To fill data gaps for this SIDS endpoint, the rate of degradation by hydroxyl radicals in the atmosphere has been estimated using the SRC AOPWIN v1.91 program.

AOPWIN also calculates a half-life, based on a hydroxyl radical concentration of 1.5E+06 molecules/cm^3. In the SIAR, a different half-life is reported, using the European standard value of 5E+05 molecules/cm^3. Both sets of half-lives, in hours, are reported in Table A.V.1 below.

Table A.V.1. Measured and predicted photodegradation rate constants and half-lives

Name	CAS	Measured OH rate constant (cm^3/molecule.sec)	Estimated OH rate constant (cm^3/molecule.sec)	Half life (h) [1]	Half life (h) [2]
1-Hexanol	111-27-3	12.5E-12	9.716E-12	30.8 [3] 39.6 [4]	10.3
1-Heptanol	111-70-6	13.7E-12	11.129E-12	28.1 [3] 34.6 [4]	9.4
1-Octanol	111-87-5	14.4E-12	12.542E-12	26.7 [3] 30.7 [4]	8.9
1-Nonanol	143-08-8		13.955E-12	27.6	9.2
1-Decanol	112-30-1		15.368E-12	25.1	8.4
1-Undecanol	112-42-5		16.781E-12	22.9	7.6
1-Dodecanol	112-53-8		18.194E-12	21.2	7.1
1-Tridecanol	112-70-9		19.607E-12	19.6	6.5
Tridecanol, branched	90583-91-8		19.884E-12	19.4	6.4
1-Tetradecanol	112-72-1		21.021E-12	18.3	6.1
1-Pentadecanol	629-76-5		22.434E-12	17.2	5.7
1-Hexadecanol	36653-82-4		23.847E-12	16.2	5.4
2-methyl pentadecanol	NA		24.123E-12	16.0	5.3
1-Hexadecanol unsaturated (Z)	NA		76.892E-12	5.0	1.7
1-Heptadecanol	1454-85-9		25.260E-12	15.3	5.1
1-Octadecanol	112-92-5		26.673E-12	14.4	4.8
9-Octadecen-1-ol, (Z)-	143-28-2		79.718E-12	4.8	1.6
1-Eicosanol	629-96-9		29.499E-12	13.1	4.4
1-Docosanol	661-19-8		32.325E-12	11.9	4.0
1-Butanol, 3-methyl-	123-51-3	13.1E-12	8.295E-12	29.4 [3] 46.4 [4]	

Notes:
1 – using EU standard concentration of OH radicals, 5E+05 molecules/cm^3
2 – using SRC AOPWIN, i.e. 1.5E+06 molecules/cm^3
3 – based on measured rate constant
4 – based on SRC estimated rate constant

From this set of measured and estimated data, certain conclusions can be drawn:

- Available measured data for relevant linear and branched structures suggest that the estimated half lives are likely to be realistic and slightly conservative.

- Estimated half-lives for branched structures are slightly shorter than for linear structures of equivalent carbon number.

- Estimated half-lives for unsaturated structures are very much shorter than for saturated structures of equivalent carbon number.

ABIOTIC DEGRADATION

Abiotic degradation in water is not expected due to the absence of labile groups.

BIODEGRADATION

There is a very limited range of quantitative structure-activity relationship methods available which address biodegradation. Some of these are effectively highly specialised research tools. The program BIOWIN is effectively an expert system with limited quantitative application. It, by its nature, recognises that linear or singly-branched hydrocarbon chains are susceptible to microbial degradation. This is enhanced by the presence of the OH group. It can be seen from the BIOWIN outputs below that it provides very little differentiation between linear C14 and C22 alcohols. The magnitude of the BIOWIN scores is consistent with rapid biodegradation in the environment; it could be argued from these data that all the category members would degrade fast in the environment. The variation in the ready test results is thus explained as simply reflecting the lower bioavailability of the longer chain members.

DATA SET FOR LONG CHAIN ALCOHOLS

For single component alcohols, ready biodegradability tests show that for up to C14, the alcohols are readily biodegradable within a 10-day window. C16-18 are readily biodegradable but not within the 10-day window. Longer chain lengths >C18 are not readily biodegradable; no inherent biodegradability test results are available, but a significant level of degradation was observed. However, in non-standard studies with low-concentrations of the alcohol, uniformly high degradation rates can be found. In general terms for non-adapted bacteria, biodegradation rates are expected to be lower at higher carbon numbers because uptake by the bacteria is slower, and dissolution of excess substance can limit bioavailability.

Rapid degradation is also indicated by the difficulties encountered in aquatic toxicity tests for these substances, caused by rapid removal of the substance from the test medium, presumably by biodegradation by micro-organisms.

PREDICTED VALUES

Predicted biodegradation rates, using all methods in the SRC BIOWIN v 4.00 program, show (Table A.V.2) that linear alcohols are predicted to biodegrade rapidly. Three endpoints of this program are referred to in the TGD discussion of screening approaches to persistence assessment in the context of PBT. All of these structures would be considered not persistent on the basis of the criteria given.

Table A.V.2. Predicted biodegradation probability rates for linear alcohols

CAS	Carbon no.	Linear Model[1]	Non-Linear Model[1]	Ultimate Biodegradation[2]	Primary Biodegradation[2]	MITI Linear Model[3]	MITI Non-Linear Model[3]
No P, if all 3 are met:			*>0.5*	*>2.2*			*>0.5*
111-27-3	6	0.9661	0.9892	3.4317	4.0988	0.8168	0.9397
111-70-6	7	0.9594	0.9869	3.4007	4.0786	0.8245	0.9411
111-87-5	8	0.9527	0.9840	3.3697	4.0584	0.8322	0.9425
143-08-8	9	0.9460	0.9806	3.3387	4.0381	0.8398	0.9438
112-30-1	10	0.9393	0.9764	3.3077	4.0179	0.8475	0.9451
112-42-5	11	0.9327	0.9713	3.2767	3.9977	0.8552	0.9463
112-53-8	12	0.9260	0.9652	3.2457	3.9774	0.8629	0.9476
112-70-9	13	0.9193	0.9579	3.2147	3.9572	0.8706	0.9488
112-72-1	14	0.9126	0.9491	3.1837	3.9369	0.8783	0.9499
629-76-5	15	0.9060	0.9386	3.1527	3.9167	0.8860	0.9511
36653-82-4	16	0.8993	0.9260	3.1217	3.8965	0.8936	0.9522
1454-85-9	17	0.8926	0.9112	3.0907	3.8762	0.9013	0.9533
112-92-5	18	0.8859	0.8937	3.0597	3.8560	0.9090	0.9544
1454-84-8	19	0.8792	0.8732	3.0287	3.8357	0.9167	0.9555
629-96-9	20	0.8726	0.8495	2.9977	3.8155	0.9244	0.9565
	21	0.8659	0.8222	2.9667	3.7953	0.9321	0.9575
661-19-8	22	0.8592	0.7912	2.9357	3.7750	0.9398	0.9585

Notes:

[1] A Probability Greater Than or Equal to 0.5 indicates --> Biodegrades Fast; A Probability Less than 0.5 indicates --> Does NOT Biodegrade Fast

[2] Result Classification (Primary & Ultimate): 5.00 -> hours 4.00 -> days 3.00 -> weeks 2.00 -> months 1.00 -> longer

[3] A Probability Greater Than or Equal to 0.5 indicates --> Readily Degradable; A Probability Less than 0.5 indicates --> NOT Readily Degradable

Branched alcohols are present in many of the commercial products. No measured results are available for branched alcohols specifically. It is possible that branched components might be less biodegradable than linear ones, but this might not be picked up in a standard study. (Q)SAR methods indicate that as a general rule mono-branched structures degrade at essentially the same rate as the linear unsaturated alcohol of equivalent carbon number.

Unsaturation does not appear to be detrimental to biodegradation rate; in two ready tests, a commercial mixture (C16-18 components, containing C18 unsaturated components) was readily biodegradable. C18 unsaturated alcohol was predicted by (Q)SAR to degrade at essentially the same rate as the linear unsaturated alcohol, i.e. a screening assignment of ‘no P’.

The table (A.V.3) shows the BIOWIN results for branched structures and one unsaturated structure:

Table A.V.3. BIOWIN outputs for branched and unsaturated alcohols

CAS	Carbon no.	Linear Model[1]	Non-Linear Model[1]	Ultimate Biodegra-dation[2]	Primary Biodegra-dation[2]	MITI Linear Model[3]	MITI Non-Linear Model[3]
No P, if all 3 are met:			*>0.5*	*>2.2*			*>0.5*
Branched alcohols							
123-51-3	5, 4Me	0.8643	0.9466	3.1643	3.8500	0.6600	0.8561
	6, 2Me	0.8576	0.9356	3.1333	3.8298	0.6677	0.8591
	10, 2Me	0.9393	0.9764	3.3077	4.0179	0.6984	0.8705
	14, 2Me	0.9126	0.9491	3.1837	3.9369	0.7292	0.8812
	18, 2Me	0.8859	0.8937	3.0597	3.8560	0.7599	0.8911
	22, 2Me	0.8592	0.7912	2.9357	3.7750	0.7907	0.9003
	10, 2Bu	1.0478	0.9962	3.6060	4.2870	0.6984	0.8705
	14, 2Bu	1.0211	0.9916	3.4820	4.2060	0.7292	0.8812
	22, 2Bu	0.9676	0.9599	3.2341	4.0441	0.7907	0.9003
	18, 2Oc	0.9944	0.9815	3.3580	4.1251	0.7599	0.8911
	22, 2Oc	0.9676	0.9599	3.2341	4.0441	0.7907	0.9003
Unsaturated alcohols							
143-28-2	18, 9Z	0.8869	0.8964	3.0642	3.8589	0.8286	0.9087

Notes:

[1] A Probability Greater Than or Equal to 0.5 indicates --> Biodegrades Fast; A Probability Less than 0.5 indicates --> Does NOT Biodegrade Fast

[2] Result Classification (Primary & Ultimate): 5.00 -> hours 4.00 -> days 3.00 -> weeks 2.00 -> months 1.00 -> longer

[3] A Probability Greater Than or Equal to 0.5 indicates --> Readily Degradable; A Probability Less Than 0.5 indicates --> NOT Readily Degradable

It is concluded that in studies where both linear and essentially-linear components are present, all would degrade rapidly.

BIOCONCENTRATION

BCF values for the alcohols are predicted by three (Q)SARs. For alcohols with log K_{ow} below 6, the Veith *et al* (1979) equation is used. For those with log K_{ow} greater than 6, the recalculated Connell and Hawker (1988) equation is used. Both equations are discussed in the TGD. For purposes of comparison, BCF was also calculated using SRC BCFWIN. The values calculated by the Veith *et al* and Connell and Hawker methods are generally considered to be more authoritative. The estimates using the BCFWIN method are much lower, as shown in Table A.V.4 and Figure A.V.1.

Predicted data should be validated by comparison with measurements. Unfortunately, there are no reliable measured data for bioconcentration. Across the Category, BCF is available for only one linear alcohol: hexadecanol, C16; the value originates in a short study and is considered to be invalid.

The natural ability of biochemical systems in the body to metabolise alcohols may mean that predictions will tend to be overestimates. Measured data available for three iso-alcohols support this view, though there are too few data to think of this as a trend.

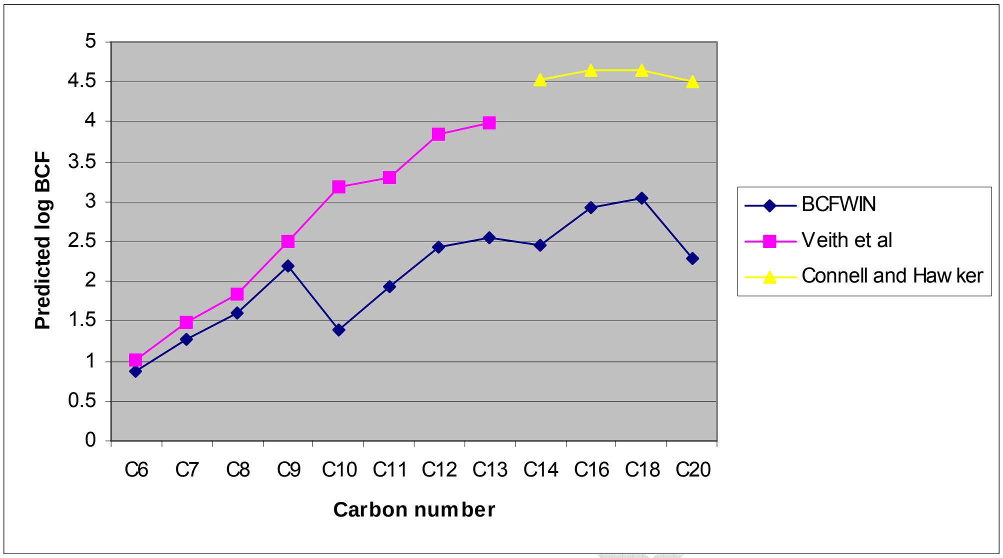
Table A.V.4. Predicted BCFs for linear alcohols

Carbon Number	Log K_{ow}	BCFWIN		Veith *et al*		Connell & Hawker	
		log BCF	BCF	log BCF	BCF	log BCF	BCF
6	2.03	0.86	7	1.03	11		
7	2.57	1.28	19	1.48	31		
8	3.15	1.61	41	1.98	95		
9	3.77	2.20	160	2.50	320		
10	4.57	1.40	25	3.18	1529		
11	4.72	1.93	86	3.31	2051		
12	5.36	2.43	267	3.86	7178		
13	5.51	2.54	349	3.98	9627		
14	6.03	2.44	277			4.53	33886
15	6.43[1]	2.61	405			4.63	42581
16	6.65	2.92	834			4.66	45342
17	7. 08[1]	3.00	1002			4.65	45073
18	7.19	3.05	1122			4.64	43791
18 unsat.	7.07[1]	2.62	420			4.65	45167
19	7.50[1]	1.94	87			4.58	38019
20	7.75	2.28	191			4.50	31805
21	7.75[1]	1.94	87			4.50	31805
22	7.75[1]	1.94	87			4.50	31805

Note:

[1] Estimated log K_{ow}, derived from SRC KOWWIN as described in Annex I (measured value not available). NB, For C21 and 22 the value is read-across from the measured value for C20.

Figure A.V.1. Predicted BCF of linear alcohols by different methods



Values predicted for 2-methyl branched alcohols are fairly consistent with the predicted values for the linear structures of corresponding carbon number (Table A.V.5). Branched structures present are predicted to have slightly lower BCF than the corresponding linear alcohol and hence the value predicted for the linear alcohol is the more conservative.

Table A.V.5. Predicted BCFs for 2-methyl branched alcohols

Carbon Number	Log K_{ow}[1]	BCFWIN		Veith *et al*		Connell & Hawker	
		log BCF	BCF	log BCF	BCF	log BCF	BCF
6	2.04	0.65	4	1.03	11		
8	3.12	1.40	25	1.95	89		
10	4.15	2.16	145	2.83	669		
12	5.12	1.92	82	3.65	4478		
14	5.98	2.67	470	4.38	23976		
16	6.69	2.93	849			4.66	45667
18	7.23	2.43	269			4.64	43239
20	7.54	1.94	87			4.57	37143
22	7.56	1.94	87			4.56	36635

Note:

[1] Estimated log K_{ow}, derived from SRC KOWWIN as described in Annex I (measured value not available)

For the multi-component sponsored substances, there cannot be a single value of BCF. However, the values for the components present are relevant. The presence of branched components is not expected to significantly affect the predicted value.

ADSORPTION

The TGD gives several equations for calculation of K_{oc} for specific substance types. Three are of relevance to alcohols:

Hydrophobics: $\log K_{oc} = 0.81 \log K_{ow} + 0.10$
(n = 81, r2 = 0.89, standard error = 0.45)

This equation is valid up to log K_{ow} = 7.5. Values for substances with log K_{ow} >7.5 are shown in italics in the table.

Non-hydrophobics: $\log K_{oc} = 0.52 \log K_{ow} + 1.02$
(n = 390, r^2 = 0.63, standard error = 0.56)

This equation is valid up to log K_{ow} = 8.

Alcohols and organic acids: $\log K_{oc} = 0.47 \log K_{ow} + 0.5$
(n = 36, r^2 = 0.72, standard error = 0.39)

Alcohols: $\log K_{oc} = 0.39 \log K_{ow} + 0.5$
(n = 13, r^2 = 0.77, standard error = 0.40)
Both are valid up to log K_{ow} = 5. Values for substances with log K_{ow} >5 are shown in italics in the table.

Van Compernolle:

$\log K_{oc}$ = Chain Length * 0.235 + 1.420 r^2 = 0.99, n =4, and
$\log K_{oc}$ = log K_{ow} * 0.766 + 0.111 r^2 = 0.994, n = 4

Due to being based on a mixed set of substance types, including types of alcohols not relevant to the current set, the method for Alcohols and organic acids is not shown here.

K_{oc} was also calculated using SRC PCKOCWIN. This method is based on structural considerations and is not influenced by other property values.

Predicted data should be validated by comparison with measurements. Only a limited set of measurements is available.

Results are brought together in table A.V.6.

Table A.V.6. Predicted and measured K_{oc} values for linear alcohols

Carbon Number	Log K_{ow}	PCKOCWIN		TGD (Hydrophobic)		TGD (Non-hydrophobic)		TGD (Alcohols)		Available measured data	References
		log Koc	Koc	log Koc	Koc	log Koc	Koc	log Koc	Koc		
C6	2.03	0.92	8.3	1.74	56	2.08	119.0	1.29	19.6		
C7	2.57	1.19	15.3	2.18	152	2.36	227.2	1.50	31.8		
C8	3.15	1.45	28.3	2.65	448	2.66	455.0	1.73	53.5		
C9	3.77	1.72	52.1	3.15	1425	2.98	955.9	1.97	93.4		
C10	4.57	1.98	96.2	3.80	6334	3.40	2491.2	2.28	191.6		
C11	4.72	2.25	177.4	3.92	8379	3.47	2981.3	2.34	219.2		
C12	5.36	2.51	327.1	4.44	27644	3.81	6415.0	*2.59*	*389.4*	Koc = 17980	Van Compernolle et al. (2006)
C13	5.51	2.78	603.4	4.56	36568	3.89	7677.1	*2.65*	*445.6*		
C14	6.03	3.05	1113.0	4.98	96450	4.16	14308.7	*2.85*	*710.7*	Koc = 50830	Van Compernolle et al. (2006)
C15	6.43[1]	3.31	2053.0	5.31	203376	4.36	23099.4	*3.01*	*1017.9*		
C16	6.65	3.58	3786.0	5.49	306549	4.48	30060.8	*3.09*	*1240.2*	Koc = 143000	Van Compernolle et al. (2006)
C17	7. 08[1]	3.84	6982.0	5.83	683597	4.70	50303.7	*3.26*	*1824.7*		
C18	7.19	4.11	12880.0	5.92	839267	4.76	57385.2	*3.30*	*2014.2*	Koc = 471000	Van Compernolle et al. (2006)
C18 unsat.	7.07[1]	4.11	12880.0	5.83	670965	4.70	49705.0	*3.26*	*1808.4*		
C19	7.50[1]					4.92	83176.4	*3.43*	*2660.7*		
C20	7.75	4.64	43810.0	*6.38*	*2385064*	5.05	112201.8	*3.52*	*3330.4*		
C21	7.75[1]					5.05	112201.8	*3.52*	*3330.4*		
C22	7.75[1]	5.17	149000.0	*6.38*	*2385064*	5.05	112201.8	*3.52*	*3330.4*		

Note:

[1] Estimated log K_{ow}, derived from SRC KOWWIN as described in Annex I (measured value not available). NB, For C21 and 22 the value is read-across from the measured value for C20.

None of these approaches stands out in terms of reliability or performance. The values predicted by specific methods may possibly be preferred by certain reviewers, or more applicable in particular contexts or applications. The value calculated by the TGD Non-hydrophobics equation is the most conservative across the category.

For the multi-component sponsored substances, there cannot be a single value of log Koc. However, the values for the components present are relevant. The presence of branched components is not expected to significantly affect the predicted value.

References

Connell DW and Hawker DW (1988). Use of polynomial expressions to describe the bioconcentration of hydrophobic chemicals by fish. Ecotox. Environ. Safety 16: 242-257.

Veith GD, Defoe DL and Bergstedt BV (1979). Measuring and estimating the bioconcentration factor of chemicals in fish. J. Fish. Board Can. **36**: 1040-1048.

ANNEX VI: ENVIRONMENTAL DISTRIBUTION MODELLING

Several approaches to distribution modelling are described below. Two models have been used:

- The 1997 Level I model implemented as 'EQC'
- The 1999 Level III model, available on the Canadian government web site.

Both models use key property data as inputs (molecular weight; melting point, vapour pressure, water solubility, log K_{ow}) and also use degradation half lives.

In modelling the long chain alcohols, some degradation has been allowed for in both the Level I and Level III models. The half-life for degradation in air is estimated using the SRC AOPWIN model, which predicts the rate of reaction with hydroxyl radicals in the atmosphere. This is converted into a half-life using the standard EU atmospheric concentration of hydroxyl radicals. The half-lives in soil and in water are both set to 720 hours, i.e. 30 days, for all of the alcohols, to reflect that they are all aerobically biodegradable. The use of a single, relatively high, value of the half life does not have a major effect on the models; also only relative data are reported.

The basic results for each of the sponsored substances in this Category are recorded in the substance dossiers and tabulated in the SIAR. The results for EQC level I are the simplest and assume equal kg/d releases into air, water and soil.

The Level III model has been used to indicate the fate modelled for separate releases into different compartments. No inflow from outside the modelled area (the default settings) has been included. The results are presented in Table A.VI.1.

In Level III the % in each compartment varies according to the point of release. For most of the substances it is relevant to note that there is relatively little movement between soil and water, because transfer via the air compartment is very slow, for a substance of low volatility.

