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Environmental properties of long chain alcohols. Part 1: Physicochemical, environmental fate and acute aquatic toxicity properties

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ABSTRACT

This paper summarises the physicochemical, biodegradation and acute aquatic ecotoxicity properties of long chain aliphatic alcohols. Properties of pure compounds are shown to follow somewhat predictable trends, which are amenable to estimation by quantitative structure–activity relationships ((Q)SARs). This allows predictions of data relating to human and environmental safety profiles and patterns. These alcohols have been shown to be rapidly degradable under standard conditions up to C_{18} . Furthermore, evidence suggests that longer chain lengths are also rapidly biodegradable. While $\log K_{ow}$ values suggest possible bioaccumulation potential, available data suggest that these substances are not as bioaccumulative as estimations would predict. For acute aquatic toxicity, solubility limits the possibility of effects being appropriately observed and become increasingly challenging above C_{12} . Further, a model has been developed for multi-component mixtures which give an excellent account of aquatic ecotoxicity allowing for the prediction of acute effects of un-tested mixtures.

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1. Introduction

The long chain aliphatic alcohols category is based upon a homologous series of compounds with increasing carbon chain lengths. Members of the category span chain lengths from 6 to 22 carbons. The commercial industrial processes used to produce alcohols in some cases necessarily result in products that usually contain homologues across a range of carbon chain lengths, and in some products may include unsaturated alcohol components, and essentially linear (mono-alkyl branched) components, as well as linear alcohols. The data set presented here has been reviewed by the Organisation for Economic Co-operation and Development (OECD) High Production Volume (HPV) Chemicals Programme as a Category (a grouped approach, in which data for individual members are presented and discussed together as part of a whole set, rather than substance-by-substance) at the OECD SIDS (Screening Information Data Set) Initial Assessment Meeting

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¹ Present address: National Environmental Research Institute of Denmark, P.O. Box 358, Frederiksborgvej 399, DK-4000 Roskilde, Denmark. (SIAM) 22 (Paris, France, April 2006). All components of all commercial products relevant to this category are primary alcohols (long chain aliphatic alcohol category SIDS Initial Assessment Report, OECD, 2006a).

The hydroxyl group in alcohols confers upon the hydrocarbon chain a considerable degree of polarity and, therefore, affinity for water. It is susceptible to oxidation by metabolic processes. Linear or essentially linear hydrocarbon chains are also readily oxidised metabolically. Substances that contain a number of homologous components can be expected to behave in a way consistent with the carbon number distribution, allowing the substances to be considered as a group, or category (refer to OECD Manual for Investigation of HPV Chemicals, OECD, 2004a). Key features that the members share are the same structural features, similar metabolic pathways, common mode of ecotoxicological action, and common levels and mode of human-health-related effects (Veenstra et al., 2008, this issue). It is normally the case that the strongest features for a category will be the presence of predictable physical-chemical properties that emerge from the sharing of common chemical attributes. Long chain alcohols are a series of homologous structures varying by carbon number along an essentially linear alkyl chain.

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This paper summarises the fundamental physicochemical, biodegradation and acute aquatic ecotoxicity properties of long chain aliphatic alcohols. Properties of pure compounds follow somewhat predictable trends, and are amenable to estimation by quantitative structure–activity relationships ((Q)SARs). With this understanding, and awareness of biodegradation patterns, models were developed to allow the rational understanding of the way multi-component commercial grade products behave. This allows predictions of data relating to human and environmental safety profiles and patterns to be made.

CAS number was used as a primary descriptor for data management and in some cases there was a need to differentiate commercial products which are multi-component substances with dissimilar compositions sold under the same CAS number. These are referred to as 'Types'. The specific composition of each 'type' is confidential, but limited generic definitions are stated where it is particularly useful to the discussion. Further nonconfidential information is available in the SIAR (OECD, 2006a).

In accordance with the OECD HPV Programme and processes used by contributors, all physicochemical, biodegradation, fate and ecotoxicity data were evaluated using the Klimisch scoring system (Klimisch et al., 1997; OECD, 2004b). Studies and reports achieving Klimisch scores 1 and 2 comprised the vast majority of information used that is reported in this paper. Use of such studies are considered reliable without restriction (score of 1) or reliable with restriction (score of 2). Studies with a score of 2 were scientifically and technically justified, but may not have been documented by GLP (a peer-reviewed literature citation, for example, in the absence of a full study report would be at this level).

2. Physicochemical properties of long chain alcohols

Physicochemical properties are of fundamental importance in a chemical data set. Property data have direct significance, some are inputs for prediction of other chemical properties, and they are also used in modelling environmental distribution, fate and effects. For the long chain aliphatic alcohols, an extensive data set was drawn from many sources, which are fully described in peer-reviewed SIDS documentation and discussed in the SIAR (OECD, 2006a). (Q)SAR methods have been used to fill data gaps. For multi-component substances, the value appropriate to a particular property has usually to be represented as a range (the minimum and maximum values are of more importance in the present contexts than a mid-range value, bearing in mind the significance of physicochemical properties of individual components for modelling; some of these substances encompass ranges of properties that are particularly sensitive for fate modelling and prediction of other properties).

For the most part data are presented in relation to their dependence upon carbon chain length, because this shows any trends more clearly. These patterns are useful for understanding relationships among and between substances so that gap filling by read-across and (Q)SAR is robust. Alternative means to express patterns other than carbon number, such as molecular weight, dimensions, and so forth are also considered valid. However, pragmatically, these aspects are inter-related and regulatory definitions (e.g., CAS numbers) revolve around descriptions based on carbon number.

2.1. Pure long chain alcohols

2.1.1. Melting point

Measured and predicted melting point values are shown in Fig. 1A. The SRC MPBPVP program was used to develop initial

predictions (EPI Suite v. 3.12; SRC, 2005). Melting point is estimated by two methods (adapted Joback method (1982); Gold and Ogle method (Lyman, 1985)) and then derives a recommended value as the mean of these two predictions. Measured data for some substances are available from published and unpublished sources (refer to SIAR, OECD, 2006a for full details). For long chain aliphatic alcohols, the set of measured data are close to complete for the 'pure' alcohols and models provide overestimates. Over-estimation increases with increasing carbon chain length from just a few °C at C_{12} , up to 50 °C at C_{22} . The melting points of branched isomers tend to be a few degrees lower than the linear alcohol of corresponding carbon number. The presence of a small proportion of branched isomers in commercial *n*-alcohols is expected to lower the observed melting point of those substances slightly.

2.1.2. Boiling point

Measured and predicted boiling points for long chain alcohols are presented in Fig. 1B. Predictions were generated by the SRC MPBPVP program (EPI Suite v. 3.12; SRC, 2005). This program estimates boiling point using a method adapted from Stein and Brown (1994). Measured data are close to complete for the 'pure' alcohols, and most of these data suggest that the predictions are highly accurate. Data for the longest chain lengths are scarce and the single value available is rather lower than the prediction and is omitted from the calculations and the figure.

Measured data for some substances are available from published and unpublished sources (refer to SIAR, OECD, 2006a, for full details). In the absence of reliable measured data for some substances, it is considered acceptable to use the value estimated by MPBPVP to fill data gaps. The regression statistics confirm the appropriateness of the estimations and could be used to adjust the prediction if necessary. The slope of the measured versus predicted BP relationship is close to 1 (0.954) with an R^2 exceeding 99%.

The boiling points of branched isomers tend to be a few degrees lower than the linear alcohol of corresponding carbon numbers. The presence of a small proportion of branched isomers in commercial *n*-alcohols is expected to raise the observed boiling point of those substances slightly.

2.1.3. Vapour pressure

Predicted and measured values of vapour pressure at 25 °C for linear alcohols are presented in Fig. 1C. Measured data for some substances are available from published and unpublished sources (refer to SIAR, OECD, 2006a for full details). For predicted values, the SRC MPBPVP program was used (EPI Suite v. 3.12). The strong correlation (R^2 of 97%) between the predicted and measured values suggests these predictions are reliable for linear alcohols.

2.1.4. Density

Relative density values at 20 °C for linear alcohols are around 0.827 (mean, 95% confidence interval 0.006, 19 values). Measured data for some substances are available from published and unpublished sources (refer to SIAR, OECD, 2006a for full details).

2.1.5. Partition coefficient

The octanol–water partition coefficient K_{ow} is widely used a parameter to help in the interpretation of environmental and health property data. Measured data for some substances are available from published and unpublished sources (refer to SIAR, OECD, 2006a for full details). The majority of measured values originate from published data (Tewari et al., 1982; Hansch et al., 1989, 1995; Burkhard et al., 1985; Hansch and Leo, 1979; Veith et al., 1980; Pearson and Eadsforth, 1984; Sasol, Sastech



Fig. 1. Relationships of measured and predicted physical-chemical properties of aliphatic alcohols: (A) melting point, (B) boiling point, (C) vapour pressure, and (D) K_{ow} (octanol-water partition coefficient).

Research and Development, 1998). Note that some reliable measured values approach 8. These are assumed to have been appropriately measured bearing in mind the inherent challenges in measuring $\log K_{ow}$ values in this range. Reliable measured $\log K_{ow}$ values were available for most of the single-component alcohols. These were used to compare with results from the SRC KOWWIN program (EPI Suite v. 3.12; SRC, 2005). Plotting measured vs. predicted $\log K_{ow}$, as shown in Fig. 1D, trends of expected decreased accuracy of prediction by the model beyond a $\log K_{ow}$ of 6 are evident. By relating the data to carbon number (not shown, but which follows a similar trend), regression of the data allowed a simple formula to be developed to describe the measured $\log K_{ow}$ values (the curved line shown in Fig. 1D)

$$log K_{ow} = 0.0584 + (1.142 \times log KOWWIN)$$
$$- (1.482E - 05 \times carbon-number^{4})$$
(1)

The straight line in the figure represents the expected linear correlation, found for the lower carbon numbers and shown extrapolated. This non-linear trend is found irrespective of the modelling program used, and several others were considered. Thus, to fill data gaps, $\log K_{ow}$ is estimated by using the SRC KOWWIN program and applying this amendment to the result. The adjusted R^2 for the regression is 0.992 and the carbon number and KOWWIN terms are highly significant (p < 0.001). Refinement of K_{ow} predictions might be anticipated by including melting point in the relationship (e.g., Mackay and Shiu, 1984); however, the strength of this relationship without melting point.

plus the fact that most of the substances are already liquids in the environmental temperature range of interest makes this unnecessary.

The value of $\log K_{ow}$ derived by the equation reaches a peak at around C_{20} , and then begins to drop again. It would be expected that experimentation would yield values of $\log K_{ow}$ which would reach a plateau and would not drop again; such a pattern is typical of $\log K_{ow}$ values in homologous series. Therefore for C_{21} and C_{22} , the same value is read-across from C_{20} . It is normal practice that values of $\log K_{ow}$ are limited to a maximum value of 8 because of the inherent difficulties in measuring values above this; values > 8 are meaningless in the context of most applications of the value (e.g. in risk assessment; in prediction of other chemical property values). Values predicted as part of this work were limited to a value of 8 as necessary.

The form of the regression used is an empirical one, but also has a reasonable theoretical basis. Powers other than 4 in the C number were investigated, but 4 worked most successfully. As carbon chain length increases, molecules in solution can 'fold', i.e. adopt non-linear conformations. This will be particularly the case for longer chains where there is a possibility to 'save' the enthalpic cost of dissolving in water by minimising the surface area achieved by adopting a shape as close as possible to spherical. The form of fit used in the regression retains the expected linear relationship of true $\log K_{ow}$ on KOWWIN at low C number—this latter predicts a linear increment for every CH_2 group added. Then, as C increases molecular volume does not increase in proportion to the C number.



Fig. 2. Physical chemical relationships of water solubility (A) and partitioning to organic carbon (K_{oc} , B).

2.1.6. Solubility in water

Reliable measured water solubility (WS) values were available for most of the single-component alcohols. Many established (Q)SARs derive WS based on a correlation with log $K_{ow.}$ (e.g. EPI Suite v. 3.12 and many other sources). Plotting the values against predicted log K_{ow} from EPIWIN as shown in Fig. 2A, provides a highly significant regression (p < 0.001) with an adjusted R^2 of 0.983. The regression was not improved by inclusion of further terms, such as molecular weight. Given their importance in subsequent discussion about acute aquatic ecotoxicity and chronic ecotoxicity (Schäfers et al., 2008, this issue), the values (measured and predicted) are shown in Table 1.

Table 1	
Measured and predicted water solubility values for linear alcohols.	

CAS no.	Carbon number	Chemical name	Predicted water solubility (mg/L)	Measured value used in regression (mg/L)
111273	6	1-Hexanol	7671.3	5900
111706	7	1-Heptanol	1743.6	1670
111-87-5	8	1-Octanol	400.7	551
143-08-8	9	1-Nonanol	94.2	128
112-30-1	10	1-Decanol	22.9	39.5
112-42-5	11	1-Undecanol	5.8	8
112-53-8	12	1-Dodecanol	1.6	1.93
112-70-9	13	1-Tridecanol	4.51E-01	0.38
112-72-1	14	1-Tetradecanol	1.41E-01	0.191
629-76-5	15	1-Pentadecanol	4.90E-02	0.102
36653-82-4	16	1-Hexadecanol	1.90E-02	0.013
1454-85-9	17	1-Heptadecanol	8.42E-03	0.008
112-92-5	18	1-Octadecanol	4.33E-03	0.0011
629-96-9	20	1-Eicosanol	1.93E-03	-
661-19-8	22	1-Docosanol	1.98E-03	-

2.2. Complex mixtures of long chain alcohols

The term 'mixture' in chemical terms can be defined specifically to mean a deliberate blend or preparation of substances. The term 'complex mixture' is commonly used in the chemical industry to describe multi-component substances. Some commercially significant substances in the long chain alcohols category are complex reaction products containing a range of chain-length components.

Defining the properties of "complex mixtures" (or even commercial substances containing minor components in addition to a major one) is more difficult than for essentially pure substances. The methods used for accomplishing this for long chain aliphatic alcohols are described below.