Table A.VI.1. Results of fugacity modelling

Substance	Input data used:	Results of Level I modelling	Results of Level III modelling	Conclusions
1-hexanol 111-27-3	Molecular weight 102.2 Data temperature 25 deg C Log Kow 2.03 Water Solubility 5900 mg/L Vapour pressure 122 Pa Melting point –50 deg C half life in air 30.8 h half life in water and soil 720 h	Air 28% Soil 6.23% Water 65.6% Fish 3.52E-04% Sediment 0.14%	Release: To air To water To soil % in air 66.8 0.0375 0.0379 % in water 8.11 99.9 14.6 % in sediment 0.00728 0.0897 0.0131 % in soil 25.1 0.0141 85.3	The results reflect that the ultimate fate of 1-hexanol is dependent on its route of release into the environment. 1-Hexanol released to air would partially precipitate to soil.
1-octanol 111-87-5	Molecular weight 130.2 Data temperature 25 deg C Log Kow 3.15 Water Solubility 551 mg/L Vapour pressure 10 Pa Melting point –16 deg C half life in air 26.7 h half life in water and soil 720 h	Air 17.3% Soil 45.4% Water 36.3% Fish 2.56E-03% Sediment 1.01%	Release: To air To water To soil % in air 63.6 0.0407 0.00446 % in water 4.02 98.7 1.6 % in sediment 0.0504 1.24 0.02 % in soil 32.3 0.0207 98.4	The results reflect that the ultimate fate of 1-octanol is dependent on its route of release into the environment. 1-Octanol released to air would partially precipitate to soil.
1-decanol 112-30-1	Molecular weight 158.3 Data temperature 25 deg C Log Kow 4.57 Water Solubility 39.5 mg/L Vapour pressure 1.13 Pa Melting point 6.4 deg C half life in air 25.1 h half life in water and soil 720 h	Air 2.57% Soil 92.5% Water 2.81% Fish 5.22E-03% Sediment 2.06%	Release: To air To water To soil % in air 71.9 0.0324 0.000287 % in water 3.18 45.9 0.0674 % in sediment 3.74 54 0.0792 % in soil 21.2 0.00954 99.9	The results reflect that the ultimate fate of 1-decanol is dependent on its route of release into the environment. 1-Decanol released to air would partially precipitate to soil and water. In water, the adsorption coefficient of 1-decanol results in adsorption to sediment.
1-undecanol 112-42-5	Molecular weight 172.3 Data temperature 25 deg C Log Kow 4.72 Water Solubility 8 mg/L Vapour pressure 0.39 Pa Melting point 14 deg C half life in air 22.9 h half life in water and soil 720 h	Air 3.37% Soil 92.5% Water 1.99% Fish 5.22E-03% Sediment 2.06%	Release: To air To water To soil % in air 77.9 0.0414 0.000334 % in water 2.67 36.6 0.0458 % in sediment 4.64 63.4 0.0794 % in soil 14.8 0.00784 99.9	The results reflect that the ultimate fate of 1-undecanol is dependent on its route of release into the environment. 1-Undecanol released to air would partially precipitate to soil and water. In water, the adsorption coefficient of 1-undecanol results in adsorption to sediment.

Substance	Input data used:	Results of Level I modelling	Results of Level III modelling	Conclusions
1-tridecanol 112-70-9	Molecular weight 200.4 Data temperature 25 deg C Log Kow 5.51 Water Solubility 0.38 mg/L Vapour pressure 0.057 Pa Melting point 32 deg C half life in air 19.6 h half life in water and soil 720 h	Air 2.02% Soil 95.5% Water 0.33% Fish 5.39E-03% Sediment 2.12%	Release: To air To water To soil % in air 69.1 0.018 0.000171 % in water 1.36 9.38 0.0121 % in sediment 13.1 90.6 0.117 % in soil 16.4 0.00428 99.9	The results reflect that the ultimate fate of 1-tridecanol is dependent on its route of release into the environment. 1-Tridecanol released to air would partially precipitate to soil and water. In water, the adsorption coefficient of 1-tridecanol results in adsorption to sediment.
1-tetradecanol 112-72-1	Molecular weight 214.4 Data temperature 25 deg C Log Kow 6.03 Water Solubility 0.191 mg/L Vapour pressure 0.014 Pa Melting point 40 deg C half life in air 18.3 h half life in water and soil 720 h	Air 0.33% Soil 97.3% Water 0.10% Fish 5.50E-03% Sediment 2.16%	Release: To air To water To soil % in air 38.4 0.00395 0.000033 % in water 1.57 4.61 0.0106 % in sediment 32.5 95.4 0.219 % in soil 27.6 0.00284 99.8	The results reflect that the ultimate fate of 1-tetradecanol is dependent on its route of release into the environment. 1-Tetradecanol released to air would partially precipitate to soil and water. In water, the adsorption coefficient of 1-tetradecanol results in adsorption to sediment.
1-pentadecanol 629-76-5	Molecular weight 228.4 Data temperature 25 deg C Log Kow 6.43 Water Solubility 0.102 mg/L Vapour pressure 0.00512 Pa Melting point 45 deg C half life in air 17.2 h half life in water and soil 720 h	Air 0.10% Soil 97.6% Water 0.04% Fish 5.51E-03% Sediment 2.17%	Release: To air To water To soil % in air 21.1 0.00128 1.12E-05 % in water 1.47 3.32 0.0107 % in sediment 42.7 96.7 0.31 % in soil 34.7 0.00211 99.7	The results reflect that the ultimate fate of 1-pentadecanol is dependent on its route of release into the environment. 1-Pentadecanol released to air would partially precipitate to soil and water. In water, the adsorption coefficient of 1-pentadecanol results in adsorption to sediment.
1-hexadecanol 36653-82-4	Molecular weight 242.4 Data temperature 25 deg C Log Kow 6.65 Water Solubility 0.013 mg/L Vapour pressure 0.0014 Pa Melting point 50 deg C half life in air 16.2 h half life in water and soil 720 h	Air 0.13% Soil 97.6% Water 0.03% Fish 5.51E-03% Sediment 2.17%	Release: To air To water To soil % in air 9.88 0.00125 1.34E-05 % in water 1.25 2.98 0.0103 % in sediment 40.7 97 0.335 % in soil 48.2 0.00609 99.7	The results reflect that the ultimate fate of 1-hexadecanol is dependent on its route of release into the environment. 1-Hexadecanol released to air would partially precipitate to soil and water. In water, the adsorption coefficient of 1-hexadecanol results in adsorption to sediment.

Substance	Input data used:	Results of Level I modelling	Results of Level III modelling	Conclusions
9z-octadecenol 143-28-2	Molecular weight 268.5 Data temperature 25 deg C Log Kow 7.07 Water Solubility 0.0077 mg/L Vapour pressure 0.00198 Pa Melting point 17 deg C half life in air 4.8 h half life in water and soil 720 h	Air 0.13% Soil 97.6% Water 9.38E-03% Fish 5.51E-03% Sediment 2.17%	Release: To air To water To soil % in air 8.01 0.000579 9.86E-06 % in water 1.17 2.65 0.0105 % in sediment 42.9 97.3 0.383 % in soil 47.9 0.00347 99.6	The results reflect that the ultimate fate of 9Z-octadecen-1-ol is dependent on its route of release into the environment. 9Z-octadecen-1-ol released to air would partially precipitate to soil and water. In water, the adsorption coefficient of 9Z-octadecen-1-ol results in adsorption to sediment.
1-eicosanol 629-96-9	Molecular weight 298.5 Data temperature 25 deg C Log Kow 7.75 Water Solubility 0.0011 mg/L Vapour pressure 0.000015 Pa Melting point 66 deg C half life in air 13.1 h half life in water and soil 720 h	Air 1.61E-03% Soil 97.8% Water 1.96E-03% Fish 5.52E-03% Sediment 2.17%	Release: To air To water To soil % in air 0.639 2.52E-05 2.41E-07 % in water 1.22 2.5 0.0111 % in sediment 47.5 97.5 0.433 % in soil 50.6 0.00199 99.6	The results reflect that the ultimate fate of 1-eicosanol is dependent on its route of release into the environment. 1-Eicosanol released to air would partially precipitate to soil and water. In water, the adsorption coefficient of 1-eicosanol results in adsorption to sediment.
1-docosanol 661-19-8	Molecular weight 326.6 Data temperature 25 deg C Log Kow 7.75 Water Solubility 0.001 mg/L Vapour pressure 0.00000815 Pa Melting point 72.5 deg C half life in air 11.9 h half life in water and soil 720 h	Air 1.05E-03% Soil 97.8% Water 1.96E-03% Fish 5.52E-03% Sediment 2.17%	Release: To air To water To soil % in air 0.582 1.72E-05 1.71E-07 % in water 1.22 2.5 0.0111 % in sediment 47.5 97.5 0.434 % in soil 50.7 0.00149 99.6	The results reflect that the ultimate fate of 1-docosanol is dependent on its route of release into the environment. 1-Docosanol released to air would partially precipitate to soil and water. In water, the adsorption coefficient of 1-docosanol results in adsorption to sediment.

ANNEX VII: MEASURED ENVIRONMENTAL CONCENTRATIONS

Long Chain Aliphatic Alcohols in Wastewater Treatment Plant Influent and Effluents

Several methods that measure long chain aliphatic alcohols in environmental matrices are available. Dunphy *et al*. (2001) devised and executed a method whereby alcohols present in an environmental sample can be detected at extremely low concentrations, often less than 10 ng/L. The method involves extraction of wastewater effluent and associated solids followed by derivatization with 2-fluoro-N-methylpyridinium p-toluenesulfonate to a permanent cation for quantitation by HPLC/MS. Morrall *et al*. (2006) reported influent levels of long chain alcohols for 9 wastewater treatment plants across the United States and 3 additional plants were reported in MRI (2004). Influents ranged from 102.8 to 2332.6 µg/L (sum of $C12_{-18}$ long chain aliphatic alcohols) and averaged 698.4 µg/L across all influents that were sampled (Annex VII, Table A.VII-1). Individual chain lengths averaged 64.0 µg/L (C_{13}) to 160.0 µg/L (C_{18}). When considering these data further, it should be clear that the analytical procedure includes both free and sorbed alcohol in the measurement. For further consideration of measured exposures in the environment, it is important to understand the amount that is sorbed.

Van Compernolle *et al*. (2006) report the adsorption of several long chain alcohols (C12, C14, C_{16}, and C_{18}) to wastewater treatment plant solids in a manuscript devoted to developing a sorption (Q)SAR for alcohol ethoxylates. Based on the alcohol only subset of data, the following SARs are derived (data in Table A.VII.2):

Log K_d = Chain Length x 0.235 + 0.642 ($R^2 = 0.999$, n = 4)
Log K_{oc} = Chain Length x 0.235 + 1.420 ($R^2 = 0.999$, n = 4)

These two relationships can be used to predict the relevant levels of long chain alcohol initially in solution in the wastewater influents and effluents. Measured log Kd for these long chain aliphatic alcohols ranged from 3.477 (± 1.892 SD) (C12) to 4.896 (± 3.728 SD) (C_{18}).

Measured levels of long chain aliphatic alcohols in municipal wastewater effluents have been made with the same methodology cited for influents above and have been reported by Eadsforth *et al*. (2006), Morrall *et al*. (2006), and MRI (2004). These studies have taken place in United States, Canada, and 5 countries in Western Europe (Annex VII, Table A.VII-3). Due to extremely rapid and extensive degradation concentrations in effluent are quite low. For this reason the methods of Dunphy *et al*. (2001) were developed as individual analytes typically are well below 0.1 µg/L thereby requiring large extraction volumes (4 L) and accounting of both free and sorbed alcohol on wastewater solids.

Determination of average regional wastewater concentrations varies in relation to the amount of specific data available on types of treatment employed within different geographies. In Europe only Activated Sludge (AS) treatment was monitored whereas in Canada, Activated Sludge and fixed film treatment (Trickling Filter [TF] and Rotating Biological Contactor [RBC]) were monitored. However, because the number of plants and their wastewater flow volumes in Canada are not available for the entire country, it is not known how to appropriately weight the individual measurements of long chain alcohol by treatment to achieve a national average. This data is available for the United States (USEPA, 1997). For example, activated sludge (AS) treatment accounts for 80.6% of total US wastewater flow versus 7.1% for Trickling Filters. Therefore, individual measurements can be weighted to achieve a national average concentration. For the US, Canada, and Europe, the average total long chain aliphatic alcohol concentrations (C12 to C_{18}) in effluent are 1.442, 2.811, and 2.169 µg/L, respectively. The 90th centile (all measurements at this concentration or lower) for individual monitored effluent measurements worldwide, not accounting for treatment type and flow, is 4.407 µg/L and the global average for the three regional measurements is 2.141 µg/L. These values include both free and bound alcohol to wastewater solids, see Table A.VII-3.

Table A.VII-1. Measured long chain alcohols in sewage treatment plant influents from monitoring studies in the US

[(Concentrations expressed in µg/L) (data from Morrall *et al*., 2006 (A) and MRI, 2004 (B)). AS-activated sludge L-lagoon; OD-oxidation ditch; RBC-rotating biological contactor; TF-trickling filter]

Location	Treatment Type	C12	C13	C14	C15	C16	C18	Total	Data Source
Influent									
San Benito, Texas	L	40.1	39.9	51.2	165.6	55.6	37.1	389.5	A
Rockaway Valley, New Jersey	OD	82.1	25.4	83.7	57.6	78.6	102.9	430.3	A
St. Clairsville, Ohio	RBC	51.5	15.0	55.6	34.7	40.1	37.2	234.1	A
Oskaloosa, Iowa	TF	139.2	68.5	168.7	122.7	178.2	176.4	853.7	A
Sedalia, Missouri	TF	201.3	64.5	163.6	102.7	150.9	164.3	847.3	A
Rosehill, Kansas	L	26.1	4.25	26.62	10.49	15.62	19.75	102.8	A
Lodi, California	AS	69.2	12.3	71.8	52.0	78.6	90.1	374.0	A
Durham, Oregon	AS	23.2	5.0	31.8	32.9	53.6	79.0	225.5	A
Opelika, Alabama	OD	124.7	90.8	83.8	403.1	203.5	190.4	1096.3	A
Lowell, Indiana	AS	409.6	268.5	277.4	254.3	505.3	617.5	2332.5	B
Wilmington, Ohio	AS	30.0	19.5	21.1	20.8	45.0	43.7	180.1	B
Bryan, Ohio	AS	213.1	154.2	143.4	119.9	322.6	361.7	1314.9	B
Influent Average		84.2	36.2	81.9	109.1	95.0	99.7	506.1	
Effluent									
San Benito, TX USA	L	0.958	0.067	0.626	0.329	0.888	1.555	4.423	A
Rockaway Valley, NJ USA	OD	0.603	0.025	0.093	0.021	0.142	0.641	1.525	A
St. Clairsville, OH USA	RBC	0.023	0.008	0.025	0.007	0.017	0.050	0.130	A
Oskaloosa, IA USA	TF	0.965	0.134	0.448	0.422	0.832	1.466	4.267	A
Sedalia, MO USA	TF	1.892	0.499	1.952	0.578	4.752	3.812	13.485	A
Rosehill, KS USA	L	0.552	0.067	0.406	0.062	0.221	1.982	3.290	A
Lodi, CA USA	AS	0.134	0.015	0.041	0.026	0.060	0.294	0.570	A
Durham, OR USA	AS	0.132	0.007	0.057	0.027	0.063	0.538	0.824	A
Opelika, AL USA	OD	0.140	0.128	0.032	0.010	0.010	0.438	0.758	A
Lowell, Indiana	AS	0.160	0.004	0.004	0.385	0.035	0.352	0.941	B
Wilmington, Ohio	AS	0.097	0.004	0.056	0.086	0.116	0.400	0.759	B
Bryan, Ohio	AS	0.051	0.004	0.004	0.004	0.004	0.073	0.140	B
Effluent Average		0.270	0.038	0.1601	0.070	0.287	0.656	1.442	
Removal (%)									
San Benito, Texas	L	97.6	99.8	98.8	99.8	98.4	95.8	98.9	A
Rockaway Valley, New Jersey	OD	99.3	99.9	99.9	100.0	99.8	99.4	99.6	A
St. Clairsville, Ohio	RBC	100.0	99.9	100.0	100.0	100.0	99.9	99.9	A
Oskaloosa, Iowa	TF	99.3	99.8	99.7	99.7	99.5	99.2	99.5	A
Sedalia, Missouri	TF	99.1	99.2	98.8	99.4	96.9	97.7	98.4	A
Rosehill, Kansas	L	97.9	98.4	98.5	99.4	98.6	90.0	96.8	A
Lodi, California	AS	99.8	99.9	99.9	100.0	99.9	99.7	99.8	A
Durham, Oregon	AS	99.4	99.9	99.8	99.9	99.9	99.3	99.6	A
Opelika, Alabama	OD	99.9	99.9	100.0	100.0	100.0	99.8	99.9	A
Lowell, Indiana	AS	100.0	100.0	100.0	99.8	100.0	99.9	100.0	B
Wilmington, Ohio	AS	99.7	100.0	99.7	99.6	99.7	99.1	99.6	B

Bryan, Ohio	AS	100.0	100.0	100.0	100.0	100.0	100.0	100.0	B
Removal Average		**99.8**	**99.9**	**99.9**	**99.9**	**99.8**	**99.6**	**99.8**	

Table A.VII.2. Sorption (K_d and K_{oc}) of radiolabeled long chain alcohols to wastewater solids

[The data for the C15 alcohol is reported here for completeness, but is not considered in the alcohol sorption SAR because of technical discrepancies discussed in Van Campernolle *et al.* (2006). Based on the time course data, sorption was concluded to be in equilibrium at 72 hr.]

Chain Length	K_d	K_{oc} at measured f_{oc} of 0.167
12	3,002	17,981
14	8,486	50,828
15	3,084	-----
16	23,790	142,492
18	78,695	471,350

Table A.VII.3. Summary of measured long chain alcohols in sewage treatment effluents cited from monitoring studies in the United States

[(Data from Morrall *et al*. 2006), Canada, and Europe (data from Eadsforth *et al*., 2006) (all concentrations expressed in µg/L). L = lagoon; OD = oxidation ditch; TF = trickling filter; AS = activated sludge; RBC = rotating biological contactor. The US average is not a simple arithmetic mean, but reflects the national distribution of each form of waste treatment based on flow.]

Location	Treatment Type	C12	C13	C14	C15	C16	C18	Total
San Benito, TX USA	L	0.958	0.067	0.626	0.329	0.888	1.555	4.423
Rockaway Valley, NJ USA	OD	0.603	0.025	0.093	0.021	0.142	0.641	1.525
St. Clairsville, OH USA	RBC	0.023	0.008	0.025	0.007	0.017	0.050	0.130
Oskaloosa, IA USA	TF	0.965	0.134	0.448	0.422	0.832	1.466	4.267
Sedalia, MO USA	TF	1.892	0.499	1.952	0.578	4.752	3.812	13.485
Rosehill, KS USA	L	0.552	0.067	0.406	0.062	0.221	1.982	3.290
Lodi, CA USA	AS	0.134	0.015	0.041	0.026	0.060	0.294	0.570
Durham, OR USA	AS	0.132	0.007	0.057	0.027	0.063	0.538	0.824
Opelika, AL USA	OD	0.140	0.128	0.032	0.010	0.010	0.438	0.758
Lowell, Indiana	AS	0.160	0.004	0.004	0.385	0.035	0.352	0.941
Wilmington, Ohio	AS	0.097	0.004	0.056	0.086	0.116	0.400	0.759
Bryan, Ohio	AS	0.051	0.004	0.004	0.004	0.004	0.073	0.140
Average		0.255	0.035	0.147	0.135	0.283	0.587	1.442
Vernon, BC, Canada	TF	0.393	0.174	0.428	0.886	0.452	0.718	3.051
Kelowna, BC, Canada	AS	0.243	0.102	0.107	0.181	0.095	0.121	0.849
Toronto, ON, Canada	AS	0.027	0.235	0.548	0.312	0.883	0.492	2.497
La Prairie, QC, Canada	AS	0.070	0.030	0.029	0.041	0.057	0.068	0.295
Victoriaville, QC, Canada	AS	0.069	0.019	0.014	0.048	0.026	0.109	0.285
Paris, ON, Canada	AS	0.036	0.030	0.033	0.059	0.083	0.060	0.301
Cardston, AB, Canada	RBC	1.251	0.961	3.354	3.257	3.180	2.174	14.177
Waterloo, ON, Canada	AS	0.301	0.122	0.156	0.172	0.160	0.127	1.038
Average		0.299	0.209	0.584	0.619	0.617	0.483	2.811
Northwich, UK	AS	0.468	0.319	0.305	0.154	0.485	0.591	2.322
Cannock, UK	AS	0.104	0.087	0.069	0.084	0.179	0.318	0.841
Rushmoor, UK	AS	0.134	0.104	0.095	0.125	0.338	0.408	1.204

Kralingse Veer, NL	AS	0.410	0.147	0.138	0.125	0.368	0.138	1.326
De Meern, NL	AS	0.282	0.208	0.174	0.155	0.472	0.239	1.53
Horstermeer, NL	AS	0.360	0.211	0.212	0.136	0.598	1.209	2.726
Estepona, ES	AS	0.214	0.073	0.182	0.148	0.999	1.144	2.76
La Vibora, ES	AS	1.179	0.533	1.741	1.181	4.172	2.426	11.232
Munich, G	AS	0.010	0.023	0.007	0.034	0.005	0.008	0.087
Torino, IT	AS	0.070	0.094	0.057	0.058	0.419	0.038	0.736
Robecco, IT	AS	0.092	0.130	0.072	0.206	0.187	0.266	0.953
Ratingen, G	AS	0.046	0.052	0.033	0.083	0.037	0.068	0.319
Average		0.281	0.165	0.257	0.207	0.688	0.571	2.322
Global Average		0.278	0.136	0.329	0.320	0.529	0.547	2.141

Wastewater effluent measurements in the previously cited studies include the levels of long chain aliphatic alcohol initially sorbed to wastewater solids. Using the bioavailability SAR above, adjusted to a common level of organic carbon for wastewater ($f_{oc} = 0.32$), free long chain aliphatic alcohol in effluents can be estimated (Annex VII, Table A.VII-4). For US, Canada and Europe, the average total long chain alcohol concentrations (C12 to C_{18}) following adjustment due to sorption are 0.644, 1.487, 1.041 µg/L. The 90th centile (all measurements at this concentration or lower) for individual monitored effluent measurements worldwide, not accounting for treatment type and flow, is 2.121 µg/L and the global average of regional measurements is 1.057 µg/L. A reduction in the longest chain lengths, that possess the highest Koc values, account for the largest change in predicted total AE exposure concentration. This observation in particular has high importance when considering the structure-activity-relationships for aquatic toxicity to the long chain aliphatic alcohols.

Long Chain Aliphatic Alcohols in Sediments

Few reliable data are available for the sediment compartment. Dyer *et al.* (2006) recently performed a study to determine the appropriateness of the Dunphy *et al*. (2001) analytical method for measuring alcohol ethoxylate in coarse sediments. The method was applied at three sites of varying sediment composition. Further refinements to the methods were instituted to potentially measure free long chain aliphatic alcohols and alcohol ethoxylates in pore water, surface waters, and chemical sorbed to coarse and fine sediments. Analytical results without further interpretation were recently reported by MRI (2004) to the Soap and Detergent Association (SDA). Three additional sites were considered in this latter study and considered points upstream of the discharge, in the immediate point of entry for the discharge, at the end of the mixing zone, downstream of the mixing zone and far downstream of the mixing zone (Table A.VII-5) (MRI, 2004). Long chain aliphatic alcohols were ubiquitous and primarily associated with fine particulate matter in river sediments. Measurements by chain length and location were variable and the highest measurements (up to 12 µg/g) were recorded far downstream of sewage treatment plant inputs (above that recorded in the mixing zones and discharge proper). Levels of alcohols upstream of sewage inputs highly overlapped those in discharge and mixing zone samples (circa 0.1 to 1 µg/g). These observations are indicative of and consistent with the widespread natural presence of long chain aliphatic alcohols in sediments reviewed by Mudge (2005).