2.2.1. Melting point, boiling point, vapour pressure, octanol-water partition coefficient

It is not scientifically realistic or necessary to attempt a detailed prediction of the melting point of the multi-component commercial products. Therefore, it is not possible to estimate what the boiling range of such substances might be from the available data set, with any useful level of reliability. However, an indication can be gained from the boiling points of the individual carbon chain lengths present. Vapour pressures for multi-component substances can be calculated from compositional data and values for the pure substances. This has been done (OECD, 2006a) in accordance with basic physicochemical principles, by calculation of the partial vapour pressure of each component and then summing the partial vapour pressures.

For the multi-component substances, there cannot be a single value of $\log K_{ow}$. However, the $\log K_{ow}$ values for the individual components present are relevant. A similar approach has also been accomplished for the related non-ionic surfactant series of ethoxylated alcohols (Boeije et al., 2006).

2.2.2. Solubility in water

Useful and reliable chemical property data were available for some test substances, which were complex reaction products containing a range of chain-length components. There was therefore a need to use modelling to understand the behaviour of these substances in solution at given loading rates, in order to correctly interpret the data available for these substances in terms of the dissolved components, as well as forming a basis upon which data gaps may be filled. Multi-component substances, such as several of the sponsored long chain alcohols (those substances included in the OECD SIAR for long chain alcohols, OECD, 2006a), have a more complex behaviour in water due to the role of partitioning effects. Furthermore, a model of such effects, developed primarily for use in predicting ecotoxicity, also allows the estimation of solubility of the mixture. By manipulation of various factors, it is possible to determine the loading rate at which ~100% is dissolved, which is effectively the solubility of the mixture. This model is of particular interest when considering the dissolved component across a range of loading rates. The model itself is described in more detail in Section 2.2.3.

2.2.3. Physicochemical description of solubility of multi-component liquids as a partitioning process

This section develops a reasonably simple model of solubility of multi-component substances with particular reference to the long chain alcohols. 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. However, the model does not apply to surfactants. It is useful both to consider solubility in water and also to understand the composition of aqueous media produced for testing toxicity to aquatic organisms.

The model described below gives the same results as an analysis based on considering the mole fraction of each component (i.e., based on Raoult's Law); however, it has an advantage over that approach under some conditions. This is because the volume change of the alcohol mixture is included in the description, a measure which is vital when considering the small amounts of alcohol added when test media for aquatic studies are generated.

If a quantity W(mg) of a multi-component alcohol substance is added to a volume of water V_{aq} (L), then by definition equilibrium for each component of the substance is

$$K_{\rm al-w} = \frac{C_{\rm s}}{C_{\rm aq}} \tag{2}$$

where $K_{\rm alc-w}$ is the alcohol-water partition coefficient of the component, and $C_{\rm s}$ and $C_{\rm aq}$ refer to its concentration in the substance and aqueous solution, respectively (mg/l). In this case, the alcohol that the component partitions out from is the substance itself. If the proportion dissolved out of the substance is very small, $C_{\rm s}$ 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 xW

$$xW = V_{\rm s}C_{\rm s} + V_{\rm aq}C_{\rm aq} \tag{3}$$

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 *xW* and the density *d* (g/ml). V_s is approximated as a fraction *f* of the initial volume, i.e.

$$V_{\rm s} = \frac{fW}{d} \tag{4}$$

Combining these equations, and setting $V_{aq} = 1 L$ gives the expression for C_{aq}

$$C_{\rm aq} = \frac{XW}{(fWK_{\rm alc-w}/10^6d) + 1} \tag{5}$$

The factor of 10^6 is needed to get the correct units. The value of f depends on C_{aq} so iteration of the calculation is needed and evaluated for each loading. The Eq. (3) is similar in principle to methods used by previous authors to model toxicity of

hydrocarbon fractions (Peterson, 1994; Verhaar et al., 1997; Di Toro et al., 2007). The main and very important difference is that in this work we estimate the final volume of the undissolved phase by calculation from the amount dissolved. This correction is very important when a high proportion of the added substance has dissolved, particularly at low loading rates. To demonstrate the use of the model, an example of a hypothetical twocomponent mixture of dodecanol and tridecanol has been modelled, using $K_{\rm alcohol-water}$ values as developed below. The results are shown in Fig. 3.

The appropriate alcohol–water partition coefficient suitable for each carbon chain length present should be used to describe the partitioning in the 'substance–water' system. In order to model alcohol–water solubility and partition as accurately as possible, K_{alc-w} values are needed for each carbon number. One way to obtain these is to use the measured solubilities. Table 2 shows values of K_{alc-w} needed to obtain the literature measured water solubility. Whilst it is sensible to avoid over-interpretation of the data, a large increase in K_{alc-w} above the $K_{octanol-water}$ value is not surprising for the higher carbon numbers. Consider dodecanol: the difference was 0.27 log units above the measured log K_{ow} value, consistent with the expectation that dodecanol will be more lipophilic than octanol. The K_{alc-w} values will be used in subsequent modelling.

The values in Table 2 are for pure substances, whereas for a multi-component substance ideally the partition coefficient of the individual component in the whole substance would be known. There are no fully reliable measured data to make such a prediction, so a compromise is necessary. The K_{alc-w} of each component is taken from Table 2 whatever the substance composition. It is hard to predict what the errors might be for each substance so this approximation needs to be borne in mind when the data available for ecotoxicity test media are considered below. Such uncertainties are inherent in any method of modelling solubility in complex media. The present method allows complexity and volume change in water accommodated fractions to be addressed, even though ideally more calibration data would be available to the modeller than in fact there are.

There are no solubility data to allow calculation of K_{alc-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 this value will be used to reduce K_{alc-w} for the present work. Work by Roberts and Marshall (1995) suggests much higher differences, yet since these values are based on biological data they are not useful for the present purpose.



Fig. 3. Effect of loading rate on amount dissolved for a hypothetical mixture of dodecanol and tridecanol (60:40 by weight).

Table 2		
Data us	ed to ob	otain K _{alc}

-water

Carbon number	Measured log <i>K</i> ow	Measured water solubility (mg/L)	Fitted log K _{alc-w}	Difference in log K values	Ref $(\log K_{ow})$	Ref (WS)
6	2.03	5900	2.145	0.115	Tewari et al. (1982)	Yalkowsky and Dannenfelser (1992)
7	2.57	1313	2.791	0.221	Tewari et al. (1982)	Tewari et al. (1982)
8	3.15	551	3.168	0.018	Hansch et al. (1989) ^a	Yalkowsky and Valvani (1980)
9	3.77	128	3.805	0.035	Tewari et al. (1982)	Letinski et al. (2002)
10	4.57	39.5	4.348	0.222	Hansch et al. (1995)	Yalkowsky and Valvani (1980)
11	4.72	8	5.003	0.283	Abraham et al. (1994)	Letinski et al. (2002)
12	5.36	1.93	5.629	0.269	Burkhard et al. (1985)	Letinski et al. (2002)
13	5.51	0.38	6.33	0.82	Hansch and Leo (1979), Veith	Letinski et al. (2002)
					et al. (1980)	
14	6.03	0.191	6.642	0.612	Burkhard et al. (1985)	Yalkowsky and Dannenfelser (1992)
15	6.43 est	0.102	6.905	-		Yalkowsky and Valvani (1980)
16	6.65	0.013	7.293	0.643	Burkhard et al. (1985)	Yalkowsky and Dannenfelser (1992)
18	7.19	0.0011	7.86	0.67	Burkhard et al. (1985)	OECD (1993), Budavari (1996)

 Table 3

 Compositions of four substances, and average dissolved concentrations in WAFs prepared at a loading rate of 9.6 mg/L (Wenzel, 2003).

Substance	Dodecan	nol (C ₁₂ OH)	Trideca	anol (C ₁₃ OH)	Tetradeo	canol (C ₁₄ OH)	Pentade	canol (C ₁₅ OH)	Hexadec	anol (C ₁₆ OH)	Octadeo	canol (C ₁₈ OH)
	%	М	%	М	%	М	%	М	%	М	%	М
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 (μ g/L) at 9.6 mg/L loading.

Data sets from a number of case studies are available against which the capability of the model for predicting the solubility of multi-component alcohols can be assessed. In the following discussion, measured values are from the cited reference and predictions are made according to Eq. 5.

In a study with the alga *Pseudokirchneriella subcapitata* (Wenzel, 2003) a substantial amount of analytical data across several loading rates was available. Analytical determinations were made of the water-accommodated fractions (WAFs) prepared for testing. Table 3 provides information about their composition and average dissolved concentrations at a WAF loading rate of 9.6 mg/L (percent compositions have been rounded). This shows how the method has been applied to several substances and how detailed useful data can be obtained for substances that could at first be viewed as similar in composition.

The first substance is similar to the example given above. Using the new predicted $\log K_{\rm alc-w}$ values, the model predicts 302 and 82 µg/L of C₁₂ and C₁₃, respectively. The discrepancy with the measured values of around 225 and 50 µg/L is not substantial, but could be due to a number of factors, including the $K_{\rm alcohol-water}$ between the substance and algal media could be different to that in pure water, equilibrium may not have been achieved, and the substance was degrading or adsorbing.

Considering more complex substances, the model predicts 147.4, 41.4, 19.9 and $5.6 \,\mu\text{g/L}$ for the C₁₂, C₁₃, C₁₄ and C₁₅ alcohols, respectively, again over-predicting the higher molecular weight homologues by comparison with measured data, but predicting the order of magnitude reasonably well. The algal growth study by Wenzel (2003) gives a full set of data and these show that the model over-predicts some of the dissolved concentrations. For this substance at 1.2 mg/L loading (data not shown above), the model predicts 26.0, 18.9, 8.84 and 2.55 μ g/L, whereas the measured

values were 45.9, 18.3 and $4.7\,\mu g/L$, and were not detected, respectively.

Palmer and Cann (2000a) tested three commercial variants of C_{12-16} linear alcohols (CAS no. 68855-56-1) in algal growth and *Daphnia* test media. In WAFs prepared at a loading rate of 1 mg/L the initial dissolved concentrations were 0.43, 0.64 and 0.36 mg/L. The predicted value from the partition model is 0.38 mg/L.

Whale et al. (2000) similarly tested C_{14-16} (CAS no. 68333-80-2) at two loading rates. Measured and predicted dissolved concentrations in WAFs prepared at loading rates of 1 and 100 mg/L were 0.23 and 0.15 (100 mg/L loading rate) and 0.07 and 0.15 mg/L (1 mg/L loading rate), respectively. The predicted values show that a loading rate of 1 mg/L should have been high enough to achieve saturation concentrations of the substance in the WAF. The amount dissolved at 100 mg/L was higher, which could have been due to slower attainment of equilibrium at the lower loading rate. The lower levels of measured dissolved concentrations at the start of test are unlikely to be complicated by biodegradation or complexation to colloidal materials because WAFs were prepared in sterile conditions without additional organic material present other than the alcohols themselves. However, adsorption on to surfaces could occur.

The results of a study reported by Palmer and Cann (2000b) and summarised in Table 4 show that there can be differences between media prepared for tests with invertebrates or algae. Measured dissolved concentrations were consistently lower in algal media versus invertebrate water and below predicted concentrations; the reasons are not known since they would be expected to be the same; however, it is possible that water qualities (hardness, nutrients, etc.) for various test media could result in some differences.

The results of a further series of ecotoxicity studies with C_{10-16} (CAS no. 67762-41-8) (Sasol, Sastech Research and Development,

Table 4

Measured and predicted total concentrations of dissolved components of multi-component alcohols in two different test media (Palmer and Cann, 2000b).

CAS no.	Loading rate	Measured dissolved con	Predicted concentration in	
		Invertebrate medium	Algal medium	invertebrate medium (mg/L)
67762-41-8 Type C; 80–95% Linear; >95% C_{12}/C_{13} [range	1 mg/L	0.60	0.53	0.68
C ₁₁₋₁₅ , Even and oud chain lengths present	LL ₅₀	0.28	0.23	0.48
67762-41-8 Type B; 5–50% Linear; ≥95% C_{12}/C_{13} [range	1 mg/L	0.60	0.50	0.68
C ₁₁₋₁₄]; Even and out chain lengths present	LL ₅₀	0.23	0.24	0.49

2000a) provide insight to the inherent difficulties of working with WAFs. Predicted and measured concentrations of dissolved components are reported for test media prepared at three loading rates of 10, 32 and 100 mg/L. Measured total dissolved alcohol (mg/L) and predicted total dissolved alcohol were 1.3 versus 1.0, 8.8 versus 1.1 and 9.8 versus 1.1 mg/L, respectively.

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) because such high dissolved concentrations were reported. The loading rate for a 50% effect, EL₅₀, was reported as 15 mg/L.

In the parallel *Daphnia* ecotoxicity study on the same C_{10-16} material (Sasol, Sastech Research and Development, 2000b) a WAF loading rate of 10 mg/L gave a 5.5 mg/L dissolved concentration and an EL₅₀ of 2.8 mg/L. The algal study (Sasol, Sastech Research and Development, 2001) was more in line with expectations. A dissolved concentration of 0.63 mg/L was reported in a 1 mg/L WAF and the E_bL_{50} was approx. 0.23 mg/L, at which loading almost all the substance would be modelled to dissolve.

Kirch (1998a) reported the results of an ecotoxicity study with C_{12-18} (CAS no. 67762-25-8 (Type A; 100% Linear; >50% C_{12}/C_{14} ; >10% C_{16}/C_{18} [range C_{8-20}]; even chain lengths present)) 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 5. Agreement between measured and predicted values is high. However, with a loading rate of 10 mg/L, the predicted values are numerically very similar to those at 1000 mg/L, but the measured results were very different: $C_{16} > C_{14} > C_{12}$ (in terms of quantity of each dissolved), which is somewhat inconsistent and perhaps indicative of analytical difficulties at low concentration, or the approximations regarding K_{alc-w} are not valid.

The modelled data and measurements do not fully agree, but given the difficulties in test media preparation and analysis (see also Schäfers et al., 2008, this issue), and the fact that aquatic testing is conducted on a large scale relative to physicochemical property measurement, the model provides a good framework for the interpretation of results. Other approaches based on physicochemical properties would be likely to do no better because of the limitations of experimental data availability. There are studies that are predicted well and a smaller number that are predicted less well. For the present purpose of trying to understand toxicity of complex mixtures the approach represents a realistic balance of ideal and pragmatic necessity.