Table A.VII.4. Summary of measured long chain alcohols in sewage treatment effluents following adjustment for bioavailability for the long chain alcohol (Q)SAR

[(all concentrations expressed in µg/L). L = lagoon; OD = oxidation ditch; TF = trickling filter; AS = activated sludge; RBC = rotating biological contactor. The US average is not a simple arithmetic mean, but reflects the national distribution of each form of waste treatment based on flow.]

Location	Treatment Type	C12	C13	C14	C15	C16	C18	Total
San Benito, TX USA	L	0.821	0.052	0.419	0.178	0.362	0.294	2.126
Rockaway Valley, NJ USA	OD	0.517	0.019	0.062	0.011	0.058	0.121	0.788
St. Clairsville, OH USA	RBC	0.020	0.006	0.017	0.004	0.007	0.009	0.063
Oskaloosa, IA USA	TF	0.827	0.104	0.300	0.229	0.339	0.277	2.076
Sedalia, MO USA	TF	1.621	0.388	1.308	0.313	1.937	0.721	6.288
Rosehill, KS USA	L	0.473	0.052	0.272	0.034	0.090	0.375	1.296
Lodi, CA USA	AS	0.115	0.012	0.027	0.014	0.024	0.056	0.248
Durham, OR USA	AS	0.113	0.005	0.038	0.015	0.026	0.102	0.299
Opelika, AL USA	OD	0.120	0.099	0.021	0.005	0.004	0.083	0.332
Lowell, Indiana	AS	0.137	0.003	0.003	0.209	0.014	0.067	0.433
Wilmington, Ohio	AS	0.083	0.003	0.038	0.047	0.047	0.076	0.294
Bryan, Ohio	AS	0.044	0.003	0.003	0.002	0.002	0.014	0.067
Average		0.219	0.027	0.098	0.073	0.115	0.111	0.644
Vernon, BC, Canada	TF	0.337	0.135	0.287	0.480	0.184	0.136	1.559
Kelowna, BC, Canada	AS	0.208	0.079	0.072	0.098	0.039	0.023	0.519
Toronto, ON, Canada	AS	0.023	0.183	0.367	0.169	0.360	0.093	1.195
La Prairie, QC, Canada	AS	0.060	0.023	0.019	0.022	0.023	0.013	0.160
Victoriaville, QC, Canada	AS	0.059	0.015	0.009	0.026	0.011	0.021	0.141
Paris, ON, Canada	AS	0.031	0.023	0.022	0.032	0.034	0.011	0.153
Cardston, AB, Canada	RBC	1.072	0.747	2.247	1.765	1.296	0.411	7.538
Waterloo, ON, Canada	AS	0.258	0.095	0.105	0.093	0.065	0.024	0.640
Average		0.256	0.162	0.391	0.335	0.252	0.091	1.487
Northwich, UK	AS	0.401	0.248	0.204	0.083	0.198	0.112	1.246
Cannock, UK	AS	0.089	0.068	0.046	0.046	0.073	0.060	0.382
Rushmoor, UK	AS	0.115	0.081	0.064	0.068	0.138	0.077	0.543
Kralingse Veer, NL	AS	0.351	0.114	0.092	0.068	0.150	0.026	0.801
De Meern, NL	AS	0.242	0.162	0.117	0.084	0.192	0.045	0.842
Horstermeer, NL	AS	0.309	0.164	0.142	0.074	0.244	0.229	1.162
Estepona, ES	AS	0.183	0.057	0.122	0.080	0.407	0.216	1.065
La Vibora, ES	AS	1.010	0.414	1.167	0.640	1.701	0.459	5.391
Munich, G	AS	0.009	0.018	0.005	0.018	0.002	0.002	0.054
Torino, IT	AS	0.060	0.073	0.038	0.031	0.171	0.007	0.380
Robecco, IT	AS	0.079	0.101	0.048	0.112	0.076	0.050	0.466
Ratingen, G	AS	0.039	0.040	0.022	0.045	0.015	0.013	0.174
Average		0.241	0.128	0.172	0.112	0.280	0.108	1.041
Global Average		0.239	0.106	0.220	0.173	0.216	0.103	1.057

Table A.VII.5. Levels of long chain aliphatic alcohols (ng/g) determined on coarse and fine sediment fractions in several small mid-western USA streams

[(MRI 2004 – Lowell, IN; Wilmington, OH; Bryan, OH, and Dyer *et al*, 2006 – East Fork, OH; Glendale, OH; Winton Woods, OH). C and F indicate alcohol associated with coarse and fine particulate matter isolated by centrifugation. NR indicates levels were not reportable based on laboratory blank samples reported in MRI (2004). Samples were simultaneously analyzed such that NR levels for C12, C13, C14, C15, C16, and C18 were <5.9, <6.5, <8.4, < 72, and <78 ng/g, respectively.]

Site	C12		C13		C14		C15		C16		C18		Total	
Upstream	C	F	C	F	C	F	C	F	C	F	C	F	C	F
Lowell, Indiana	NR	33	NR	46	NR	38	NR	43	NR	NR	NR	NR	NR	160
Wilmington, Ohio	NR	32	NR	29	NR	63	NR	143	NR	201	NR	145	NR	613
Bryan, Ohio	NR	29	NR	11	NR	43	NR	58	NR	358	NR	317	NR	816
Discharge Zone														
Lowell, Indiana	6.1	99	8.6	28	NR	141	NR	191	NR	535	NR	200	14.7	1208.7
Wilmington, Ohio	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Bryan, Ohio	--	--	--	--	--	--	--	--	--	--	--	--	--	--
East Fork LMR, Ohio	2	--	1.9	--	7.4	--	9.8	--	13.8	--	11.5	--	46.4	--
Glendale, Ohio	23.1	--	31.4	--	69.7	--	58.4	--	152.6	--	210.6	--	545.8	--
Winton Woods, Ohio	7.4	--	3.6	--	24.9	--	23.8	--	42.6	--	33.1	--	135.4	--
End of Mixing Zone														
Lowell, Indiana	11	49	8	28	11	49	NR	41	NR	83	NR	NR	30	250
Wilmington, Ohio	NR	104	NR	65	NR	160	NR	146	NR	852	NR	731	NR	2058
Bryan, Ohio	36	NR	11	NR	99	NR	53	NR	444	NR	961	NR	1604	NR
Downstream														
Lowell, Indiana	No Access Available at this Site													
Wilmington, Ohio	NR	24	NR	24	NR	22	NR	81	NR	73	NR	NR	NR	224
Bryan, Ohio	NR	7	NR	7	NR	10	NR	NR	NR	NR	NR	NR	NR	24
Far Downstream														
Lowell, Indiana	13	112	10	72	28	229	72	285	112	1273	NR	957	235	2928
Wilmington, Ohio	7	390	10	122	NR	649	NR	282	NR	5836	NR	5045	17	12324
Bryan, Ohio	NR	11	NR	NR	NR	20	NR	NR	NR	89	NR	NR	NR	120

Long Chain Alcohols in Manufacturing Discharges

No data are available for the presence of long chain alcohols in manufacturing discharges although it is realistic to expect exposure from production of any chemical, derived from process and handling losses, cleaning processes and the like. Due to the rapid and extensive biodegradation known for of alcohols it has been viewed as a low priority for work. Typically, manufacturing sites are structured to minimize potential inadvertent loss of materials due to process or production inefficiency. Specifically, so-called "fat traps" are in use to capture aliphatic substances on-site and prior to any environmental release. However, as with any engineered process and design some loss to the environment is inevitable. Because long chain aliphatic alcohols are aerobically and anaerobically biodegradable, and rapidly mineralized by unacclimated microbial consortia they are expected to decline quickly even while in discharge systems and subsequently after release into surface waters and sediments.

In order to gain insight into potential for release from manufacturing discharges in a local situation, EUSES v. 2 (EU TGD Volume 4, 2004) with Emission Scenarios for chemical production in industrialized Western Europe was used. The following inputs were utilized in these scenarios:

Input Parameter	Value
Production tonnage per year per chain length	3000 metric tonnes
Days of facility operation per year	300 days
Alcohol production per day	10,000 kg/day
Fraction to wastewater	0.0001
Daily loss rate	1 kg/day
Influent flow rate	10,000 m^3/d
In-stream Dilution	40

Influent and dilution values are taken from EU Technical Guidance Document Volume 4, "Emissions Scenarios for Chemical Production". EUSES SIMPLETREAT predictions for release from wastewater treatment plants are found in Section 2.2.4.3 and suggest loss rates lower than those measured in monitoring studies (discussed in Annex VII). Typical removal for C12-C_{18} chain lengths during sewage treatment are between 99.6-99.9% (Eadsforth *et al*., 2006; Morrall *et al*. 2006) which has also been confirmed experimentally under controlled laboratory conditions by Wind *et al*., 2006). To be conservative, a removal value of 99.5% was used for the C12-C18 range. It is likely that biodegradation rate constants used in simulations like SIMPLETREAT used for typical hydrophobic organics are inappropriate. Biodegradation rate constants for C12 and C16 LCOH were reported by Federle and Itrich (2006) and were used in these simulations. Furthermore, sorption estimates (K_{oc}) for C12-C18 long chain aliphatic alcohols were developed by Van Compernolle *et al*. (2006) and were applied to the same chain length range in the simulations. Koc values for long chain aliphatic alcohols below C12 were based on the alcohol (Q)SAR in the EU TGD (2004). It should be pointed out that SIMPLETREAT does not allow for anaerobic biodegradation in primary treatment, although anaerobic biodegradation of long chain aliphatic alcohols in a wastewater treatment context has been demonstrated (Federle and Itrich, 2006) thus the predictions should be considered conservative.

Table A.VII-6 summarizes SIMPLETREAT output for C_6-C_{20} alcohols. Predicted in-stream concentrations range from 0.003 to 0.113 µg/L for individual chain lengths. If a dilution factor of 10 is assumed following effluent discharge in the monitoring studies (see Table A.VI-5 where the global average measured effluent concentrations from wastewater treatment plants ranged from 0.103 to 0.239 µg/L for individual chain lengths) then in-stream predictions for wastewater treatment plant effluents and discharge from manufacturing are quite similar. Further, all of these predictions do not yet account for subsequent degradation in the receiving water. Given the rapid and extensive degradation rates confirmed in benchtop simulation studies (Federle and Itrich, 2006, Wind *et al*, 2006), high rates of removal demonstrated in sewage treatment (Eadsforth *et al*., 2006; Morrall *et al*, 2006), inherent metabolism of long chain aliphatic alcohols by micro and macrobiota, and the ubiquitous presence of natural sources of long chain aliphatic alcohols in the environment (Mudge 2005) exposure to long chain aliphatic alcohols will be of low concern.

Table A.VII.6. Summary of SIMPLETREAT output from EUSES for manufacturing scenarios with long chain aliphatic alcohols (C6-C20)

[Values common to all simulations include rate constant per hour (100), loss rate to waste (1.0 kg/d), influent flow rate (10000 m^3/d), influent concentration (100 µg/L), and dilution into receiving water (40)].

Substance	Koc predicted by (Q)SAR:	Koc value	Fraction to air	Fraction to water	Fraction to sludge	Fraction degraded	Clocalwater
			Fstp_air	Fstp_water	Fstp_sludge		**µg/l**
1-Hexanol	TGD Alcohols	1.96E+01	0.004	0.001	0.002	0.993	0.003
1-Heptanol	TGD Alcohols	3.18E+01	0.005	0.001	0.003	0.991	0.003
1-Octanol	TGD Alcohols	5.35E+01	0.004	0.001	0.005	0.990	0.003
1-Nonanol	TGD Alcohols	9.34E+01	0.006	0.0014	0.0083	0.984	0.004
1-Decanol	TGD Alcohols	1.92E+02	0.0076	0.0014	0.017	0.974	0.004
1-Undecanol	TGD Alcohols	2.19E+02	0.013	0.0014	0.019	0.967	0.004
1-Dodecanol	Van Compernolle et al.	1.65E+04	0.0048	0.0038	0.47	0.521	0.010
1-Tridecanol	Van Compernolle et al.	2.15E+04	0.00755	0.00417	0.498	0.490	0.010
1-Tetradecanol	Van Compernolle et al.	5.37E+04	0.00277	0.0077	0.597	0.393	0.019
1-Pentadecanol	Van Compernolle et al.	1.09E+05	0.00136	0.012	0.648	0.339	0.030
1-Hexadecanol	Van Compernolle et al.	1.60E+05	0.00172	0.0152	0.671	0.312	0.038
1-Octadecanol	Van Compernolle et al.	4.15E+05	0.00163	0.0273	0.729	0.242	0.068
1-Eicosanol	Van Compernolle et al.	1.12E+06	1.36E-04	0.045	0.796	0.159	0.113
1-Docosanol	Van Compernolle et al.	1.12E+06	0.000094	0.045	0.796	0.159	0.113

ANNEX VIII: ECOTOXICOLOGICAL (Q)SARs PREDICTIONS AND COMPARISON WITH MEASURED VALUES

This Annex considers the acute and chronic aquatic ecotoxicity data for the essentially pure substances. It is unwise to rely too heavily on predictions since it is not always known how reliable the studies were that the (Q)SARs are based on. Nevertheless, it is shown that the data set available makes a coherent whole.

Testing single component substances

Measured concentrations are the preferred source of information about exposure in laboratory studies. Nominal values may not be reliable since there may be problems of instability. However, for short term tests with easily soluble substances, nominal values are likely to be reliable.

This Annex shows that the acute E(L)C_{50} values follow the trend expected for non-polar narcosis.

(Q)SAR Models

There has been extensive discussion in the open literature and elsewhere of (Q)SAR approaches applicable to alcohols. For simplicity, restricting the discussion to pure linear alcohols, the following ecotoxicity and regression data (Table A.VIII.1) were obtained for fish acute studies, with the data used for the regression in italic. EC_{50} values units are transformed to log mmolar to be consistent with the normal methods in the literature:

Table A.VIII.1. Measured data for acute effects in fish

Chemical Name	Acute Fish 96h LC_{50} (mg/L)	Carbon No	*log (fish LC_{50}, mmol/L)*	MW	*log Kow*
1-Hexanol	97.20	6	*-0.022*	102.2	*2.03*
1-Heptanol	38.00	7	*-0.486*	116.2	*2.57*
1-Octanol	13.00	8	*-1.001*	130.3	*3.15*
1-Nonanol	5.50	9	*-1.419*	144.3	*3.77*
1-Decanol	2.30	10	*-1.838*	158.3	*4.57*
1-Undecanol	1.04	11	*-2.219*	172.4	*4.72*
1-Dodecanol	1.01	12	*-2.266*	186.4	*5.36*

Regression statistics:

Regression Statistics	
Multiple R	0.9876
R Square	0.9753
Adjusted R Square	0.9704
Standard Error	0.1484
Observations	7

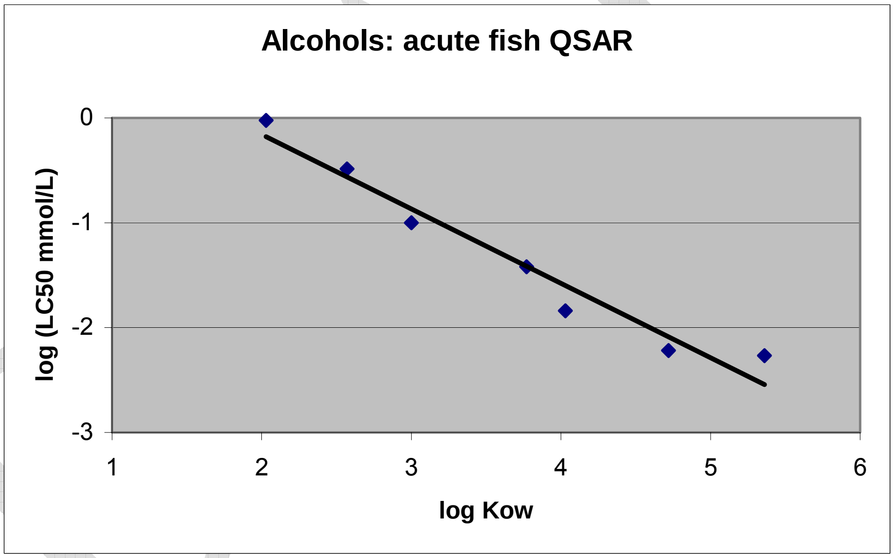
ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1	4.355227	4.355226964	197.7061	3.27E-05
Residual	5	0.110144	0.022028799		
Total	6	4.465371			

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	1.291	0.194116	6.653191209	0.001157	0.7925	1.7905
log Kow	-0.6989	0.049707	-14.06079851	3.27E-05	-0.8267	-0.5711

The results are shown in Figure A.VIII.1:

Figure A.VIII.1. Acute effects in fish



In summary:

Log EC_{50} = 1.29 – 0.691 log K_{ow}
R^2 = 0.975
Where EC_{50} is measured in mmol/litre.

Whilst the results are acceptable, they should not be over-interpreted due to the low number of points. The expression suggests that dependence of the EC_{50} on log K_{ow} is somewhat lower than the usual gradient for non-polar organics (approximately 0.94, e.g. in ECOSAR). This is further reflected in the evident trend in the fit from the Könemann equation (14-d LC_{50}), see Table A.VIII.2.

Table A.VIII.2. Comparison of regressions

Chemical Name	Carbon No	Acute Fish 96h LC_{50} (mg/L)	Predicted mg/L from above regression on $logK_{ow}$	Predicted by – ECOSAR (freshwater Fish 96h LC50, mg/L)	Predicted mg/L by Könemann - ECOSAR
1-Hexanol	6	97.2	68.0	111.0	129.22
1-Heptanol	7	38.0	32.0	44.0	49.76
1-Octanol	8	13.0	17.7	18.0	23.54
1-Nonanol	9	5.5	5.6	6.4	5.57
1-Decanol	10	2.3	4.0	2.4	3.63
1-Undecanol	11	1.0	1.4	0.9	0.99
1-Dodecanol	12	1.0	0.5	0.3	0.30

For carbon chain lengths of 6 to 8, the regression analysis presented here overestimates toxicity, whereas ECOSAR and Könemann methods both underestimate toxicity. For C10 to12, all values are closer to the observed toxicity, with the toxicity of calculated C12 being overestimated by all three methods. For C13 and C14 the predicted LC_{50} from the new regression are 0.45 mg/L and 0.2 mg/L, which are subject to being close to the limit of solubility in water. The ECOSAR values are 0.12 mg/L and 0.04 mg/L respectively. The order of magnitude is certainly consistent with a narcosis mechanism. Therefore, it seems unnecessary to address why the data are less sensitive to log K_{ow} than the usual predictions for non-polar narcosis. The acute *Daphnia magna* data are very similar to the fish data.

Table A.VIII.3. Measured data for acute effects in *Daphnia magna*

Chemical Name	Carbon No	CAS No	MW	*log Kow*	duration	Acute Daphnia EC_{50} (mg/L)	*log (Daphnia EC_{50}, mmol/L)*
1-Hexanol	6	111273	102.2	*2.03*	24	201	*0.293745*
1-Heptanol	7	111706	116.23	*2.57*	24	82	*-0.1515*
1-Octanol	8	111875	130.26	*3.15*	24	20	*-0.81378*
1-Decanol	10	112301	158.32	*4.57*	48	2.9	*-1.73714*
1-Undecanol	11	112425	172.35	*4.72*	96	1	*-2.23641*
1-Dodecanol	12	112538	186.38	*5.36*	48	0.77	*-2.38391*

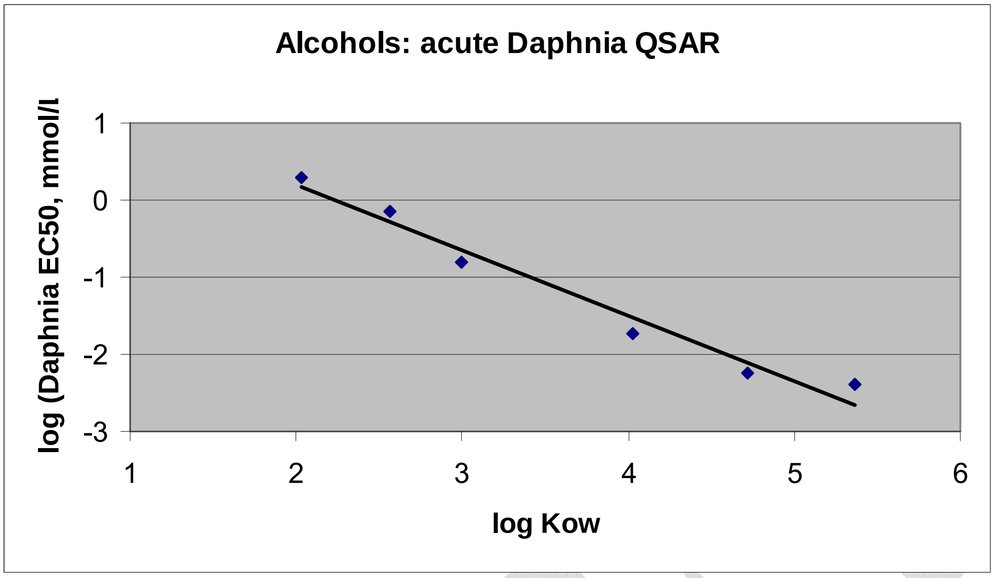
Regression Statistics	
Multiple R	0.9905
R Square	0.9811
Adjusted R Square	0.9764
Standard Error	0.1715
Observations	6.0000

ANOVA

	df	SS	MS	F	Significance F
Regression	1.0000	6.1216	6.1216	208.1327	0.0001
Residual	4.0000	0.1176	0.0294		
Total	5.0000	6.2392			

	Coefficients	Standard Error	t Stat	P-value	Lower 95%	Upper 95%
Intercept	1.9222	0.2256	8.5211	0.0010	1.2959	2.5485
log Kow	-0.8287	0.0574	-14.4268	0.0001	-0.9881	-0.6692

Figure A.VIII.2. Acute effects in *Daphnia magna*



In summary:

Log EC_{50} = 1.92 – 0.83 log K_{ow}
R^2 = 0.981
Where EC_{50} is measured in mmol/litre.