2.3. General trends

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:

Table 5

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 (Kirch, 1998a).

Carbon number	Concentration (mg/L)	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			

(1) melting point and 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; (2) water solubility decreases because the free energy required for a molecule to dissolve becomes less favourable for larger molecules; and (3) 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.

3. Environmental fate properties of long chain alcohols

3.1. Photodegradation

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. The rate of degradation by hydroxyl radicals in the atmosphere can be estimated for other chain lengths using the SRC AOPWIN v1.91 program (part of the EPI Suite v3.12, SRC, 2005).

AOPWIN also calculates a half-life, based on a hydroxyl radical concentration of 1.5×10^6 molecules/cm³. An alternative half-life, more applicable to European environmental conditions, can be developed using the European standard value of 5×10^5 molecules/cm³. Both sets of half-lives, in hours, are reported in Table 6. The half-life for linear alcohols for photo-oxidation in air, based on a hydroxyl radical concentration of 5×10^5 molecules/cm³ varies between 12 h (estimated for 1-docosanol) and approximately 30 h (measured for 1-hexanol).

From this set of measured and estimated data the following conclusions are drawn: (1) available measured data for relevant linear and branched structures suggest that the estimated half-lives are likely to be realistic although slightly overestimated; (2) estimated half-lives for branched structures are similar to linear structures of equivalent carbon number; and (3) estimated

Table 6				
Measured and selected	predicted	photodegradation	rate constants	and half-lives.

Name	CAS	Measured OH rate constant (cm ³ /molecule s)	Estimated OH rate constant (cm ³ /molecule s)	Half-life (h) ^a	Half-life (h) ^b	Reference
1-Hexanol	111-27-3	12.5E-12	9.716E-12	30.8 ^c 39.6 ^d	10.3	Kwok and Atkinson (1994)
1-Heptanol	111-70-6	13.7E-12	11.129E-12	28.1 ^c 34.6 ^d	9.4	Kwok and Atkinson (1994)
1-Octanol	111-87-5	14.4E-12	12.542E-12	26.7 ^c 30.7 ^d	8.9	Atkinson (1994)
1-Tridecanol	112-70-9	-	19.607E-12	19.6	6.5	SRC (2005)
Tridecanol, branched	90583-91-8	-	19.884E-12	19.4	6.4	SRC (2005)
1-Octadecanol	112-92-5	-	26.673E-12	14.4	4.8	SRC (2005)
9-Octadecen-1-ol, (Z)-	143-28-2	-	79.718E-12	4.8	1.6	SRC (2005)
1-Docosanol	661-19-8	-	32.325E-12	11.9	4.0	SRC (2005)

^a Using EU standard concentration of OH radicals, 5E+05 molecules/cm³.

^b Using SRC AOPWIN, i.e. 1.5E+06 molecules/cm³.

^c Based on measured rate constant.

^d Based on SRC estimated rate constant.

half-lives for unsaturated structures are very much shorter than for saturated structures of equivalent carbon number.

3.3. Biodegradation

3.3.1. Overview of measured degradation properties

Many biodegradation assays have been carried out on long chain alcohols (see OECD, 2006a for a full reporting of results). In general, carbon chain lengths less than 16 are all readily biodegradable meeting the 10-day window (60% CO₂ evolved or greater) in the standard 28-day test, chain lengths of C_{16-18} are rapidly biodegradable but occasionally do not meet the 10-day window, and above C18 degradation ranged from 21% to 60% evolved CO₂ (more information about specific results is discussed below). Compounds that have almost achieved the pass level in the ready biodegradability test (e.g. OECD 301 series) are considered to possess inherent biodegradability in a regulatory and scientific context ('inherent' biodegradability is most usually defined on the basis of levels of degradation under specific test conditions, e.g. the OECD 302 series, but in certain circumstances such a conclusion may be drawn from the results of a ready test). These results were concluded from tests that closely conform to OECD 301 series ready test biodegradability methods using nonacclimated inocula. Results were similar for branched and linear alcohols. Tests which allow microbial adaptation have significant methodological deficiencies for the present purpose and were not considered in this summary. 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 (Richterich, 1993, 2002a, b; Huntingdon Life Sciences Ltd., 1996; Henkel KGaA, 1992a). Chain lengths of C₁₆₋₁₈ achieved ready test pass levels, although not within the 10-day window (Mead, 1997; Henkel KGaA, 1992b, c). The one test on a single carbon chain length greater than C₁₈ (docosanol) showed degradation of 37% (Mead, 2000) in a ready biodegradability study conducted to OECD 301.

Several non-standard studies are useful in the overall understanding of the biodegradability of the LCOH category. Federle and Itrich (2006) studied the fate of free (linear alcohols) and linear alcohol ethoxylate (AE)-derived fatty alcohols in activated sludge, in a non-standard study conducted using a scientifically sound method. Radiolabelled $({}^{14}C)$ C₁₂, C₁₄ and C₁₆ alcohols metabolism in a batch-mode activated sludge die-away system. Disappearance of parent, formation and disappearance of metabolites, uptake into biomass and mineralisation to ¹⁴C CO₂ were monitored over time. Activated sludge from a municipal wastewater treatment plant (WWTP) was obtained, and used at 2500 mg/L. The test substance was dosed at a concentration that is low relative to most standard OECD guideline studies, but relevant to environmental conditions. Dosed levels were 9.3, 10.0 and 10.7 µg/L for dodecanol, tetradecanol and hexadecanol, respectively. Typical concentrations for OECD 301 series tests range from 10 to 100 mg/L which for some compounds can influence their interpretation for environmental relevance (Federle and Itrich, 2006). Recoveries were high (>83% from biological test systems and >90% from abiotic controls). After 48 h incubation, only a few percent of the radiolabelled carbon remained in the form or parent compounds. Over 65% was recovered in the form of radiolabelled carbon dioxide. The results are summarised in Table 7.

Concentration time dependence data were modelled with

$$C = A e^{-k_1 t} + B e^{-k_2 t}$$
(6)

(a two compartment first order decay model) and the fitted results were as shown in Table 8.

The results show the high biodegradability of C_{12-16} alcohols in activated sludge. The trend in the fitted parameters suggests a very rapid removal of dissolved alcohol as the dominant process, with a slower removal of adsorbed substance. It is hypothesised that desorption of alcohol from solids likely controls the overall

Table 7

Removals and fate of linear alcohols in a non-standard study (Federle and Itrich, 2006).

C Form that the radiolabelled carbon is present in (%) after 48 h incubation

	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

Table 8

Model parameters for degradation of linear alcohols in a non-standard study (Federle and Itrich, 2006).

С	А	$k_1 (h^{-1})$	В	$k_2 (h^{-1})$
C12 C14 C16	82 ± 2 82 ± 2 41 ± 3	$113 \pm 8 \\ 87 \pm 5 \\ 103 \pm 23$	9 ± 1 12 ± 1 48 ± 2	$\begin{array}{c} 0.36 \pm 0.1 \\ 0.30 \pm 0.1 \\ 0.43 \pm 0.04 \end{array}$

rate of biodegradation. Such a trend would be consistent with the pattern of the ready test data. In the European Technical Guidance Document (TGD) (EC, 2003), the SIMPLETREAT model uses a rate constant of $1 h^{-1}$ for readily biodegradable substances meeting the 10-day window which is clearly lower than those derived for alcohols in this study.

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 AE homologues in a laboratory continuous activated sludge unit (Wind et al., 2006) useful data about the properties and environmental exposures of alcohols are presented because alcohols are members of an AE distribution. The waste water organisms were exposed principally to ethoxylates, which are also generated by the degradation of the ethoxylates. An AE mixture (C_{12-18}) was dosed at 4 mg/L in the influent. Removals exceeded 98% were for alcohols and over 99% removal across all chain lengths based on high-quality specific analytical with limits of detection around 0.1 µg/L. Detailed results are presented in Table 9. This study also showed that of the small amount of LCOH that did not degrade was found in recovered solids at the end of the study. The extent of removal of alcohols is very high from an exposure route that can realistically be anticipated based on the known uses of alcohols.

Another line of evidence for rapid degradation is 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. This is more fully explored in a related paper by Schäfers et al. (2008, this issue).

Predicted data from the SRC BIOWIN v4.00 program (part of the EPI Suite v3.12; SRC, 2005) support rapid degradation for the linear alcohols. However, the extent of measured data for long chain aliphatic alcohols 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 were identified in the SIAR (OECD, 2006a) that show lower levels of degradation. In the context of ca. 15 studies of high reliability for alcohols in the range C_{8-16} (single- and multi-component test substances), which showed consistently high levels of degradation, these two low-degradation results 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. This interpretation is

Table 9

Removal of alcohols during an activated sludge test on alcohol ethoxylates (Wind et al., 2006).

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

strongly supported by the results of the more recent and definitive studies by Federle and Itrich (2006) and Morrall et al. (2006), along with a broader understanding of biological transformations summarised by Mudge et al. (2008).

3.3.2. Structural issues in respect of biodegradation rate

Mono-branched alcohols are present in many of the commercial products. No measured results are available for these 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 it is unlikely this could be discerned in a standard study as they are usually only a small component of the mixture. Prediction by (Q)SAR (SRC BIOWIN v4.00) allows for a screening assessment of persistence. (Q)SAR (BIOWIN) indicates that mono-branched structures degrade at essentially the same rate as the linear unsaturated alcohol of the same carbon number. These conclusions are supported by reliable measured data for more highly branched alcohols which are members of the Oxo Alcohols Category (OECD, 2006b).

Unsaturation does not appear to be detrimental to biodegradation rate. In ready biodegradation tests, a commercial multicomponent substance (C_{16-18} components, containing C_{18} unsaturated components) was found to be readily biodegradable in a reliable study (using a non-standard inoculum; garden soil microorganisms; Borner, 1999), and in several studies of non-assignable reliability. C_{18} unsaturated alcohol was predicted by (Q)SAR (BIOWIN) to degrade at essentially the same rate as the linear unsaturated alcohol.

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

3.3.3. Biodegradation under anaerobic conditions

The anaerobic biodegradability of C_8 , C_{16} (three reliable studies) and $C_{16-18}+C_{18}$ unsaturated (one reliable study), has been investigated. All test substances were anaerobically degradable (>75–95% degradation in tests of 4–8 weeks duration; Shelton and Tiedje, 1984; Nuck and Federle, 1996; Steber and Wierich, 1987; Steber et al., 1995). These findings are considered as additional information to the more standard aerobic biodegradation for concluding biodegradability status. Detailed results are presented in the OECD SIAR (2006a).

3.3.4. Biodegradation prediction

A limited range of quantitative structure–activity relationship methods are available which address biodegradation with many being effectively highly specialised research tools. The program BIOWIN v4.00 is effectively an expert system with limited quantitative application. BIOWIN recognises that linear or singly branched hydrocarbon chains are susceptible to microbial degradation. This is enhanced by the presence of the OH group. BIOWIN predicts very little differentiation between linear C_{14} and C_{22} alcohols. The magnitude of the BIOWIN scores is consistent with rapid biodegradation in the environment; it could be argued from these data alone 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 which is also consistent with Federle and Itrich (2006).

Predicted biodegradation probability rates, using all methods in the BIOWIN program, show that linear alcohols are predicted to biodegrade rapidly (SRC, 2005). Linear and non-linear models give probabilities of 0.91 ± 0.03 and 0.93 ± 0.06 , respectively. Ultimate biodegradation (mineralisation to CO₂ and water) was modelled to occur in the range of days to weeks although experimental evidence discussed above would suggest ultimate degradation may be more likely in hours. Three models in this program are referred to in the TGD discussion of screening approaches to persistence assessment in the context of PBT (EC, 2003). The MITI linear and non-linear models within BIOWIN provide very similar estimates to the other models (0.87 ± 0.04 and 0.95 ± 0.01 , respectively). All of these category members would be considered not persistent on the basis of the discussion above.

3.4. Bioaccumulation and bioconcentration

It is important to note that in respect of this section and subsequent discussions on ecotoxicity, all studies involving experimental animals were conducted in accordance with national and international guidelines for the protection of animal welfare. No reliable guideline-standard measured bioconcentration data are available for long chain alcohols. Chain lengths C₁₁ and above have $\log K_{ow} > 4.5$ and so could be considered to be potentially bioaccumulative. The rapid degradation described above, combined with evidence of rapid metabolism in mammalian studies (Veenstra et al., 2008, this issue), 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 $\log K_{ow}$ alone, absent metabolism, range from 7.0 for C₆ to a maximum of 46,000 for C₁₆ reducing to 1100 for C₂₂ (EC, 2003 after Veith et al., 1979 and recalculated from Connell and Hawker, 1988) (Fig. 4).

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 (EC, 2003). For purposes of comparison, BCF was also calculated using the BCFWIN program (part of the EPIWIN v3.12 suite; SRC, 2005). The values calculated by the Veith et al. and Connell and Hawker methods are generally considered more reliable (Weisbrod et al., 2007; Environment Canada, 2006; Mudge et al., 2008).

Predicted data should be validated by comparison with measurements. Unfortunately, there are no reliable measured data for bioconcentration, though weight of evidence of available data can be taken into account as below (OECD, 2005).