Table A.VIII.4. Comparison of regressions

Chemical Name	Carbon No	Acute *Daphnia* 48h EC_{50} (mg/L)	Predicted mg/L from above regression on logK_{ow}	Predicted by – ECOSAR (acute Daphnid 48h LC_{50}, mg/L) – neutral organics
1-Hexanol	6	201	175.6	76.2
1-Heptanol	7	82	71.2	28.0
1-Octanol	8	20	26.3	9.30
1-Decanol	10	2.9	2.12	0.58
1-Undecanol	11	1	1.73	0.46
1-Dodecanol	12	0.77	0.55	0.13

The ECOSAR neutral organics equation provides a result that gives a lower EC50 than all the measured examples.

USE OF READ-ACROSS AND EXPERT JUDGMENT FOR ALGAL TOXICITY

For comparison and for filling in data gaps the acute toxicity of essentially single carbon chain length alcohols has been estimated by expert judgment of qualified members of the Industry Consortium, with reference to measured and predicted results for other trophic levels.

The basis of the judgment is that examination of the available measured data suggest that algal EC_{50} values are of the same order, or possibly slightly lower, than the *Daphnia magna* EC_{50} values. However, there must always be uncertainty in such read across so in Table A.VIII.5 below, ranges have been stated. Table A.VIII.5 also shows the fish and invertebrate results used as part of the estimations. Where these data are themselves estimates, they are shown in italics. Available measured data for algae are shown with underlining. All other values for algae are estimated by read-across as described above. Data gaps for 'supporting' substances have not been filled as part of this process.

Table A.VIII.5. Estimated acute toxicity to algae for essentially pure commercial products (using expert judgment where no data are available)

CAS #	Comment [1]	Water solubility (mg/L)	Fish LC50 (mg/L) [2]	Invert EC50 (mg/L)[2]	Algae EC50 (mg/L)[2]
111-27-3	6	5900 at 20°C	97	201	80
111-70-6	7– SUPPORTING	1313 at 20°C	38	82	
111-87-5	8	551 at 25°C	13	20	6.5-14
143-08-8	9 - SUPPORTING	128 at 20 °C	5.5		
112-30-1	10	39.5	2.3	2.9	1.0-10 (read across)
68516-18-7	10 (hydroform) – SUPPORTING	-		4.2	
112-42-5	11	8.0 at 20°C	1.0	0.8-1.1	0.1-1.0 (read across)
68603-15-6	11 (branched) (Type A)	9.7 mg/L at a loading rate of 1000 mg/L [modelling]	*1.7* [3]	*1.7* [3]	1-10 (read across)
112-53-8	12– SUPPORTING	1.93 at 20°C	1.0	0.77	0.62 (biomass) -2.6 (growth) Other result agrees closely (EC50 0.97)
112-70-9	13	0.38 at 20°C	LC50 not reached *>LOS* [3]	0.51 - effects seen but this is slightly >LOS. *>LOS* [3]	0.1-1.0 (read across)
90583-91-8	13 (branched)	0.38 mg/L at a loading rate of 1000 mg/L [modelling]	*>LOS* [3]	*>LOS* [3]	>LOS [read across]
112-72-1	14	0.191 at 25°C	LC50 not reached *>LOS* [3]	Effects seen *0.18* [3]	Effects seen >LOS
629-76-5	15	0.102 at 25°C	*No effects expected at LoS* [3]	*No effects expected at LoS* [3]	No effects expected at LoS (read across)
36653-82-4	16	0.013 at 25°C	LC50 not reached *>LOS* [3]	*No effects expected at LoS* [3]	Effects seen >LOS
143-28-2	18 (unsaturated)	0.042 (prediction)	*No effects expected at LoS* [3]	*No effects expected at LoS* [3]	No effects expected at LoS (read across)
112-92-5	18– SUPPORTING	0.0011 at 25°C	LC50 not reached		
629-96-9	20	0.0027 mg/L at a loading rate of 1000	*No effects expected at LoS* [3]	*No effects expected at LoS* [3]	No effects expected at LoS

CAS #	Comment [1]	Water solubility (mg/L)	Fish LC50 (mg/L) [2]	Invert EC50 (mg/L)[2]	Algae EC50 (mg/L)[2]
		mg/L [modelling][1]			(read across)
661-19-8	22	0.0027 mg/L at a loading rate of 1000 mg/L [modelling] [1]	LC50 not reached *>LOS [3]*	*No effects expected at LoS [3]*	No effects expected at LoS (read across)

Notes:

1 – compositional Types are discussed in SIAR section 1.3

2 – LOS = Limit of solubility.

3 – estimated using QSAR (see Annex IX and earlier in this Annex)

ANNEX IX : ECOTOXICOLOGICAL INTERPRETATION OF DATA FOR MULTI-COMPONENT SUBSTANCES, AND FILLING OF DATA GAPS

1 INTRODUCTION

This Annex describes the approach to understanding the acute toxicity of members of the category which contain many components.

It is established in the scientific literature that aquatic organisms are exposed to a test substance *via* what is dissolved in the aqueous solution, rather than by what is undissolved. In order to interpret acute ecotoxicity data, information needs to be available about the composition of the test medium (i.e. the components dissolved) at the various dose levels used. Such information might be available via measurement or modelling.

Preparation of test media, for pure and multi-component substances, requires care and is ideally substantiated by appropriate analysis. It might not be realistic to quantify all components. For multi-component substances, there exists the possibility that some components could dissolve more (in absolute terms and as a proportion of the amount present) than others, as a consequence of differential solubility/partitioning into water. Analysis can be important for substances which degrade in the test system, or which adsorb to surfaces, or which volatilise. When test media have been prepared as water-accommodated fractions (i.e. by addition of an excess of substance, the components of which do not all dissolve fully in the medium), analysis is important or a predictive model might be useful.

For this category, valid measured acute data are not available for each substance and each trophic level. The purpose of this document is to provide a theoretical description of the toxicity which adequately explains the available data and which could allow data gaps to be filled by estimation. This approach uses (Q)SARs (see also Annex VIII) and a model for the solubility of substances.

One consequence of the foregoing discussion is the realisation that study results taken from the literature may be unreliable in respect of the actual exposure, particularly for poorly soluble and readily degradable substances. Therefore, any (Q)SARs used or developed using such data are subject to assessment of the reliability of the studies on which they are based.

It has been shown in the SIAR text and in Annex VIII to the SIAR that the acute $E(L)C_{50}$ values follow the trend expected for non-polar narcosis.

Multi-component substances do not present a major problem for measurement in the laboratory if all the components dissolve freely at the loading used, since it can reasonably be assumed that the effects can be added, although the method to do this is not straightforward (see section 3 of this annex for discussion). However, the pure substance solubility is not without problems as a guide to what could dissolve. For example, consider a multi-component product containing alcohols in the range C6 to C10. The total amount of that substance which dissolves in water cannot be easily predicted from the solubility of the individual alcohols present. This is addressed in detail in 3.1.

2. PHYSICOCHEMICAL DESCRIPTION OF SOLUBILITY OF LIQUIDS AS A PARTITIONING PROCESS

2.1 Theory

This section develops a reasonably simple model of solubility of multi-component substances with particular reference to the LCA category. It is general in that it applies to freely soluble substances, poorly soluble substances and liquid pure substances, assuming that problems of time needed to achieve equilibrium, degradation, volatilisation and adsorption can be ignored. It does not apply to surfactants.

If a quantity W (mg) of a multi-component alcohol substance is added to a volume of water V_{aq} (L), then at equilibrium by definition for each component of the substance:

$$K_{alc-w} = \frac{C_s}{C_{aq}} \quad (1)$$

Where K_{alcsw} is the alcohol-water partition coefficient of the component, and C_s and C_{aq} refer to its concentration in the substance and aqueous solution respectively. In this case, the alcohol that the component partitions out from is the substance itself. If the proportion dissolved out of the substance was very small, C_s would be similar to the initial concentration before addition to water. However, at low loading rates mass balance must be explicitly accounted for.

Thus if the proportion by weight of the substance is x:

$$xW = V_s C_s + V_{aq} C_{aq} \quad (2)$$

Where V_s and C_s are the volume of the alcohol and the concentration of the component in alcohol, at equilibrium. The initial volume is simply derived from the weight W and the density d. V_s is approximated as a fraction f of the initial volume. i.e.:

$$V_s = \frac{fW}{d} \quad (3)$$

Combining these equations, and setting V_{aq} = 1 L gives the expression for C_{aq}:

$$C_{aq} = \frac{xW}{(fWK_{sw}/10^6 d) + 1} \quad (4)$$

It is relevant to note that when $f = 0$ the substance is fully dissolved giving the expected result. When the substance is added to a high loading rate $f = 1$ and the equation 1 is returned. The value of f depends on C_{aq} so iteration is needed.

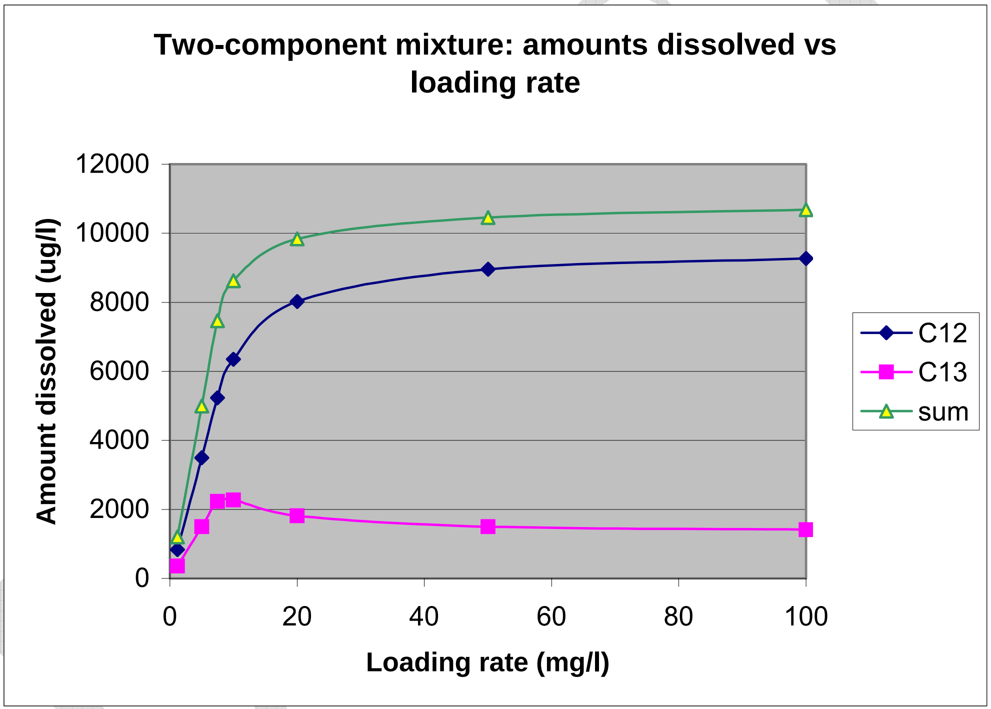
The equation (4) is very similar to methods used by previous authors to model toxicity of hydrocarbon fractions (for example, Peterson, 1994, and Verhaar, 1997,

As an example, a hypothetical two component mixture of dodecanol and tridecanol has been modelled using SRC KOWWIN (v. 3.12) values for the octanol-water partition coefficients. The results are shown in Table A.IX.1 and Figure A.IX.1.

Table A.IX.1. Effect of loading rate on amount of substance dissolved for a hypothetical two component mixture of dodecanol and tridecanol

	Amount dissolved (µg/L)			
Loading	C12	C13	sum	Fraction dissolved
1.2	840	360	1200	1
5	3499	1498	4997	0.999
7.5	5236	2231	7467	0.996
10	6346	2275	8621	0.862
20	8023	1817	9841	0.492
50	8957	1502	10460	0.209
100	9270	1412	10683	0.107

Figure A.IX.1. Effect of loading rate on amount dissolved for hypothetical mixture of dodecanol and tridecanol



Octanol-water partition coefficients are used in the example since this is the standard system and is relevant here. However as an important refinement, this treatment is improved below by the use of an alcohol-water partition coefficient suitable for each carbon chain length present.

2.2 Comparison to measured data

Pure substance data

It is of interest to note that the partition model given above gives a predicted solubility of pure octanol equal to the measured value of 550 mg/L with a log $K_{ow} = 3.17$, at any loading rate exceeding the solubility. The literature measured values of log K_{ow} are around 3.1, which is a good corroboration.

In order to model alcohol-water solubility and partition as accurately as possible, $K_{alcohol\text{-}water}$ ($K_{alc\text{-}w}$) values are needed for each carbon number. One way to obtain these is to use the measured solubilities. Table A.IX.2 shows values of $K_{alc\text{-}w}$ needed to obtain the literature measured water solubility.

Table A.IX.2. $K_{alc\text{-}w}$ values derived from measured solubilities

CAS No	C	Chemical Name	Measured log Kow	Water Solubility (mg/L)	Fitted log Kalc-w	Difference in log K values
111273	6	1-Hexanol	2.03	5900	2.145	0.115
111706	7	1-Heptanol	2.57	1313	2.791	0.221
111-87-5	8	1-Octanol	3.15	551	3.168	0.018
143-08-8	9	1-Nonanol	3.77	128	3.805	0.035
112-30-1	10	1-Decanol	4.57	39.5	4.348	0.222
112-42-5	11	1-Undecanol	4.72	8	5.003	0.283
112-53-8	12	1-Dodecanol	5.36	1.93	5.629	0.269
112-70-9	13	1-Tridecanol	5.51	0.38	6.33	0.82
112-72-1	14	1-Tetradecanol	6.03	0.191	6.642	0.612
629-76-5	15	1-Pentadecanol	6.43 est	0.102	6.905	-
36653-82-4	16	1-Hexadecanol	6.65	0.013	7.293	0.643
112-92-5	18	1-Octadecanol	7.19	0.0011	7.86	0.67

Whilst it is sensible to avoid over-interpretation of the data, a large increase in $K_{alc\text{-}w}$ above the $K_{octanol\text{-}water}$ value is not surprising for the higher carbon numbers. Consider dodecanol: the difference was 0.27 above the measured log K_{ow} value, consistent with the fact that dodecanol will be more hydrophobic than octanol. The $K_{alc\text{-}w}$ values will be used in subsequent modelling.

The branched alcohols present in many of the substances in the category are expected to have slightly lower partition coefficients than their linear equivalents, because the molecular size is smaller, and the CH_2 groups shield each other from the surrounding water in solution (the relationship of molecular size to log K_{ow} has been discussed in many papers). There are no solubility data to allow calculation of $K_{alc\text{-}w}$ for the branched isomers. The SRC program KOWWIN suggests a difference of around 0.07 for the octanol-water system, which is probably insignificant, and therefore this value will be used to reduce $K_{alc\text{-}w}$ for the present work. Work by Roberts and Marshall (1995) suggests much higher differences but since these values are based on biological data they are not useful for the present purpose - they may be correct values but to use them could introduce a circular argument into the analysis, because the present Annex is also trying to interpret similar biological data on the basis of partition coefficients.

Data for Mixtures

Set 1

In a study (Wenzel, 2003) for which there is a substantial amount of analytical data across several loading rates, analytical determinations of the water-accommodated fractions were made. For information, 9.6 mg/L loading of four substances gave results reported in Table A.IX.3.

Table A.IX.3 provides information about their composition and average dissolved concentrations at a WAF loading rate of 9.6 mg/L (% compositions have been rounded).

Table A.IX.3. Compositions of four substances, and average dissolved concentrations, loading rate 9.6 mg/L

Sub-stance	C12OH		C13OH		C14OH		C15OH		C16OH		C18OH	
	%	M	%	M	%	M	%	M	%	M	%	M
1	40	227.7	60	50.45								
2	20	117.55	30	32.7	30	6.7	20	2				
3	60	749.75			20				10		15	
4	70	744.45			30	3.8			<5			

%: % content, rounded in order to protect confidentiality (exact values were used in the modeling)
M: Measured concentration (µg/L) at 9.6 mg/L loading

The first substance is not dissimilar to the example given above. Using the new predicted log K_{alc-w} values, the model predicts 302 µg/l and 82 µg/l of C12 and C13 respectively. The discrepancy with the measured values of around 225 µg/l and 50 µg/l is not substantial, but could be due to a number of factors, including all or some of:

1. $K_{alcohol-water}$ between the substance and algal media could be different to that in pure water;
2. Equilibrium may not have been achieved
3. The substance was degrading or adsorbing.

Considering the more complex second substance, the model predicts 147.4; 41.4; 19.9; 5.6 µg/l for the C12 to C15 alcohols, again over predicting the higher molecular weight homologues, but predicting the order of magnitude reasonably well. For this substance at 1.2 mg/L loading (data not shown above), the model predicts 26.0; 18.9; 8.84; 2.55 µg/l, whereas the measured values were 45.9; 18.3; 4.7 µg/l and not detected respectively.

The full study report is available which gives a full set of data for the Fraunhofer algal growth study, and shows that the model over-predicts some of the dissolved concentrations. These results may suggest that true equilibrium may not have been reached,. This is not a criticism of the study because the scale of media preparation presents serious operational problems for any ecotoxicology laboratory.

Set 2

Palmer and Cann (2000b) tested three commercial variants of CAS No. 68856-56-1 (Type A). At a loading rate of 1 mg/L the initial dissolved concentrations were 0.43mg/L, 0.64mg/L and 0.36mg/L. The predicted value from the partition model is 0.38 mg/L. It is not clear why there were differences between samples, since these had similar composition.

Set 3

Whale, Palmer and Cann (2000) tested 68333-80-2 (Type A) at two loading rates. Measured and predicted dissolved concentrations are given in Table A.IX.4.

Table A.IX.4. Measured and predicted dissolved concentrations of components of CAS No. 68333-80-2 (Type A) determined for two loading rates

Loading rate:	100 mg/L	1 mg/L
Measured:	0.23	0.07
Predicted:	0.15	0.15

The predicted values show that a loading rate of 1mg/L should have been high enough to achieve saturation. The amount dissolved at 100 mg/L was higher, which could have been due to slower attainment of equilibrium at the lower rate.

Set 4

The results of a study reported by Palmer and Cann (2000a) and summarised in Table A.IX.5 show that there can be differences between media prepared for tests with invertebrates (I) or algae (A).

Table A.IX.5. Measured and predicted total concentrations of dissolved components of multi-component alcohols in two different test media

CAS No.	Loading rate	Measured dissolved concentration (mg/L)		Predicted concentration in invertebrate (I) medium (mg/L)
67762-41-8 Type C	1 mg/L	0.60(I)	0.53(A)	0.68
	LL_{50}	0.28(I)	0.23(A)	0.48
67762-41-8 Type B	1 mg/L	0.60(I)	0.50(A)	0.68
	LL_{50}	0.23(I)	0.24(A)	0.49

Set 5

The results of a further series of studies with CAS No. 67762-41-8 (Type B) reported by Sasol, Sastech Research and Development (2000a) and summarised in Table A.IX.6 show the inherent difficulties of working with water accommodated fractions. Predicted and measured concentrations of dissolved components are reported for test media prepared at three loading rates.

Table A.IX.6. Measured and predicted total concentrations of dissolved components of a multi-component alcohol in test media

Loading rate (mg/L)	10	32	100
Measured total dissolved concentration (mg/L)	1.3	8.8	9.8
Predicted total dissolved concentration (mg/L)	1.0	1.1	1.1

The total maximum solubility of the components (summing their individual solubility values) is between 2 and 3 mg/L. This suggests that the laboratory analysis included dispersed material (which is not always avoidable) since such high dissolved concentrations were reported. The EL_{50} was reported as 15 mg/L.

In the parallel Daphnia study (Sasol, Sastech Research and Development, 2000b) a loading rate of 10 mg/L gave 5.5 mg/L dissolved and an EL_{50} of 2.8 mg/L. The algal study (Sasol, Sastech Research and Development, 2001) was more in line with expectations. At 1 mg/L, a dissolved concentration of 0.63 mg/L was reported, and the E_bL_{50} was approx. 0.23 mg/L.

Set 6

Kirch (1998a) have reported the results of a study with CAS No. 67762-25-8 (Type A) in which the concentrations of individual alcohols were determined at two loading rates (1000 and 10 mg/L). The results obtained at the 1000 mg/L loading rate are summarised in Table A.IX.7.

Table A.IX.7. Measured and predicted concentrations of individual carbon number alcohols determined in test media prepared from CAS No. 67762-25-8 at a loading rate of 1000 mg/L

Carbon number	Concentration (mg/L)	
	Measured	Predicted
12	>>0.2	0.9
14	0.031	0.041
16	0.013	0.006
18	0.002	0.002

Agreement between measured and predicted is good. However, with a loading rate of 10 mg/L, the predictions are very similar to those at 1000mg/L, but the measured results were very different: C16>C14>C12 (in terms of quantity of each dissolved), which is hard to understand.

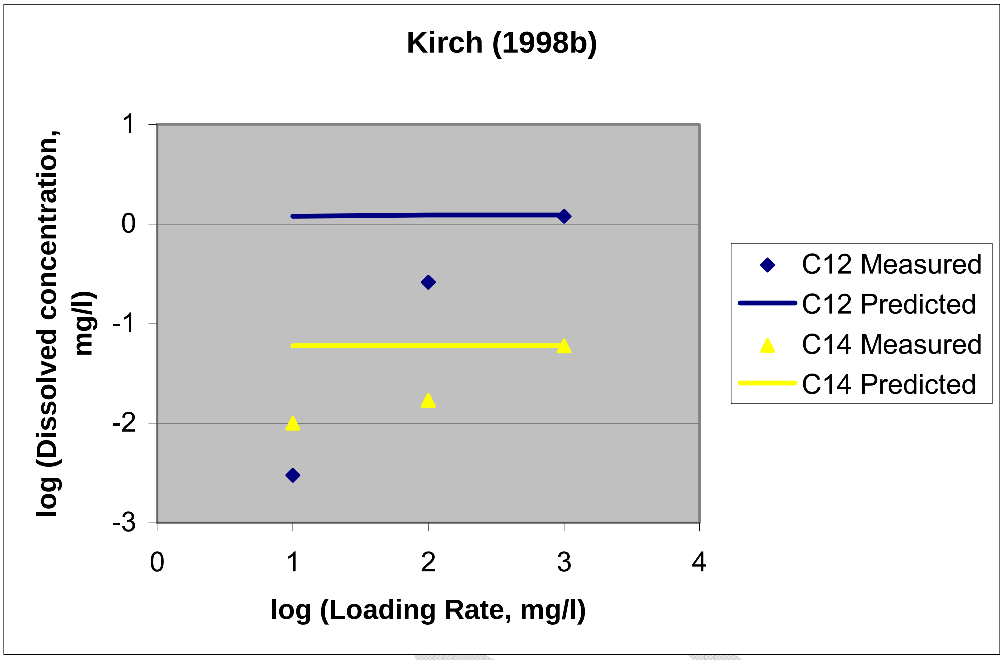
Set 7

Kirch (1998b) has reported the results of a study with CAS No. 80206-82-2 (Type A) in which measured concentrations of C12 and C14 alcohols were determined at loading rates of 10; 100; and 1000 mg/L. The results are summarised in Table A.IX.8 along with predicted concentrations of the alcohols.