For hexadecanol, the EU TGD (Q)SAR estimates a BCF value of 46,000 (EC, 2003). Freitag et al. (1982) measured a BCF of 56 for octanol (C_8) and a range of values for hexadecanol from another study (507–1550, Unilever, 1995). These measured values are all from lower quality studies in which measurements were made on total radioactivity without differentiation of the parent and any radiolabelled metabolites or bioincorporated compounds. Such measurements overestimate BCF because they cannot distinguish metabolism and incorporation from the intact parent. No attempt



Fig. 4. Predicted BCF of linear alcohols by different methods.

was made to determine if steady-state conditions had been established and some exposure concentrations were above the limit of solubility. There are no measured BCF values for any other member of the linear alcohol family. However, BCF data for alcohols similar to those in this family but with an average 2.1-2.9 branches per molecule also indicate that the BCFWIN (O)SAR (EPI Suite v3.12: SRC. 2005) overestimates BCF (EBSI, 1999). In these studies, not used within the long chain alcohols SIAR, BCFs ranged from 15.2 to 60 for branched (iso)decanol, (iso)dodecanol and (iso)tridecanol (EBSI, 1999, 2000a, b). BCFWIN results are generally around one order of magnitude lower than predicted by the TGD (Q)SAR methods. Therefore, all these data indicate that log Kow-based (Q)SAR overestimate BCF because they take no account of biotransformation and alcohols are an energy source (food) that is metabolised in a wide range of biota from bacteria to mammals (Veenstra et al., 2008, this issue; Mudge et al., 2008). These observations have recently been critically assessed using cellular biotransformation assays of ethoxylated alcohols and other aliphatic surfactants which confirm that metabolism of the alkyl chain can lower BCF by orders of magnitude (Dyer et al., 2008; Cowan-Ellsberry et al., 2008). For the more soluble chain lengths evaluated in non-guideline BCF studies on linear alcohols and those done by guidelines for branched alcohols BCFs are overestimated by at least an order of magnitude.

Values predicted for 2-methyl branched alcohols were fairly consistent with the predicted values for the linear structures of the same carbon number based on EPIWIN v3.12 estimates (SRC, 2005). Branched structures present are predicted to have slightly lower BCF than the corresponding linear alcohol consistent with $\log K_{ow}$ and other physical property determinations discussed above.

For the multi-component long chain alcohols a single BCF value is difficult to predict. However, the values for the components present are relevant. The presence of branched components is not expected to significantly affect the predicted value.

3.5. Adsorption

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 AEs. Alcohol sorption coefficients showed some time dependence, reaching a plateau by 72 h. Pentadecanol (C_{15}) was



found to be an unexplained outlier most likely associated with heterogeneous distribution of suspended solids in the test sample. K_d values ranged from 3000 (dodecanol) to 78,700 (octadecanol). Under the experimental conditions used these correspond to K_{oc} values ranging from 17,980 to 471,000, respectively (Fig. 2B). Based on these data from van Compernolle et al. (2006) the following (Q)SARs were derived:

$$Log K_d = 0.235$$
 Chain length + 0.64 ($R^2 = 0.99, n = 4$) (7)

 $Log K_{oc} = 0.235$ Chain length + 1.42 ($R^2 = 0.99, n = 4$) (8)

$$\log K_{\rm oc} = 0.766 \log K_{\rm ow} + 0.11 \quad (R^2 = 0.99, \ n = 4)$$
 (9)

A (Q)SAR based on four points should not be over-interpreted, but it is very similar to the TGD (EC, 2003) (Q)SAR for hydrophobic organic substances. 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.

Sorption to wastewater solids is relevant for understanding distribution of alcohols in the environment following waste treatment. K_{oc} , sorption corrected for organic carbon content, values were predicted using relevant (Q)SAR methods from the TGD (EC, 2003) for hydrophobics, and alcohols and the SRC PCKOCWIN v1.66 method (part of the EPI Suite v3.12; SRC, 2005). 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 TGD gives several equations for calculation of K_{oc} for specific substance types. Three are of relevance to alcohols:

Hydrophobics (EU TGD) :
$$\log K_{oc} = 0.81 \log K_{ow} + 0.10$$

($R^2 = 0.89$, $n = 81$; useful up to $\log K_{ow} = 7.5$) (10)

Alcohols and organic acids (SRC) : $\log K_{oc} = 0.47 \log K_{ow} + 0.5$ ($R^2 = 0.72$, n = 36; useful up to $\log K_{ow} = 5$) (12)

Alcohols (EU TGD):
$$\log K_{oc} = 0.39 \log K_{ow} + 0.5$$

($R^2 = 0.77$, $n = 13$; useful up to $\log K_{ow} = 5$) (13)

None of these approaches stand out in terms of reliability or performance and provide similar results. The value calculated by the TGD non-hydrophobics equation is the most conservative amongst this group of substances, but the empirically derived equation from the data of van Compernolle et al. (2006) (Eq. (9) above) is more consistent with the TGD hydrophobics (Q)SAR. For the multi-component long chain alcohols substances a single value of $\log K_{oc}$ cannot be generated, however, the values for each component is relevant. The presence of branched components is not expected to significantly affect the predicted value based on observations for branching influences on K_{ow} .

3.6. Distribution modelling for wastewater treatment plants

The distribution of long chained aliphatic alcohols in a sewage treatment plant has been estimated using the SimpleTreat model (implemented in the risk assessment program EUSES v2.0.3, ECB, 2005). Inputs to the model are the Henry's Law constant as derived from vapour pressure and water solubility (discussed in Sections 2.1.3 and 2.1.6), $\log K_{oc}$, (discussed in Section 3.5) and the biodegradability (these results reflect the levels of degradation measured by Federle and Itrich, 2006, discussed in Section 3.3.1), from which the model determines threshold rates of degradation within WWTP). The major pathways to the environment are via the sludge phase and degradation. Biodegradation dominates entry into the environment for chain lengths up to C₁₂ and for C₁₃ and above adsorption to sludge is dominant. The outputs are summarised in Table 10. It is interesting to note that a relatively constant fraction of all chain lengths is expected to pass to air or directly to water. However, as chain length increases the fraction going to sludge rises while the fraction biodegraded declines. These model results are entirely consistent with the previously discussed physical-chemical properties.

4. Aquatic toxicity

Alcohols, with the exception of some propargylic alcohols (Veith et al., 1989) that are excluded from this family, act by nonpolar narcosis (Lipnick et al., 1985). Sufficient measured data exists to allow comparison of the acute toxicity of essentially pure alcohols to fish and invertebrates with appropriate estimations by (Q)SARs (see Section 4.1). As a result, read-across for gap filling is scientifically justifiable. In addition to pure alcohols, the toxicity of a mixture that fully dissolves in water can be interpreted by the simple addition of the contribution of each component alcohol provided that the modes of toxic action are the same. Toxicity prediction for mixtures of alcohols that do not completely dissolve is less straightforward because as the carbon number increases there is not only an associated increase in toxicity (i.e. the toxic concentration decreases) but also a decrease in water solubility (see Section 4.2). Interpretations of toxicity are complicated by

Table 10

Distribution in waste water treatment plant (WWTP) predicted by SimpleTreat model (using degradation rate).

Substance	$K_{\rm oc}$ predicted by TGD (Q)SAR	Fate in WWTP:				
		Fraction to air	Fraction to water	Fraction to sludge	Fraction degraded	
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	

both uptake (true toxicity) and physical effects (such as the interactions by the undissolved alcohol with respiratory or feeding structures).

4.1. Toxicity of pure long chain alcohols

Many acute toxicity tests have been carried out on this category of alcohols. These have addressed toxicity to three key taxonomic groups of organisms; fish, invertebrates and algae. The results have been compiled, reviewed and assessed as part of the SIDS submission for the long chain alcohol substances (OECD, 2006a). Gaps in the data matrix for the category have been filled either by (Q)SAR or by read-across.