Table A.IX.8. Measured and predicted concentrations of individual carbon number alcohols determined in test media prepared from CAS No. 80206-82-2 at loading rates of 10, 100 and 1000 mg/L

Loading (mg/L)	Carbon No.	Concentration (mg/L)	
		Measured	Predicted
10	12	0.003	1.2
	14	0.01	0.06
100	12	0.26	1.23
	14	0.017	0.06
1000	12	1.2	1.23
	14	0.06	0.06

Figure A.IX.2. Measured and predicted concentrations of individual carbon number alcohols determined in test media prepared from CAS No. 80206-82-2 at loading rates of 10, 100 and 1000 mg/L



The results show similar features to those identified for the Kirch (1998a) study in that at the low loading rates, higher carbon numbers dissolved more than expected. At 100mg/L the order is as expected but the magnitude is lower than predicted. At 1000 mg/L there is good agreement between the measured and predicted concentrations. It might be concluded that the rate of attainment of equilibrium at low loading rates is a controlling factor. A mixing period of 24 hours during test medium preparation is normally considered sufficient for substances that are not too viscous. However, the method and vigour (shear forces) of stirring is also an important factor determining the rate at which the substance dissolves.

3. MODELLING TOXICITY PROPERTIES OF PURE SUBSTANCES AND COMPLEX MIXTURES

There has been extensive discussion in the open literature and elsewhere of (Q)SAR approaches applicable to single carbon number alcohols (for example, the ECOSAR program, USEPA) – see Annex VIII. However, in order to deal with the combined effects of dissolved components present in a test medium derived from a multi-component alcohol, a method for summing all effects is needed. This section pulls together the summation of toxic effects method and predicted solubility of individual components of the mixtures dissolved, as discussed in section 2.

In an aqueous solution derived from a complex mixture, in which several components are present, each below their individually measured E(L)C_{50}, then it is possible that a 50% effect on a test organism could be reached, since each component could contribute to the whole effect. In order to model such behaviour predictively then a full dose-response for every component would need to be known, and the possibility of non-additive effects would have to be investigated. This is unrealistic for all practical purposes. The total amount of substance taken up by the organism can be estimated, usually from K_{ow}, and at a certain level, the uptake is considered to be lethal. This approach is not fully validated for mixtures, but is a good basis on which to approach such substances. In common with studies in other areas of toxicology, ecotoxicologists have developed a 'toxic units' approach, where the contribution of each component is summed. A toxicity value is obtained by summing, for example:

$$SumTU = \sum_i \frac{C_i}{E(L)C_{50,i}}$$

This method has the advantage of making maximum use of the available toxicity data. This approach is valid for any toxicological end point provided the same mode of action applies for every component.

Toxicity of each component

An $E(L)C_{50}$ is needed for each component that dissolves in the test medium.

Application

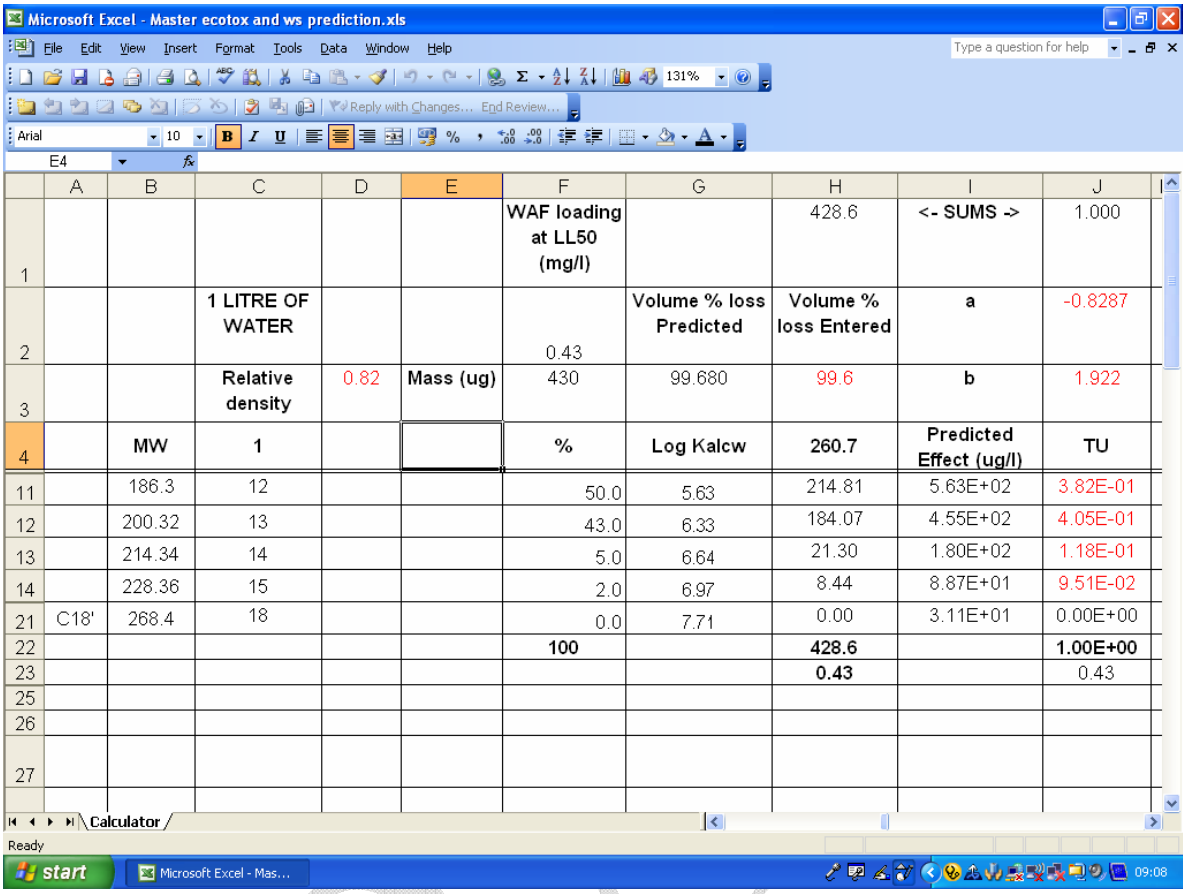
The method only works predictively if a set of conditions is found which generates Sum TU = 1. If the sum is less than 1 then it is implied that an acute $E(L)C_{50}$ cannot be reached at the limit of what can dissolve.

Spreadsheet

A spreadsheet has been used to implement the models as described.

A fragment of a cut-down version of the spreadsheet is shown below as a screen shot, and explanation of the cells follows as Figure A.IX.3:

Figure A.IX.3. Spreadsheet extract



	A	B	C	D	E	F	G	H	I	J
1						WAF loading at LL50 (mg/l)		428.6	<- SUMS ->	1.000
2			1 LITRE OF WATER			0.43	Volume % loss Predicted	Volume % loss Entered	a	-0.8287
3			Relative density	0.82	Mass (ug)	430	99.680	99.6	b	1.922
4		MW	1			%	Log Kalcw	260.7	Predicted Effect (ug/l)	TU
11		186.3	12			50.0	5.63	214.81	5.63E+02	3.82E-01
12		200.32	13			43.0	6.33	184.07	4.55E+02	4.05E-01
13		214.34	14			5.0	6.64	21.30	1.80E+02	1.18E-01
14		228.36	15			2.0	6.97	8.44	8.87E+01	9.51E-02
21	C18'	268.4	18			0.0	7.71	0.00	3.11E+01	0.00E+00
22						100		428.6		1.00E+00
23								0.43		0.43
25										
26										
27										

Points of note are:
Cell D3: density.

Cells F2 and F3: WAF loading rate in mg/L and µg/l respectively

Cell G3: % of initial volume calculated by the model to dissolve, entered manually in H3 (iterative).

Cells G11 to 21: log Kalcw values used to model dissolution

Cells H1, 22 (µg/l) and 23, J23 (mg/L): total concentrations of each chain length predicted to dissolve.

Cells I11 to 21: predicted EC50 for each component (µg/l), using the (Q)SAR coefficients in J 2 and 3.

Cells J1 and J22: sum of toxic units at the stated loading rate and amount dissolved.

Comparison to measured values

Whilst some reference has been made to dissolved concentrations measured and predicted, it is necessary to consider here a complete table of predictions and measured values. A number of comments need to be made about the table (A.IX.9) which follows:

1. All CAS numbers and types are included; even the essentially linear and pure substances do contain a range of chain lengths, and these have all been included.
2. The number of significant figures quoted is higher than can strictly be justified.
3. Data for supporting substances have not been included.
4. Columns highlighted in yellow are the predicted values from the partition model.

5. Columns highlighted in blue are the measured data; entries in bold font seem to be in contradiction to the predictions.

Given the fact that many laboratories have produced the data (over a number of years), and the difficulties of generating consistent water accommodated fractions, the consistency of measurements and predictions is good.

Table A.IX.9. Comparison of measured and estimated acute toxicity values for complex commercial products (fish and *Daphnia*)

			WS pred	WS Loading rate	FISH		Summary of fish measured data (LC50 or LL50)	DAPH		Summary of Daphnia measured data (EC50 or EL50)
					LC50/LL50	Sum TU		EC50/EL50	Sum TU	
111-27-3	1-Hexanol		5755.1	10000	63.4		97	123.6		200
	Heptanol									
68603-15-6	C6-12 Alcohols	TYPE A	9.7	1000	1.652			1.703		
68603-15-6	C6-12 Alcohols	TYPE B	43.9	1000	2.134		ca. 6	2.306		ca 6
68603-15-6	C6-12 Alcohols	TYPE C	510.0	1000	12.63		0.7-0.8	18.76		5.9
68603-15-6	C6-12 Alcohols	TYPE D	292.7	1000	3.775			4.265		
	[hexene and octene hydroformylation products mixture] - SUPPORTING									
	[hexene, octene and decene hydroformylation products mixture] - SUPPORTING									
111-87-5	Octyl alcohol		560.0	1000	15.6		13	25.45		20
85566-12-7	C8-10 Alcohols		201.7	1000	2.818			3.045		
68551-07-5	C8-18 ALCOHOLS		26.5	1000	3.6			1.313		
	Nonanol									
66455-17-2	C9-11 Alcohols		44.0	1000	2.135			2.307		
112-30-1	1-Decanol		39.5	1000	1.91		2.3	2.06		2.9
67762-41-8	C10-16 Alcohols	TYPE A	7.08	1000	0.5235			0.3136		
67762-41-8	C10-16 Alcohols	TYPE B	1.11	1000	0.619		15	0.489		0.23, 2.8
67762-41-8	C10-16 Alcohols	TYPE C	0.67	1000	0.605		ca. 10	0.48		0.28, >10
67762-41-8	C10-16 Alcohols	TYPE D	0.67	1000	2.61			0.208		
85665-26-5	Alcohols, C10-12		33.9	1000	2.135			1.133		
112-42-5	Undecyl alcohol		8.3	100	1.684		1	1.757		ca 1
	decene hydroformylation products - SUPPORTING									
	1-Dodecanol - SUPPORTING									
67762-25-8	C12-18 Alcohols	TYPE A	1.70	100	1.171			0.5		
67762-25-8	C12-18 Alcohols	TYPE B	0.35	1000	>100	0.750		17		

			WS pred	WS Loading rate	FISH		Summary of fish measured data (LC50 or LL50)	DAPH		Summary of Daphnia measured data (EC50 or EL50)
63393-82-8	C12-15 Alcohols	TYPE A	0.63	1000	2.445			0.212		
63393-82-8	C12-15 Alcohols	TYPE B	0.67	1000	2.6			0.21		
68855-56-1	C12-16 Alcohols	TYPE A	0.69	1000	2.335		Effects found, variable	0.212		Effects found, variable
68855-56-1	C12-16 Alcohols	TYPE B	3.22	1000	0.544		Effects found	0.25		
68855-56-1	C12-16 Alcohols	TYPE C	0.42	1000	100	0.823		2.2		
80206-82-2	C12-14 Alcohols	TYPE A	4.61	1000	0.483			0.282		
80206-82-2	C12-14 Alcohols	TYPE B	2.77	1000	0.774		Effects found	0.228		Effects found
75782-86-4	C12-13 Alcohols		1.12	1000	0.585			0.488		
68333-80-2	C14-16 Alcohols	TYPE A	0.15	1000	>100	0.688	No LC50 achieved	0.123		0.5
68333-80-2	C14-16 Alcohols	TYPE B	0.64	1000	2.58			0.208		
112-70-9	1-Tridecanol		0.50	1000	>100	0.866	No LC50 achieved	5.7		
90583-91-8	Tridecanol, branched and linear		0.38	1000	>100	0.695		>100	0.844	
112-72-1	1-Tetradecanol		0.20	1000	>100	0.750	No LC50 achieved	0.182		Effects found
75782-87-5	C14-15 Alcohols		0.15	1000	>100	0.688		0.29		
67762-30-5	C14-18 Alcohols	TYPE A	0.04	1000	>100	0.315		>100	0.566	
67762-30-5	C14-18 Alcohols	TYPE B	0.12	1000	>100	0.559		>100	0.844	
629-76-5	1-Pentadecanol		0.09	1000	>100	0.628		>100	0.998	EC50 possibly could be reached
36653-82-4	1-Hexadecanol		0.04	1000	>100	0.393	No LC50 achieved	>100	0.669	
67762-27-0	C16-18 Alcohols		0.03	1000	>100	0.315		>100	0.567	
143-28-2	9-Octadecen-1-ol, (9Z)-		0.04	1000	>100	0.316		>100	0.570	
68002-94-8	C16-18 and C18 Unsaturated		0.04	1000	>100	0.325	No LC50 achieved	>100	0.580	Effects seen
68155-00-0	Alcohols, C14-18 and C16-18-unsatd.		0.02	1000	>100	0.297		>100	0.553	
	Octadecanol									
97552-91-5	C18-22 Alcohol		0.01	1000	>100	0.150		>100	0.328	
629-96-9	1-Eicosanol		0.003	1000	>100	0.121		>100	0.287	
661-19-8	1-Docosanol		0.004	1000	>100	0.123	No LC50 achieved	>100	0.282	

4. SUMMARY

The combined use of (Q)SARs for fish and *Daphnia magna* combined with a model for partition (applicable to essentially pure and complex substances) means that every member of the category can be considered. The partition model provides an acceptable description of the dissolution of multi-component substances, particularly at high loadings at the time of initial preparation. The data thus generated are used within the main body of the SIAR text. The full details require access to the confidential compositional data, and are available to those authorised. Calculations for every CAS and Type have been made. Data for algae have been assessed on a read-across basis.

The overall model thus assembles all the alcohols into a single and coherent whole, and could be easily applied to any hypothetical new product of different composition to the present category members.

5. TOXICITY TO ALGAE

Acute toxicity to algae cannot easily be estimated for multi-component alcohols, but has been read across largely on the basis of the *Daphnia magna* data, which are the most applicable, although it is possible that effects on algae are slightly more severe.

Table A.IX.10 Measured and estimated acute toxicity to algae for complex commercial products (using expert judgment where necessary)

This table also shows the fish and invertebrate results used as part of the estimations. Where these data are themselves estimates, they are shown in italics. Available measured data for algae are shown with underlining. All other values for algae are estimated by read-across as described above.

CAS No.	Comment [1]	Water solubility (mg/L), sum of all components	Fish L(L)C_{50} (mg/L) [2]	Invertebrate E(L)C_{50} (mg/L) [2]	Algae E(L)C_{50} (mg/L) [2]
68603-15-6	6-12 (Type C)	510 mg/L at a loading rate of 1000 mg/L [modelling]	0.7-0.8	11	3.1
68603-15-6	6-12 (Type D)	293 mg/L at a loading rate of 1000 mg/L [modelling]	*3.8* [3]	*4.3* [3]	1.0-10
85566-12-7	8-10	202 (predicted, at a loading rate of 1000 mg/L)	6.5-10 (n)	*3.0* [3]	1.0-10
68551-07-5	8-18	26.5 (predicted, at a loading rate of 1000 mg/L)	3.6 [3]	*1.3* [3]	0.1-1.0
66455-17-2	9-11	44.0 (predicted, at a loading rate of 1000 mg/L)	2.1 [3]	*2.3* [3]	0.1-1.0
68603-15-6	6-12 (Type B)	43.9 mg/L at a loading rate of 1000 mg/L [modelling]	5.8 (n)	4.6	2.7
67762-41-8	10-16 (Type A)	7.1 mg/L at a loading rate of 1000 mg/L[modelling]	*0.52* [3]	*0.31* [3]	0.1-1.0
85665-26-5	10-12	34 (predicted, at a loading rate of 1000 mg/L)	*2.1* [3]	*1.1* [3]	0.1-1.0
67762-41-8	10-16 (Type B)	2.9	Effects seen	0.23	EL50 0.1-0.3 (both biomass and growth) Two other results support

CAS No.	Comment [1]	Water solubility (mg/L), sum of all components	Fish L(L)C_{50} (mg/L) [2]	Invertebrate E(L)C_{50} (mg/L) [2]	Algae E(L)C_{50} (mg/L) [2]
67762-41-8	10-16 (Type C)	2.4 at 25°C	Effects seen	0.28	EbL50 0.03-0.3; ErL50 One other result supports
67762-41-8	10-16 (Type D)	0.67 mg/L at a loading rate of 1000 mg/L [modelling]	*2.6* [3]	*0.21* [3]	0.1-1.0
67762-25-8	12-18 (Type A)	1.7 (predicted, at a loading rate of 100 mg/L)	*1.2* [3]	40 (i.e. effects seen >LOS *0.5* [3]	EbL50 2.3; ErL50 7.5 The value is >LOS]
67762-25-8	12-18 (Type B)	0.35 mg/L at a loading rate of 1000 mg/L [Modelling]	*>LOS* [3]	*17* [31]	10-100
63393-82-8	12-15 (Type A)	0.63 (predicted, at a loading rate of 1000 mg/L)	*2.4* [3]	*0.21* [3]	0.1-0.3
63393-82-8	12-15 (Type B)	0.67 mg/L at a loading rate of 1000 mg/L [Modelling]	*2.6* [3]	*0.21* [3]	0.1-0.3
68855-56-1	12-16 (Type B)	3.2 mg/L at a loading rate of 1000 mg/L [modelling]	Effects seen *0.54* [3]	*0.25* [3]	0.1-0.3
68855-56-1	Type C	0.42 mg/L at a loading rate of 1000 mg/L [modelling]	*>LOS* [3]	*2.2* [31]	1.0-10
68855-56-1	12-16 (Type A)	0.80 at 20°C	Effects seen >LOS *2.3* [3]	<1.0 *0.21* [3]	Results variable, mostly < 1; some valid results loaded 3-9 mg/L. Lowest (critical) result is EbL50 0.03-0.1; ErL50 = 0.1-0.3 All reported results are EL50s except one 2-day test, EC50 0.4 mg/L.
80206-82-2	Type A	4.6 mg/L at a loading rate of 1000 mg/L [modelling]	>LoS but effects seen in a study of non assignable Type. *0.48* [3]	>LOS but effects seen *0.28* [3]	EbL50 0.03-0.3 ErL50 = 0.1-0.3 Other results also EL50s; values >1 mg/L
80206-82-2	12-14 (type B)	2.8 (predicted, at a loading rate of 1000 mg/L)	>LoS but effects seen in a study of non assignable Type *0.77* [3]	>LoS but effects seen *0.23* [3]	0.1-1.0
75782-86-4	12-13	1.1 (predicted, at a loading rate of 1000 mg/L)	*0.58* [3]	*0.49* [3]	0.1-1.0
68333-80-2	Type B	0.64 mg/L at a loading rate of 1000 mg/L [modelling]	*2.6* [3]	*0.21* [3]	0.1-1.0
68333-80-2	14-16 (Type A)	0.70 at 20°C	LC50 not reached	*0.13* [3]	Effects seen >LOS. 0.1-1.0

CAS No.	Comment [1]	Water solubility (mg/L), sum of all components	Fish L(L)C$_{50}$ (mg/L) [2]	Invertebrate E(L)C$_{50}$ (mg/L) [2]	Algae E(L)C$_{50}$ (mg/L) [2]
75782-87-5	14-15	0.15 (predicted, at a loading rate of 1000 mg/L)	*No effects expected at LoS* [3]	*0.29* [31]	0.1-1.0
67762-30-5	14-18 (Type B)	0.12 (predicted, at a loading rate of 1000 mg/L)	*No effects expected at LoS* [3]	*No effects expected at LoS* [3]	>LoS
67762-30-5	14-18 (Type A)	0.035 (predicted, at a loading rate of 1000 mg/L)	*No effects expected at LoS* [3]	*No effects expected at LoS* [3]	>LoS
67762-27-0	16-18	0.03 (predicted, at a loading rate of 1000 mg/L)	*No effects expected at LoS* [3]	*No effects expected at LoS* [3]	>LoS
68002-94-8	16-18 and 18 Unsatd	0.045 (predicted, at a loading rate of 1000 mg/L)	LC50 not reached *>LOS* [3]	Effects seen - measured effects suspect *>LOS* [3]	>LoS
68155-00-0	14-18 and 16-18-unsatd.	0.024 (predicted)	*No effects expected at LoS* [3]	*No effects expected at LoS* [3]	>LoS
97552-91-5	18-22	0.0056 (predicted, at a loading rate of 1000 mg/L)	*No effects expected at LoS* [3]	*No effects expected at LoS* [3]	>LoS

Notes:

1 – compositional Types are discussed in SIAR section 1.3

2 – LoS = Limit of solubility.

3 – estimated using QSAR (see Annex VIII and earlier in this Annex)

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ANNEX X: CHRONIC TOXICITY OF LONG CHAIN ALIPHATIC ALCOHOLS TO *DAPHNIA MAGNA*

Summary – *the detail is developed in the text following*

The chronic aquatic toxicity of long chain aliphatic alcohols to *Daphnia magna* has been investigated. The practical work discussed here was carried out in part to provide measured data for (Q)SAR development due to the physical constraints of testing higher chain length alcohols and as a basis for predicting chronic toxic effects of other long chain alcohols, consistent with the category approach to the hazard assessment of long chain alcohols. Tests with pure alcohols (C10, C12, C14 and C15) were conducted in accordance with the guideline OECD 211, *Daphnia magna* Reproduction Test (Schäfers *et al*., 2005a, b, c, d) to augment existing literature data for C8 (Kuhn *et al.,* 1989). The new chronic data generated are the optimal that can be achieved reasonably. Effective testing involves real methodological complications due to the exceptionally rapid biodegradability of long chained aliphatic alcohols and the need to test as close as possible to their limits of water solubility. The apparent toxicity of C15 alcohol is measurably less than C14 alcohol based on survival and reproduction endpoints. The only method by which to make sense of the upward deflection in the toxicity profile is to investigate the relationship between toxicity, measured responses (which can combine toxicity and physical effects), and solubility. The C15 toxicity data are a mixture of both toxicity and physical effects that occur above the water solubility limit. A similar situation can be inferred to a lesser extent for C14. Reproduction is the more sensitive parameter and should be used to express toxicity and develop the (Quantitative) Structure-Activity Relationship ((Q)SAR) (developed in this Annex). NOEC and EC10 give similar (Q)SARs, although EC10 appears to be more consistently robust in (Q)SAR regression analyses. However, because the NOEC is more universally accepted in regulatory submissions, the NOEC will be used. Use of the C15 data in the (Q)SAR should be questioned and directly relates to the water solubility of C15. When C15 is not included the slope of most (Q)SARs approach -1 consistent with the expectation of a non-polar narcotic mode of action for alcohols (Veith *et al*., 1983). The acute to chronic ration (ACR) is less than 10 for 86% of the analyses and less than 100 for 100% of the analyses suggesting a non-specific narcotic ecotoxicological mode of action (ECETOC, 2003). As mentioned, the rapid biodegradability of these alcohols further complicates interpretation such that the real exposure-response profile lies somewhere between that expressed by total mean measured exposures and initial mean measured exposure. Thus, to derive the two most relevant chronic (Q)SARs for aquatic toxicity of alcohols to *Daphnia magna* the following conditions apply: (a) C15 alcohol is excluded for reasons of solubility; (b) the more sensitive reproduction endpoint is used; (c) the more accepted NOEC statistic is employed; and, (d) acknowledge that reality lies between total mean measured and initial mean measured exposure (see Box 1). Further testing the chronic aquatic toxicity of C_{16} and C_{18} chain lengths would be even more challenging than C15 due to progressively lower solubility, while exceptionally rapid biodegradability would remain unchanged. Based on the trends observed with these new toxicity data it is expected that effects on mortality and reproduction would not be observed below the level of water solubility.

Background Overview of Studies

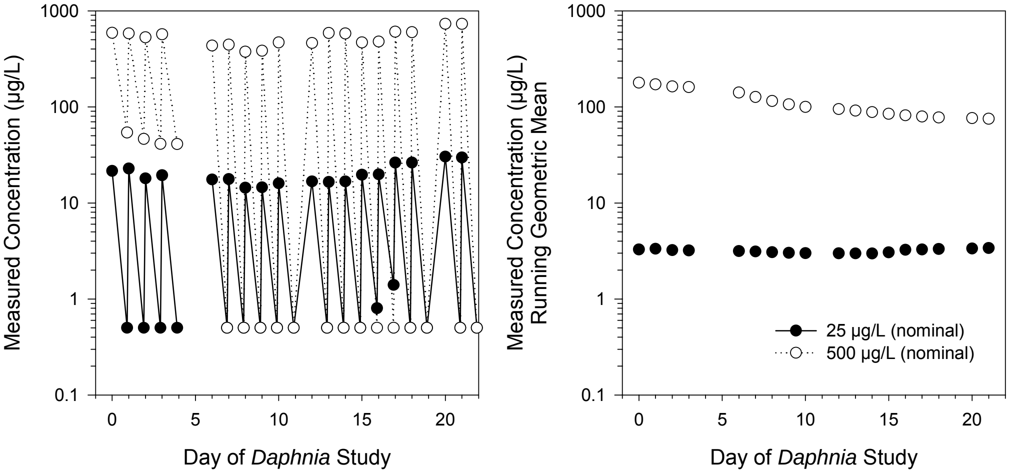
Due to the extensive and rapid biodegradation of alcohols during the conduct of aquatic toxicity tests, extreme care was taken to minimize the loss of test substances during the tests. Long chain aliphatic alcohols are extensively and rapidly mineralized to carbon dioxide and water, with half-lives in sewage treatment being less than one minute (Federle *et al*., 2006). While toxicity test dilution waters are clearly not equivalent to sewage these studies do indicate that bacteria in the environment do not require acclimation and readily utilize alcohols as a source of energy (Mudge, 2005). These aspects were confirmed in pre-studies to the full chronic toxicity tests where experimental design considerations were evaluated (Schäfers, 2005a, b). Further, two of the test substances (C14, C15) are of low water solubility (126 and 49 µg/L, respectively) and therefore required special handling and delivery. The following changes to typical protocols were therefore adopted to enable the performance of high-quality and meaningful studies:

- Vessels were closed, to reduce entry of bacteria from the atmosphere;
- Gentle aeration of test vessels was required as degradative losses of alcohol resulted in unacceptably low dissolved oxygen concentrations;
- Test solution renewals were made daily, with confirmatory analysis on both renewed and initial test solutions;
- Static renewal was determined to be the best exposure regime for long chain alcohols as this reduced the transfer of alcohol-degrading or consuming microbes (as compared to flow-through systems, where it becomes increasingly difficult to discourage acclimation and biofilm formation; see Brixham Environmental Laboratory, AstraZeneca, 2004);
- Saturated alcohol stock solutions were prepared daily for each test concentration. This involved a detailed preparatory method to reduce the possibility of insoluble material being present in the tests (Schäfers, 2005a, b);
- *Daphnia magna* were carefully rinsed with each daily transfer to reduce bacterial cross over to fresh exposure solutions. As *Daphnia magna* grow in size, this becomes less effective; and,
- Dilution water and test vessels were autoclaved prior to use each time (Schäfers *et al.*, 2005a, b, c, d).

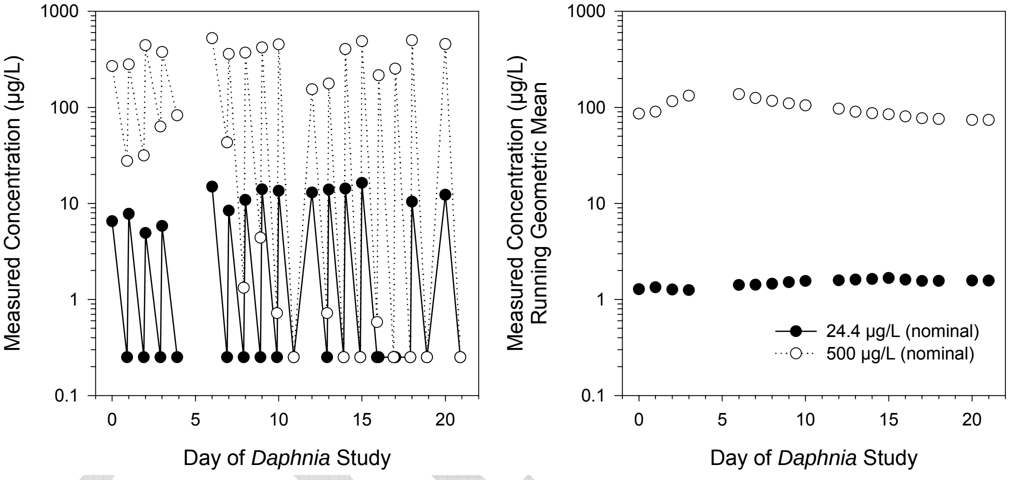
Algae have been found to metabolize alcohols and this is an unavoidable occurrence in chronic studies with *Daphnia magna* fed with algae. No modifications could be made to counter this without conducting further research into an alternative diet.

Figure A.X.1. Trends in measured exposures of dodecanol (C12) and tetradecanol (C14) at the low and high doses during the 21-d *Daphnia magna* toxicity studies

Dodecanol



Tetradecanol



In spite of the elaborate changes to reduce losses of test material, they still occurred. Figure A.X. 1 summarizes representative exposure trends for the low and high doses in C12 and C14 chronic studies. Several aspects are apparent. Beginning around the 5th to 7th day of exposure, it became increasingly difficult to maintain exposures at the high dose. Exposures declined to near background levels by 24 hours. However, the running average (average concentration determined to each point in time) exposure concentration shows the patterns are stable leading to results that can be interpreted meaningfully, in spite of noise in the daily measured data (see Figure A.X.1, Table A.X.1).

Note that by convention for this summary the following ways to express exposure will be used: (a) total mean measured concentration refers to the geometric mean of the average initial and average aged test solutions, and (b) initial mean measured concentration refers to the average of initial test solutions only.

All practicable methods, more extensive than is usually necessary, were implemented to increase the stability of exposures at and below the level of solubility in each study. However, it is expected that some initial higher treatment levels exceeded the level of solubility and during the course of each day as concentrations declined due to degradative loss, the limits of solubility were crossed (Figure A.X.2).

Table A.X.1 provides a summary of the predicted water solubility of the tested long chain alcohols along with the mean measured exposure and range. The higher chain lengths were tested in the region of water solubility, and did exceed solubility on some occasions. This is somewhat more likely than indicated because water solubility determinations are made in pure water lacking ions, whereas exposures occurred in waters with calcium and magnesium concentrations of 0.65-0.70 and 0.20-0.25 mmol/L, respectively. The usual expectation is that these would have a small effect, reducing solubility relative to pure water.

Studies with C14 and C15 were especially difficult as the predicted water solubilities for these alcohols are very low. Theory and practice in aquatic toxicology are established for testing that occurs at or below the level of solubility. Above the level of solubility physical effects enter into observed responses of the organism, but do not reflect influence of the chemical entering the body, target tissues or cells (see ECETOC 1996 for a review). Thus, interpretation is confounded and the observed responses of the test organism include a mixture of both physical effects (e.g., entrapment of particles in feeding structures, oil droplets and micro-emulsions coating organism surfaces, etc.) and toxicity. It is a reality that separating these profiles is not possible. However, it is possible to evaluate whether test observations adhere to theory and thus allow the organism to assist in the inference of solubility being exceeded or not. An example of this would be the expectation that a monotonic increase in toxicity would be observed as hydrophobicity of a chemical series increases.

Great care was taken with analytical preparations for the chronic *Daphnia magna* tests. Measured solubilities, particularly for alcohols of higher chain length (>C_{13}), become increasingly difficult and variable. Predicted solubilities then become useful to reduce the importance of variability in the data and its interpretation, and to provide grounds for comparison across all compounds. While Table A.X.1 summarizes mean measurements for the *Daphnia magna* toxicity tests, it is useful to evaluate the data graphically as in Figure A.X.2 below. Initial measured exposures routinely occur above the solubility limit. This was an unavoidable experimental outcome with consequences for interpreting the resulting effects data presented below.

First, it is important to assess effects based on both mean measured concentrations using fresh and old test solutions as well as a function of just initial solutions as the reality of exposure certainly lies between these extremes.

Table A.X.1. Relationship between solubility of long chain alcohols in pure water compared to *Daphnia magna* test waters

Chain Length	Predicted Water Solubility[a] (µg/L)	Nominal Exposure (µg/L)	Mean Total Measured Exposure[b] (µg/L)	Measured Exposure Range (µg/L)	Mean Initial Measured Exposure (µg/L)	Reference
C10	21,260	152	23	<1-161	122	Schäfers *et al.*,
		411	107	<1-414	351	2005c
		1,110	367	<1-1,352	962	
		3,000	1227	11-3,064	2,800	
C12	1420	25	3.4	<1-30	20	Schäfers *et al.*,
		69	5.3	<1-79	56	2005b
		185	14	<1-242	163	

		500	95	<1-733	534	
C14	126	24.4	1.6	<0.5-16	9.8	Schäfers *et al.*, 2005d
		68.6	3.6	<0.5-67	51	
		185	13	<0.5-188	138	
		500	77	<0.5-525	367	
C15	49	30	2.0	<0.2-22	15	Schäfers *et al.*, 2005a
		65	7.8	<0.2-127	56	
		139	19	0.2-155	104	
		300	63	0.2-387	241	

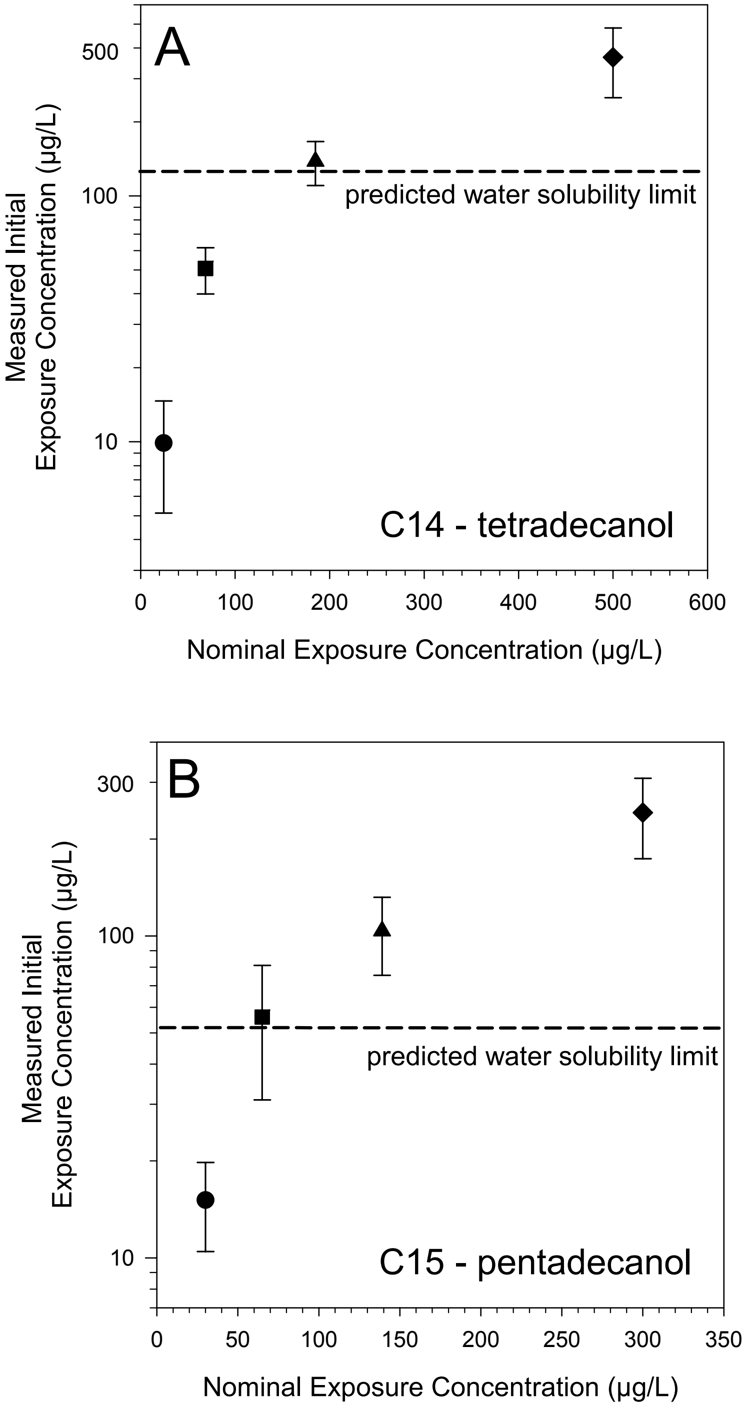
[a] Predicted values from Annex VIII. Reliable measured solubility values are available for all four substances; the use of the predicted values for solubility has the advantage of averaging any experimental variability.

[b] Mean measured exposure is based on the geometric mean of average initial exposures before addition or transfer of *Daphnia magna* and the average exposure measured in the same test vessel 24 hours later.

Secondly, testing at higher chain lengths only would become more problematic as a function of solubility. The suite of new chronic *Daphnia magna* toxicity studies on long chain alcohols presented here represents the upper bound of what can be accomplished with these highly biodegradable and insoluble materials.

Mean measured exposures and mean initial measured exposures were used in evaluations of the response of *Daphnia magna* to long chain alcohols in this sequence of studies. However, an underlying, experimentally uncontrollable pattern of variation is present, which can affect the strength of chronic structure-activity relationship interpretations. For example, this variation is not represented in the ultimate ECx and NOEC determinations as mean values are used to generate the statistical results.

Figure A.X.2. The relationship between predicted water solubility and measured initial concentrations in selected exposures in the C14 and C15 alcohol *Daphnia magna* tests



Sample sizes ranged from n of 18 to 20 across all concentrations.

The practical work discussed here was carried out in part to provide measured data for (Q)SAR development due to the physical constraints of testing higher chain length alcohols and as a basis for predicting chronic toxic effects of other long chain alcohols, consistent with the category approach to the hazard assessment of long chain alcohols.

Chronic Toxicity Results

Survival and reproduction endpoints have been summarized using standard statistical techniques. Conclusions for each test are presented as both NOEC and EC10. The OECD workshop on the statistical analysis of aquatic toxicity data concluded that regression analysis (ECx) was preferable to ANOVA (NOEC) for a number of reasons and that the latter should be phased out (OECD, 1998). Reasons for this recommendation include among others: data, such as the strength of the exposure response, are wasted in NOEC determinations, outcomes or conclusions are directly driven by choice of exposure concentrations, and the statistical outcome cannot be linked to population models. ECx estimations are generally found to be more robust for the development of structure-activity-relationships than those developed from NOECs. The influence of the choice of test concentrations on the structure-activity regression is highly diminished in the former and these can be more easily related to acute structure activity based on a similar modelling platform (for example, models already used to estimate the acute EC50).

Table A.X. 2 summarizes effect statistics for long chain alcohols with respect to survival and reproduction based on mean measured total concentrations or on mean initial concentrations. On average, responses expressed using mean initial exposure (in µg/L) are approximately 6.7 times higher than those expressed as mean total exposure. Figure A.X. 2 presents a comparison of survival and reproduction responses for all tests as a function of both expressions of exposure concentration. Effect of long chain aliphatic alcohols on *Daphnia magna* survival is generally less sensitive than the effect on reproduction. A pattern of increased toxicity with increasing chain length is also apparent. The new experimental data are combined with literature data for octanol (C8) (Kuhn *et al.*, 1989). In the octanol study, the most sensitive and only reported effect was on days to first brood release which occurred at 1000 µg/L (nominal concentration). For comparison of results across chain lengths and structure activity models the response for survival and reproduction was assumed to be equal to the effect on time to first brood.

The data indicate that for survival and reproduction, the NOEC and EC10 values increase from C14 to C15. This is almost certainly due to exceeding the boundary of water solubility as would be expected from conventional toxicological theory (Rufli *et al.*, 1998). Under these circumstances a more accurate interpretation of the results might be obtained by setting the exposure to the solubility of the substance (i.e., 49 µg/L). This has the effect of lowering the toxicity values but they are still higher than those for the C14 substance. This pattern is not in keeping with the trend of reducing toxicity values (i.e. higher toxicity) observed between the C8 and C14 alcohols. However it must be appreciated that significant uncertainty exists in identifying the true exposure concentrations in the region of the water solubility of a substance. Rufli *et al*. (1998), in a review of aquatic toxicity testing of sparingly soluble compounds, also point out that interpretation of toxicity responses observed above the solubility limit is aggravated by artefacts and that testing should only occur at or below the limit.

Table A.X.2. Chronic (21-d) aquatic toxicity of long chain alcohols to *Daphnia magna*

	Survival				Reproduction			
	NOEC		EC10		NOEC		EC10	
	µg/L	µmol	µg/L	µmol	µg/L	µmol	µg/L	µmol
	Exposure Based on Mean Total Concentration							
C8	1000	2.34	1000	7.68	1000	7.68	1000	7.68
C10	370	0.08	340	2.15	110	0.69	210	1.33
C12	14	0.06	33	0.18	14	0.08	13	0.07
C14	13	0.28	39	0.18	1.6	0.01	6.3	0.03
C15	>63	>0.28	>63	>0.28	7.8	0.03	12	0.05
	Exposure Based on Mean Initial Concentration							
C8	1000	7.68	1000	7.68	1000	7.68	1000	7.68
C10	960	6.06	934	5.90	350	2.21	610	3.85
C12	163	0.86	230	1.21	160	0.86	147	0.81
C14	140	0.65	180	0.83	9.8	0.05	70	0.33
C15	240	1.05	>240	>1.01	56	0.25	74	0.32

The chronic toxicity of alcohols should be considered in light of what is known of their acute toxicity, because survival responses are a common endpoint used in both studies. Acute toxicity tests have been performed with chain lengths up to C12 and were discussed in the Annex VIII. Acute toxicity of C14 and C15 has not been attempted due to technical experimental difficulties working above the solubility limit. Expected acute toxicity crosses the water solubility regression around C14, although confidence limits highly overlap from C12 onward (Figure A.X. 3).

Survival of *Daphnia magna* in chronic toxicity studies followed a pattern close to expectations until C15 with increasing effect with increasing hydrophobicity (Figure A.X. 4, 5). In the study on C15 alcohol, *Daphnia magna* all survived even at the highest exposure concentration of 63 µg/L (mean measured concentrations) or 240 µg/L (mean initial concentration), therefore the conclusion of this study is that the actual NOEC and EC10 would lie above these values. These responses do not conform to a pattern of monotonic decline with increasing hydrophobicity and may suggest that the test chemical does not penetrate cell membranes of the organism. While the actual regression statistics for the NOEC (Q)SAR may not provide an immediate interpretation of statistical significance ($p < 0.61$) the response is interpretable and can be considered biologically relevant (the (Q)SAR for the EC10, for example, is significant based on the same data set) (Table A.X.3).

Figure A.X.3. Comparison of acute toxicity (Q)SAR with water solubility in the range of chain lengths for which chronic toxicity data are available (with their 95% confidence intervals; bars indicate actual acute toxicity values).

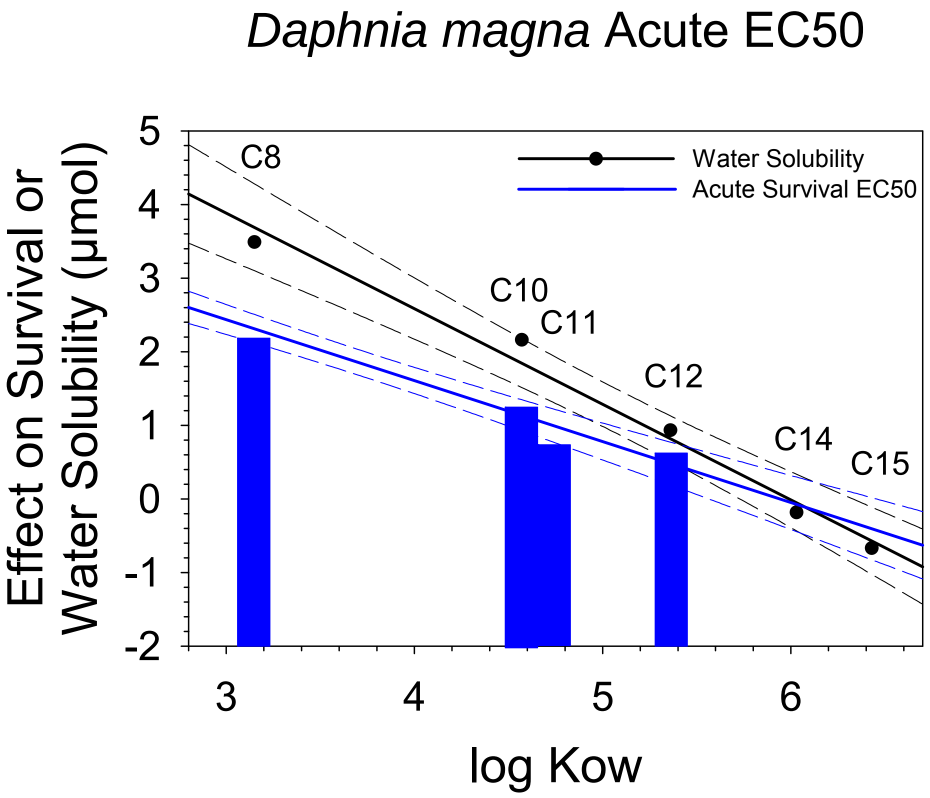
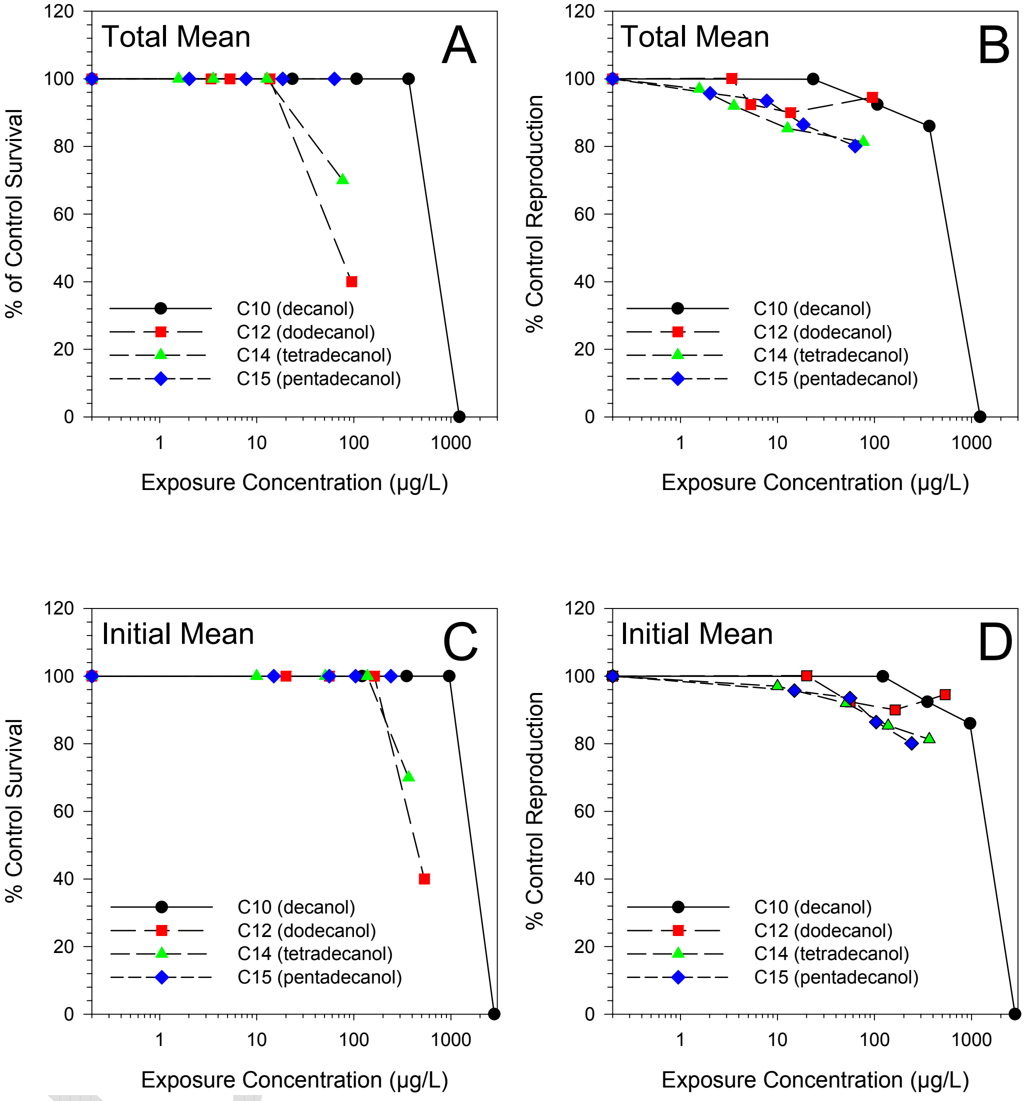


Table A.X.3. Summary of (Q)SAR regressions when C15 alcohol is excluded

Biological Endpoint	Statistical Endpoint	Expression of LCOH Exposure	Intercept	Slope	R^2	Adjusted R^2	F	p-value
Mortality	NOEC	Initial Mean	2.30	-0.41	0.82	0.73	9.10	0.10
	EC10	Initial Mean	2.13	-0.36	0.85	0.77	10.91	0.08
Reproduction	NOEC	Initial Mean	3.31	-0.70	0.84	0.76	10.40	0.08
	EC10	Initial Mean	2.54	-0.49	0.92	0.88	22.15	0.04
Mortality	NOEC	Total Mean	3.58	-0.81	0.88	0.82	14.91	0.06
	EC10	Total Mean	2.92	-0.63	0.91	0.86	19.20	0.05
Reproduction	NOEC	Total Mean	4.28	-1.03	0.97	0.96	70.62	0.01
	EC10	Total Mean	3.80	-0.88	0.95	0.92	36.89	0.03

Figure A.X.4. Exposure-response profiles for toxicity of several long chain alcohols to *Daphnia magna*



Figures A and B provide survival and reproduction responses when exposure is expressed as the total mean concentration measurement. Figures C and D provide survival and reproduction responses when exposure is expressed as the initial mean concentration measurements.

The response of *Daphnia magna* with regards to reproduction (young per female) is somewhat more sensitive than survival. Again, as with mortality, the expectation that
C15 belongs within the same structure-activity relationship appears unlikely. The effect on *Daphnia magna* in the C15 study is less than that for C14 (Figure A.X. 6). In plots of reproduction NOEC and EC10 values based on total mean concentration there is a clear deflection of apparent toxicity upward relative to C14. It is clear in both plots of reproduction NOEC and EC10 values based on initial mean concentrations that the C15 response is near or above its water solubility (Figure A.X. 7). When the survival endpoint is considered the measured responses for both C14 and C15 occur near the solubility limit (Figure A.X. 8). Because stress is apparent in these studies

near the limits of practical solubility, the effect on reproduction must also include relevant aspects of these factors.

In broad terms, the structure-activity-relationships collectively indicate that the expected non-polar narcotic mode of action is plausible (slope at or near -1) in the majority of these (Q)SARs (Table A.X. 3).

It might, however, still be argued that the C15 alcohol should be included in structure-activity-relationship regressions. If included, the effect is to flatten the slope and induce a departure from non-polar narcosis as the mode of action, which does not seem reasonable (Figure A.X. 9-12, Table A.X. 4). In addition, because the slope is flattened, an additional conclusion that testing occurred above the water solubility limit would apply to not only for C15 but for C14 as well. Further, the regressions are compromised somewhat by the fact that the C15 survival response is actually a ‘greater than’ value and if a true response would be measured (which must occur at a higher concentration) the slope would flatten further and the regression would be even less significant. This is a somewhat less environmentally conservative interpretation that is likely technically incorrect, with the resulting conclusion that C15 should be excluded from the chronic structure activity relationship.

Acute to Chronic Ratio of Long Chain Aliphatic Alcohols

Acute to Chronic Ratios (ACR) can be calculated from the data sets in a variety of ways including measured values based on total mean measured and initial mean measured concentration. Acute data are lacking for pure alcohols above C12 because these become increasingly difficult to perform due to considerations of testing above water solubility as discussed previously. Bona fide ACRs can be calculated for decanol (C10) and dodecanol (C12) (Table A.X. 5). Note that in this section exposures are expressed in mg/L so as to discuss both acute and chronic responses across a wide range of concentrations. Water solubility may still be a concern for the evaluation of the C12 ACR as the predicted water solubility (1.6 mg/L) is close to the EC50 (0.77 mg/L) and certainly some exposures in the test were above the limit.

Between C10 and C12, the ACR nearly doubles based on total mean measured concentrations providing an initial indication of solubility affecting the ACR (Table A.X. 5). ACRs could not be calculated for C14 and C15 because preliminary tests with these alcohols indicated a lack of toxicity in the range of solubility. In fact, the effect of C15 alcohol on both survival and reproduction had a very shallow exposure-response profile (Schäfers *et al.*, 2005a) indicating a lack of potency in the range of exposures that were tested (up to a nominal concentration of 300 µg/L). Zero mortality was observed during the first two days of both C14 and C15 studies at concentrations of 0.090 (C14) and 0.103 (C15) mg/L. Exposures in the chronic tests were at their highest in this period. If the acute structure-activity relationship (Annex VIII) is applied to the 48-hr EC50 of C14 and C15 alcohols to *Daphnia magna* are predicted to be 0.170 and 0.090 mg/L, respectively. However, in all these calculations both acute values are above the predicted water solubilities of C14 (0.126 mg/L) and C15 (0.049 mg/L). With these restrictions in mind, calculated ACRs on total mean measured concentrations for C14 and C15 alcohols result in ACRs of 28.3 and 7.4, respectively (Table A.X. 5). Calculated ACRs decline to 2.4 and 1.2, respectively based on initial mean measured exposures. It is interesting to note that all ACRs calculated from initial mean measured exposure concentrations are less than 10 and more or less consistent across all chain lengths.

Important empirical aspects of this analysis are that up to C12, ACRs seem reasonable and that the ACRs developed from the initial mean exposure data are more reliable and less variable. At C14 to

C15, due to uncertainties driven by the likelihood that water solubility was exceeded, it is seen that mortality effects are in order of C15 > C14 > C12 which is unexpected. It is hypothesized that insoluble particles or droplets contribute to this observation, yet at lower concentrations it is still possible that reproduction may be impaired by soluble material. This leads to the expectation that higher chain lengths of C_{16} to C_{18} would have no mortality and no reproductive effect. The experimental difficulty to test these materials is exceedingly great and adequate exposure techniques are not developed at this time.

ECETOC (2003) performed a careful review of high quality aquatic toxicology literature with several goals. One of these was to better understand the ACR for a wide range of chemicals because the ACR is often used in other forms of extrapolation in aquatic toxicology. For organics, *Daphnia magna* was found to have an ACR of <10 for 76% of the time and <100 for 100% of the time (n = 25, Table 45a of ECETOC 2003). ACRs were calculated for non-polar narcotics (all species in the data base) which have a non-specific mode of action, such as would be expected for long chain alcohols (Veith *et al.*, 1983). In the ECETOC analysis the ACRs were <10 for 87% of the time and <100 for 100% of the time (n = 38, Table 42 of ECETOC, 2003), in the present analysis ACRs were <10 for 86% and <100 for 100% of the comparisons (see Table A.X. 5), depending on how the alcohol data are expressed suggesting that long chain aliphatic alcohols have a non-specific narcotic ecotoxicological mode of action.

Conclusions of New Chronic *Daphnia magna* Toxicity Studies

1. The new chronic data generated are the best that can be achieved reasonably, yet involve real complications to due to exceptionally rapid biodegradability and the need to test as close as possible to limits of solubility for the long chained aliphatic alcohols.

2. The apparent toxicity of C15 alcohol is measurably less than C14 alcohol based on survival and reproduction endpoints.

3. The only method by which to make sense of the upward deflection in the toxicity profile for this series of long chain alcohols is to understand the relationship between toxicity, measured responses (which can combine toxicity and physical effects), and solubility.

4. The C15 toxicity data are a mixture of both toxicity and physical effects that occur above the water solubility limit. A similar situation can be inferred to a lesser extent for C14.

5. Reproduction is the more sensitive parameter and should be used to express toxicity and develop the (Quantitative) Structure-Activity Relationship ((Q)SAR).

6. NOEC and EC10 give similar (Q)SARs, although EC10 appears to be more consistently robust in (Q)SAR regression analyses. However, because the NOEC is more universally accepted in regulatory submissions, the NOEC will be used.

7. Use of the C15 data in an (Q)SAR should be questioned. This relates to the water solubility of C15. When C15 is not included the slope of most (Q)SARs approach -1 consistent with the expectation of non-polar narcotic mode of action for alcohols (Veith *et al.*, 1983).

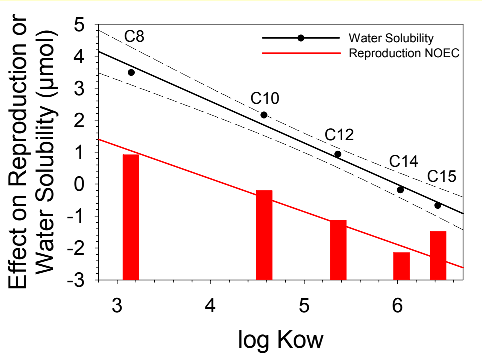
8. The ACR <10 for 73% and <100 for 100% (see Table A.X. 5) suggesting a non-specific narcotic ecotoxicological mode of action (ECETOC, 2003).

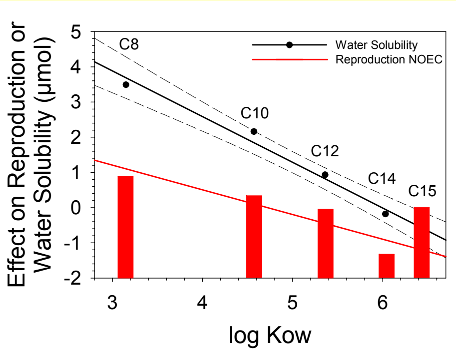
9. The rapid biodegradability of these alcohols further complicates interpretation such that the real exposure-response profile lies somewhere between that expressed by total mean measured exposures and initial mean measured exposure.

10. Thus, the two most relevant chronic (Q)SARs for aquatic toxicity of alcohols to *Daphnia magna*:
    - Exclude C15
    - Use the Reproduction NOEC
    - Reflect a reality that lies between total mean measured and initial mean measured exposure
    - See Box 1

11. Testing the chronic aquatic toxicity of C_{16} and C_{18} chain lengths would be even more challenging than C15 due to progressively lower solubility, while exceptionally rapid biodegradability would remain unchanged. Based on the trends observed with these new toxicity data it is expected that effects on mortality and reproduction would not be observed below the level of water solubility.

Box A.X.1: Chronic (Q)SAR for long chained aliphatic alcohols





log NOEC = -1.03 x log Kow + 4.28

log NOEC = -0.70 x log Kow + 3.31

Conditions	**Figure 5**	**Figure 6**
Data in SAR	C8-C14	C8-C14
Data excluded	C15	C15
Endpoint	Reproduction	Reproduction
Statistic	NOEC (µmol)	NOEC (µmol)
Exposure	Total Mean Measured (µmol)	Initial Mean Measured (µmol)
Adjusted R^2	0.959	0.758
p-value	0.014	0.084

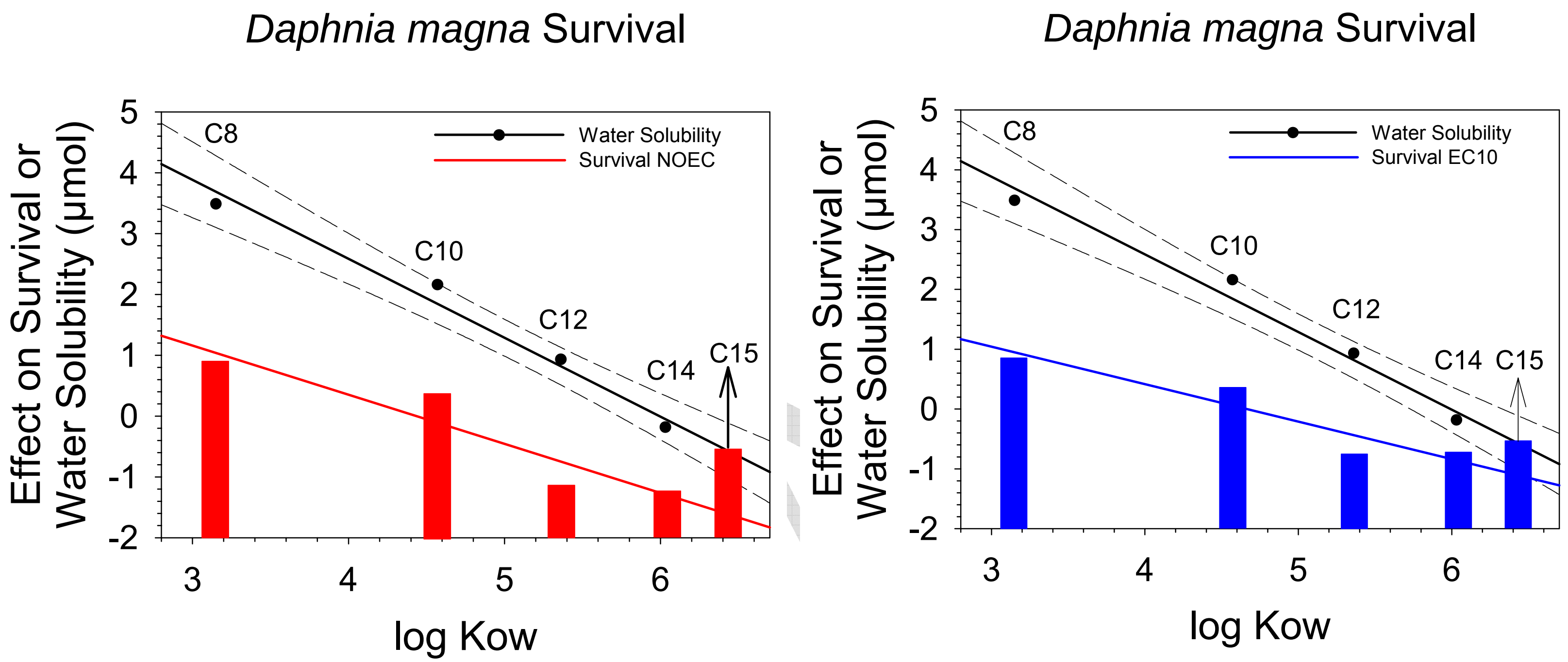


Figure A.X.5. Survival NOEC and EC10s as a function of log K_{ow} for long chain aliphatic alcohols.

[Data are plotted excluding C15 from the structure-activity relationship. Effects are expressed based on total mean measured concentrations. Bars indicate toxicity values].

Conditions of testing relevant to this figure:	Biological endpoint	Survival
	Statistical endpoint	NOEC and EC10
	Exposure expressed as	Total Mean Measured
	Chain lengths used in regression	C8, C10, C12, C14

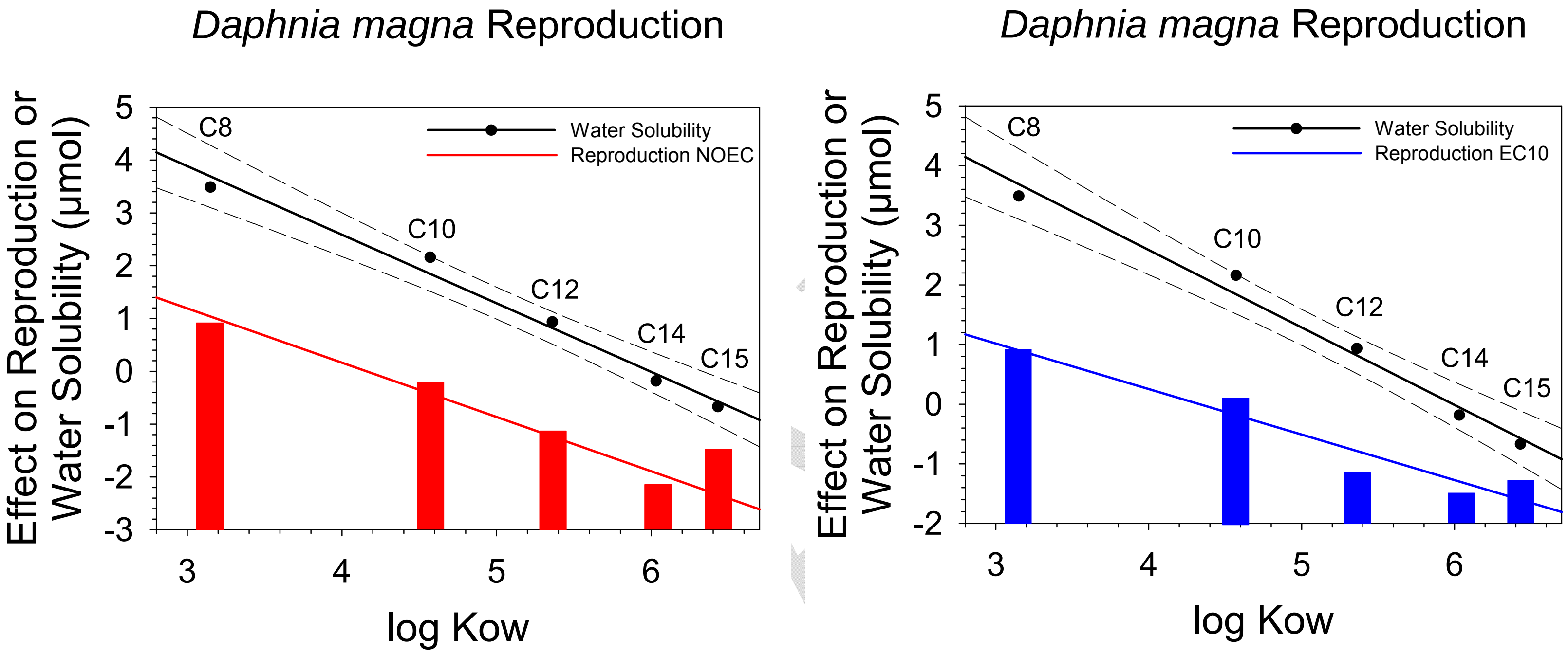


Figure A.X.6. Reproduction NOEC and EC10s as a function of log K_{ow} for long chain aliphatic alcohols.

[Data are plotted excluding C15 from the structure-activity relationship. Effects are expressed based on total mean measured concentrations. Bars indicate toxicity values].

Conditions of testing relevant to this figure:	Biological endpoint	Reproduction
	Statistical endpoint	NOEC and EC10
	Exposure expressed as	Total Mean Measured
	Chain lengths used in regression	C8, C10, C12, C14

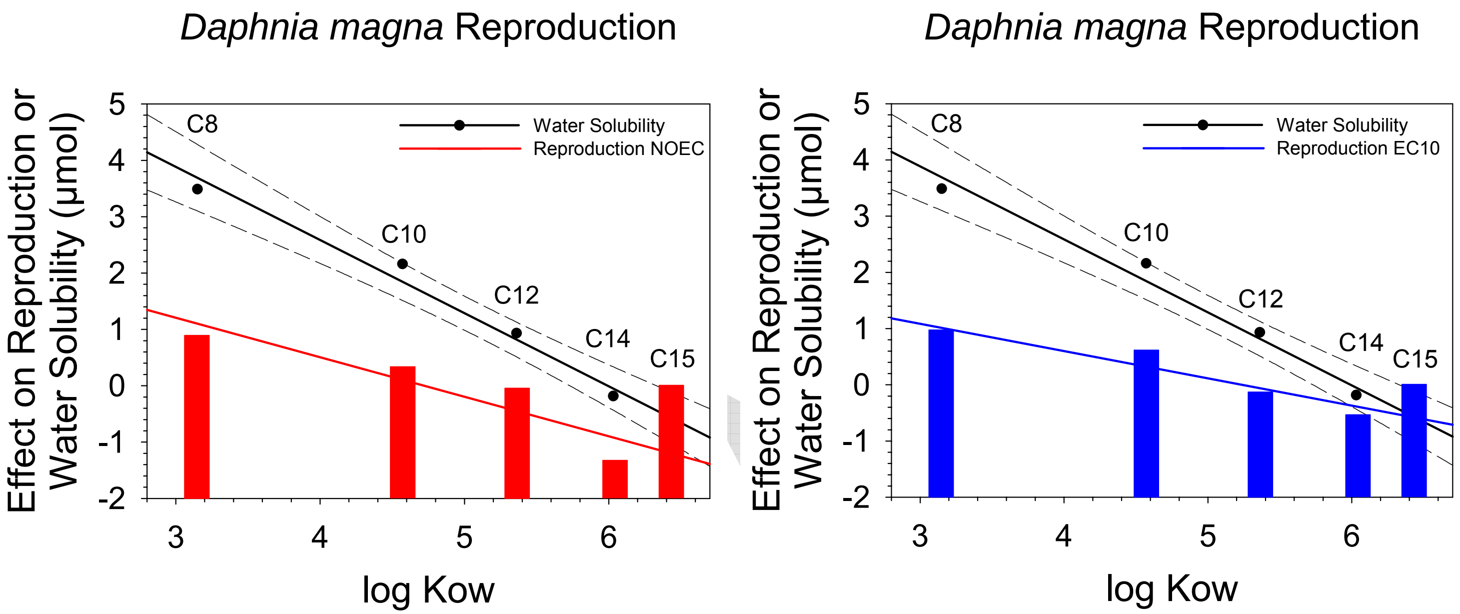


Figure A.X.7. Reproduction NOEC and EC10s as a function of log K_{ow} for long chain aliphatic alcohols.

[Data are plotted excluding C15 from the structure-activity relationship. Effects are expressed based on initial mean concentrations. Bars indicate toxicity values].

Conditions of testing relevant to this figure:	Biological endpoint	Reproduction
	Statistical endpoint	NOEC and EC10
	Exposure expressed as	Initial Mean Measured
	Chain lengths used in regression	C8, C10, C12, C14

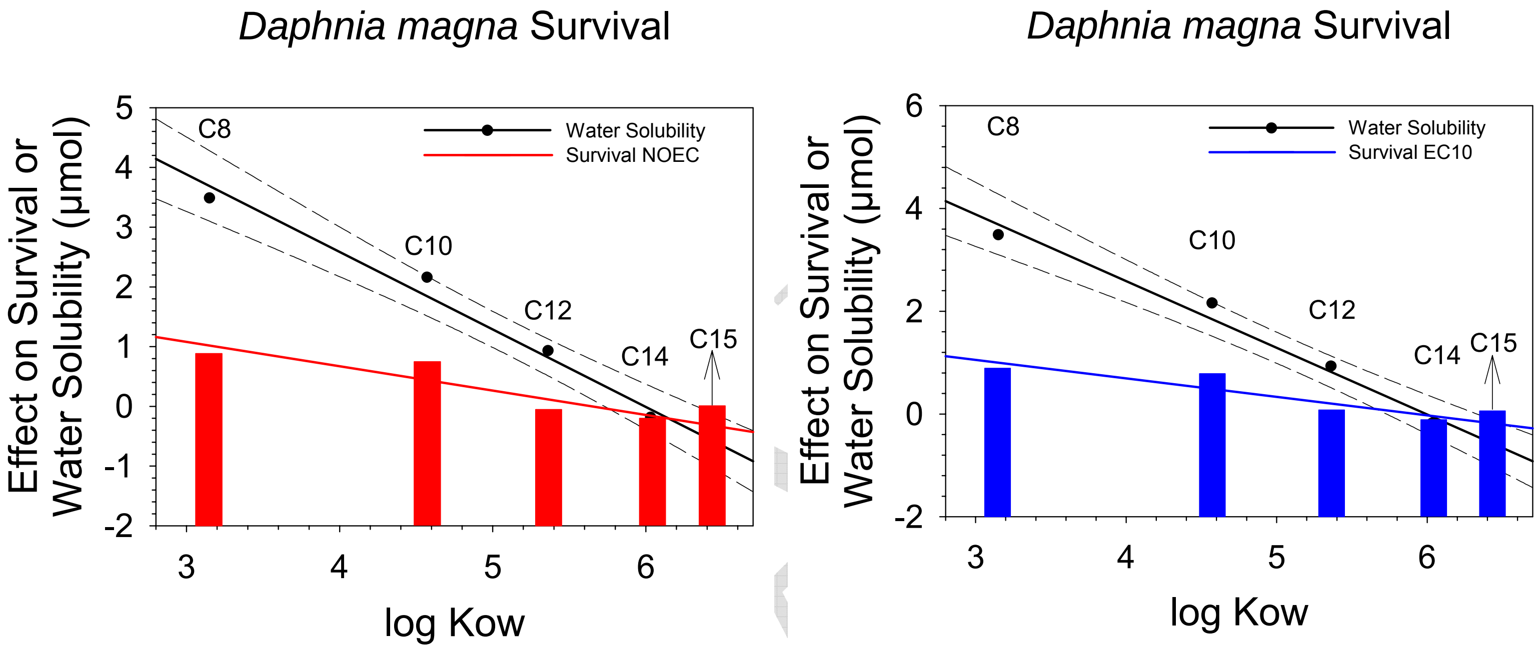


Figure A.X.8. Survival NOEC and EC10s as a function of log K_{ow} for long chain aliphatic alcohols.

[Data are plotted excluding C15 from the structure-activity relationship. Effects are expressed based on initial mean measured concentrations. Bars indicate toxicity values].

Conditions of testing relevant to this figure:	Biological endpoint	Survival
	Statistical endpoint	NOEC and EC10
	Exposure expressed as	Initial Mean Measured
	Chain lengths used in regression	C8, C10, C12, C14

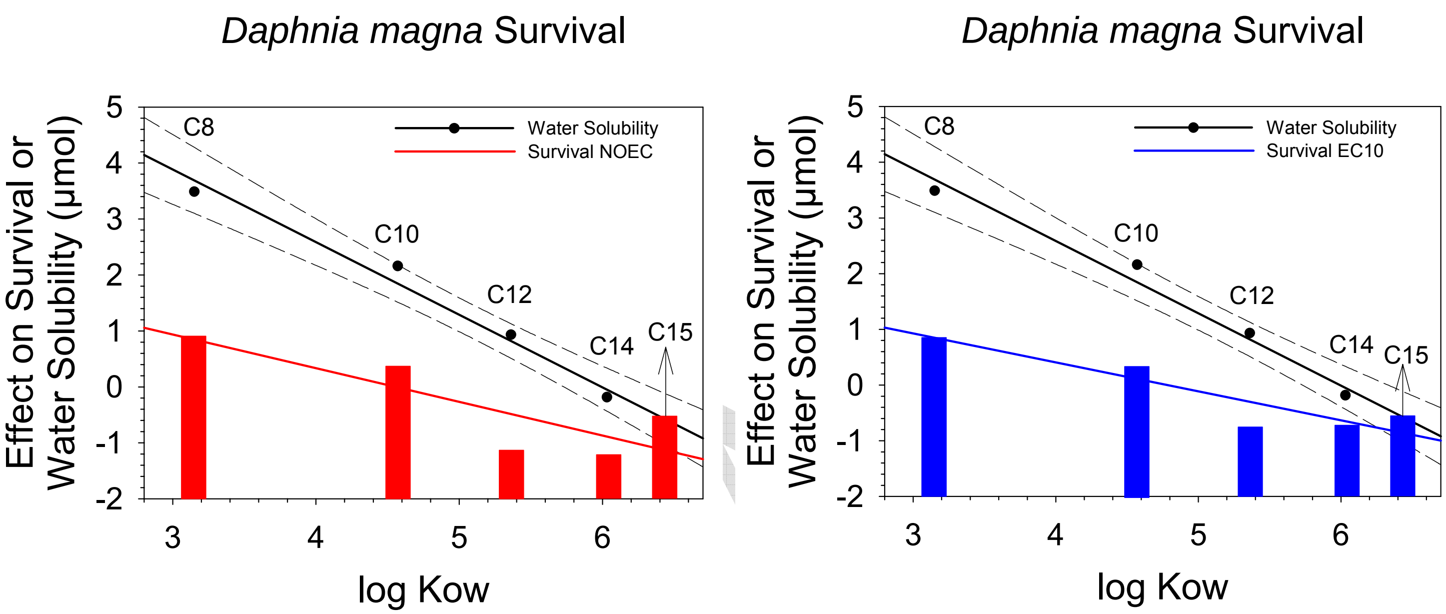


Figure A.X.9. Effect of long chain alcohols on *Daphnia magna* survival expressed as NOECs and EC10s

[Effects are expressed based on total mean measured concentrations. C15 has been included in the regressions. Bars indicate toxicity values].

Conditions of testing relevant to this figure:	Biological endpoint	Survival
	Statistical endpoint	NOEC and EC10
	Exposure expressed as	Total Mean Measured
	Chain lengths used in regression	C8, C10, C12, C14, C15

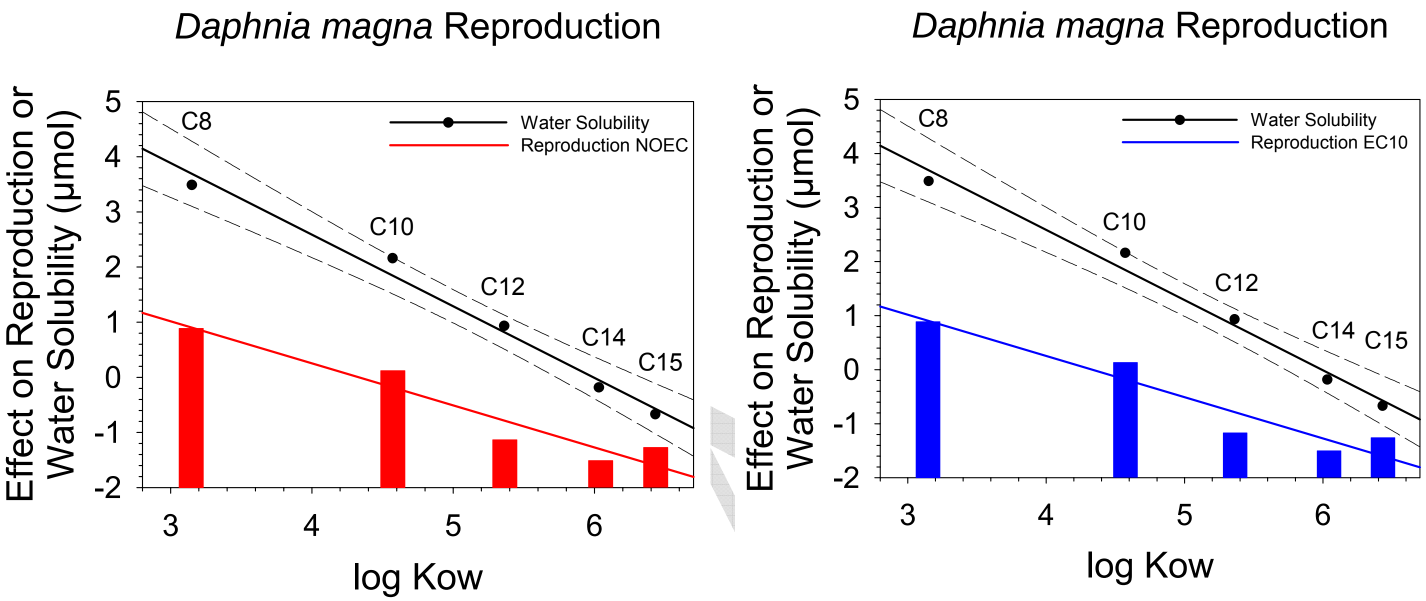


Figure A.X.10. Effect of long chain alcohols on *Daphnia magna* reproduction expressed as NOECs and EC10s.

[Effects are expressed based on Total mean measured. C15 has been included in the regressions. Bars indicate toxicity values].

Conditions of testing relevant to this figure:	Biological endpoint	Reproduction
	Statistical endpoint	NOEC and EC10
	Exposure expressed as	Total Mean Measured
	Chain lengths used in regression	C8, C10, C12, C14, C15

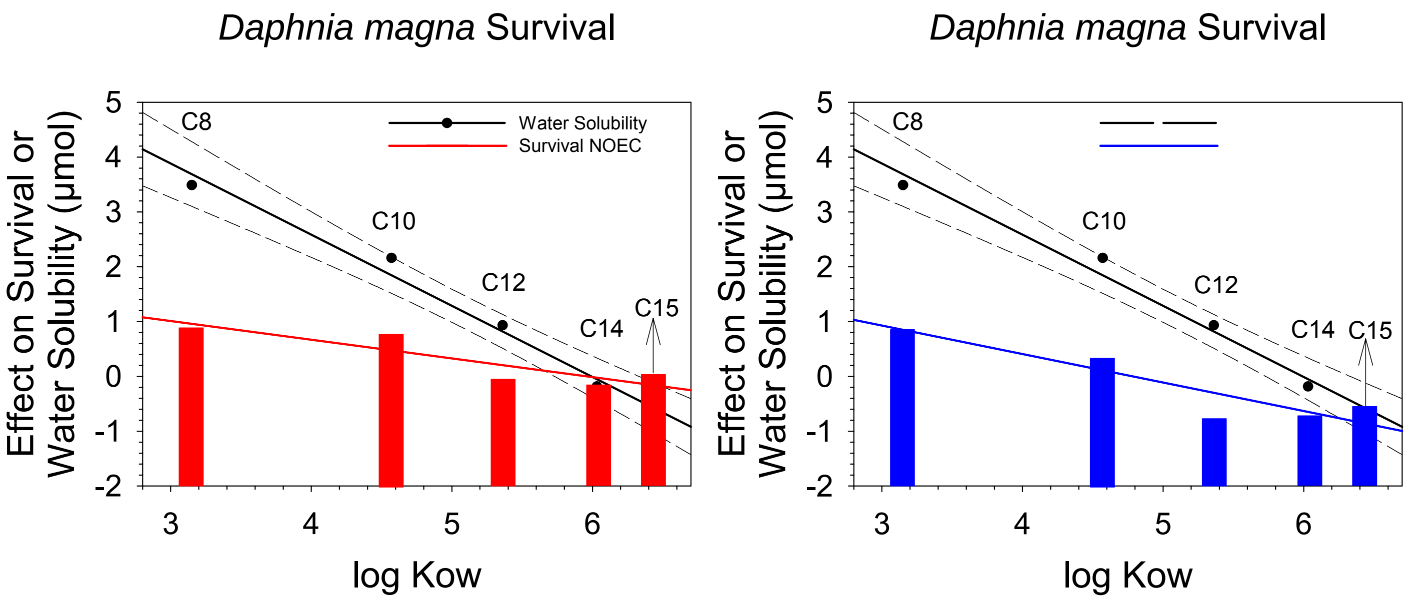


Figure A.X.11. Effect of long chain alcohols on *Daphnia magna* survival expressed as NOECs and EC10s.

[Effects are based on initial mean measured concentrations. C15 has been included in the regressions. Bars indicate toxicity values].

Conditions of testing relevant to this figure:	Biological endpoint	Survival
	Statistical endpoint	NOEC and EC10
	Exposure expressed as	Initial Mean Measured
	Chain lengths used in regression	C8, C10, C12, C14, C15

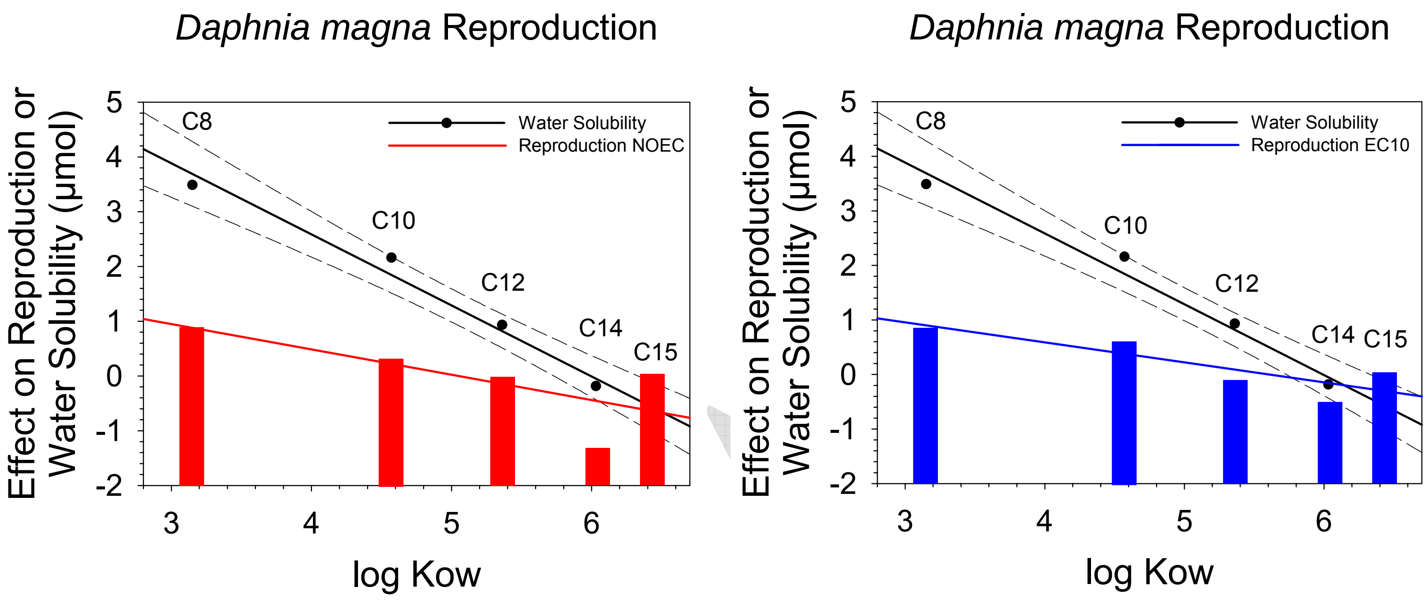


Figure A.X.12. Effect of long chain alcohols on *Daphnia magna* reproduction expressed as NOECs and EC10s.
[Effects are based on initial mean measured concentrations. C15 has been included in the regressions. Bars indicate toxicity values].

Conditions of testing relevant to this figure:	Biological endpoint	Reproduction
	Statistical endpoint	NOEC and EC10
	Exposure expressed as	Initial Mean Measured
	Chain lengths used in regression	C8, C10, C12, C14, C15

Table A.X.4. Summary of (Q)SAR regressions when C15 alcohol is included

Biological Endpoint	Statistical Endpoint	Expression of LCOH Exposure	Intercept	Slope	R^2	Adjusted R^2	F	p-value
Mortality	NOEC	Initial Mean	2.03	-0.34	0.77	0.70	10.22	0.05
	EC10	Initial Mean	1.97	-0.32	0.84	0.79	15.79	0.03
Reproduction	NOEC	Initial Mean	2.84	-0.59	0.89	0.79	11.22	0.04
	EC10	Initial Mean	2.47	-0.47	0.94	0.91	43.66	0.01
Mortality	NOEC	Total Mean	2.74	-0.60	0.71	0.61	7.34	0.07
	EC10	Total Mean	2.49	-0.52	0.84	0.79	15.61	0.03
Reproduction	NOEC	Total Mean	3.59	-0.86	0.90	0.87	27.37	0.01
	EC10	Total Mean	3.31	-0.76	0.91	0.88	29.76	0.01

Table A.X.5. Acute to Chronic Ratios (ACR) for long chain alcohols toxicity to *Daphnia magna*

[ACRs based on both survival (EC50 and EC10) and reproduction (EC10) responses were considered using mean measured concentrations of initial and aged solutions and initial solutions only].

Chain Length	Measured Acute 48-hr EC50 (mg/L)	Measured Chronic 21-d EC50 for Survival (mg/L)	Measured Chronic 21-d EC10 for Survival (mg/L)	Measured Chronic 21-d EC10 for Reproduction (mg/L)
			Total Mean Measured Concentrations	
C8	20*	---	>1[a]	>1[a]
C10	2.9	0.62	0.34	0.21
C12	0.77	0.08	0.033	0.013
C14	0.17[b]	0.13	0.038	0.006
C15	0.089[b]	> 0.063	> 0.063	0.012
		Acute EC50/Chronic Survival EC50	Acute EC50/Chronic Survival EC10	Acute EC50/Chronic Reproduction EC10
C8		---	<20[a]	<20[a]
C10		4.7	8.5	13.8
C12		9.6	23.3	59.2
C14		1.3	4.5	28.3
C15		1.4	1.4	7.4
			Initial Mean Measured Concentrations	
C8	20*	---	>1[a]	>1[a]
C10	2.9	1.50	0.93	0.61
C12	0.77	0.44	0.23	0.15
C14	0.17[b]	0.36	0.18	0.070
C15	0.089[b]	> 0.063	> 0.063	0.074
		Acute EC50/Chronic Survival EC50	Acute EC50/Chronic Survival EC10	Acute EC50/Chronic Reproduction EC10

C8	---	<20[a]	<20[a]
C10	1.7	3.1	4.8
C12	1.8	3.3	5.1
C14	0.5	0.9	2.4
C15	1.4	1.4	1.2

[a] Assumption that the EC10s for survival and reproduction are equivalent to the NOEC for days to first brood production (Kuhn et al., 1989). The actual values are likely > 1 mg/L.

[b] Predicted from alcohol acute toxicity (Q)SAR for *Daphnia magna*.

*24 hour EC50.

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