The slopes of the lines expressing the relationship between carbon number and toxicity and carbon number and solubility are not the same with the slope of the solubility line being greater. A point (cut-off) is therefore reached beyond which the carbon number distribution and thus the toxic concentration will be higher than the maximum solubility of the alcohol. Consequently the toxicity cannot be expressed.

4.1.1. Toxicity prediction by (Q)SAR

The availability of the acute toxicity database for pure linear alcohols has made it possible to develop specific (Q)SARs for this chemical category. Thus, ecotoxicity and regression data for pure linear alcohols have been obtained for fish and Daphnia magna acute studies (Fig. 5; OECD, 2006a). Acute toxicity are plotted as a function of $\log K_{ow}$ and are also compared with water solubility. The slope of all regressions are similar and it is important to note that fish and Daphnia regressions follow and are below that of water solubility. However, chain lengths above C₁₂ have been shown to be non-acutely toxic (Schäfers et al., 2008, this issue). In high-quality chronic toxicity exposures to C₁₄ and C₁₅ linear alcohols Daphnia mortality was not observed at all exposure concentrations at and below the water solubility limit. For C₁₂, C₁₄ and C_{15} the measured water solubilities are 10.3, 0.89 and 0.44 μ mol/L, respectively. The 48-h EC₅₀ for C₁₂ alcohol is 4.1 µmol/L, therefore, below the limit of solubility. In the test with C_{14} and C_{15} alcohols no mortality occurred at and slightly above the solubility limits at 0.65–1.62 and 0.44–1.1 μ mol/L, respectively.

In summary, for acute effects in fish (21 studies on 7 chain lengths, see also Fig. 5):

$$\log LC_{50} \text{ (mmol/L)} = -0.691 \log K_{ow} + 1.29$$

$$(p < 0.001, R^2 = 0.975) \tag{14}$$



Fig. 5. Acute toxicity of long chain alcohols to fish and invertebrates as a function of $\log K_{ow}$ and the relationship to water solubility for carbon chain lengths 12 and less.

While the results of the regression analysis are both statistically significant and acceptable, they should not be over-interpreted due to the low number of data points. The expression suggests that dependence of the LC_{50} on $\log K_{ow}$ is somewhat lower than the usual gradient for non-polar organics (approximately 0.94, e.g. in ECOSAR; Könemann, 1981).

The acute *Daphnia magna* data are very similar to the fish data (9 studies on 6 chain lengths, see also Fig. 5).

$$Log EC_{50} (mmol/L) = -0.83 \log K_{ow} + 1.92$$

(p<0.001, R² = 0.981) (15)

Insufficient data were available to perform a similar analysis for algae, and data gaps for pure substances in the SIDS submission had to be filled by read-across and expert judgment. The best quality (measured) algal toxicity data for single carbon chain lengths show the toxicity of the alcohols to increase from an 72-h EC_{50} of 80 mg/L for C_6 (Wenzel, 2003) to 0.62 mg/L for C_{12} (Henkel KGaA, 1994), which are of the same order of magnitude of those for Daphnia and fish, but due to a wider diversity of endpoints and exposure times used to summarise the trends than simple mortality, overall conclusions necessarily remain general. The C_{14} and C_{16} alcohols were not toxic to algae. These results indicate a toxicity cut-off at C_{14} and above.

The data for mixed carbon chain-length alcohols (commercial products) show the multi-component substances containing alcohols with carbon numbers in the ranges of C_{6-12} to C_{12-16} to be acutely toxic at concentrations of between 3.1 and 0.03–0.1 mg/L (Table 11). At these concentrations all the components are likely to have been fully dissolved. The data for acute effects on algal growth are of the same order of magnitude as the measured values for *Daphnia magna* (OECD, 2006a).

The ECOSAR equation for neutral organics gives EC_{50} values that are lower than all the measured examples, i.e. over-predicts toxicity. The measured (Q)SAR slope given in Eqs. (14) and (15) are consistent with a narcotic mode of toxic action. Because the slope is somewhat less sensitive to log K_{ow} than predicted for non-polar narcosis in detail a chemical class-specific (Q)SAR should be considered as more reliable. Acute toxicity data for chain lengths above C_{12} are not plotted here. The results suggest that acute toxicity cut-offs for effects on fish, invertebrates and algae driven by solubility lie in the region of C_{12-14} (Table 1, Figs. 2 and 5).

4.2. Toxicity of complex mixtures of long chain alcohols

Toxicity predictions for mixtures of alcohols that do not fully dissolve are complicated by the partitioning behaviour of the component alcohols within their own phase, as well as within the water phase. Partitioning models and methods of summing the contribution of multiple dissolved components allow the toxicity of complex mixtures to be predicted.

The results of tests conducted on multi-component mixtures that were assessed as part of the OECD SIAR (2006a) have been expressed using different conventions. Where the effect concentrations were below the solubility of a multi-component mixture they are reported as nominal or measured concentrations and are 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} .

The carbon number distributions present in the mixtures makes it difficult to identify an acute toxicity cut-off from the measured data. However, the results are generally supportive of the conclusion drawn from the pure substance data, i.e. that this occurs at carbon numbers in the range C_{12-14} . (Table 11).

Table 11

Comparison of measured and estimated acute toxicity values to Daphnia for complex commercial products.

CAS no.		Commercial product type	WS predicted (mg/L)	Predicted EC ₅₀ /EL ₅₀ (mg/L)	Summary of <i>Daphnia</i> measured data (EC ₅₀ or EL ₅₀ , mg/L)	
68603-15-6	C ₆₋₁₂ alcohols	TYPE B (>80% Linear; > 95% C9/10/11 [range C8-C12]; Even and odd chain lengths present)	43.9	2.306	ca 6 (nominal)	Garforth (1983), Huntingdon Life Sciences Ltd. (1991a)
68603-15-6	C ₆₋₁₂ alcohols	TYPE C > 80% Linear; > 95% C7/8/9 [range C6–C10]; Even and odd chain lengths present)	510.0	18.76	5.9	Wenzel (2005)
111-87-5	Octvl alcohol	present)	560.0	25.45	20 (nominal)	Bringmann and Kuhn (1982)
112-30-1	1-Decanol		39.5	2.06	2.9 (nominal)	Henkel KGaA (1999)
67762-41-8	C ₁₀₋₁₆ alcohols	TYPE B (5–50% Linear; ≥95% C12/13 [range C11–C14]; Even and odd chain lengths present)	1.11	0.489	0.23 (measured), 2.8 (nominal)	Sasol, Sastech Research and Development (2000b), Palmer and Cann (2000a)
67762-41-8	C ₁₀₋₁₆ alcohols	TYPE C (80–95% Linear; >95% C12/C13 [range C11–15]; Even and odd chain lengths present)	0.67	0.48	0.28 (measured), >10 (nominal)	Palmer and Cann (2000a), Huntingdon Life Sciences Ltd. (1991b)
112-42-5	Undecvl alcohol		8.3	1.757	ca 1 (nominal)	Bengtsson et al. (1984)
67762-25-8	C ₁₂₋₁₈ Alcohols	TYPE A (100% Linear; >50% C12/C14; >10% C16/C18 [range C8–C20]; even chain lengths present)	1.70	0.5	40 (nominal)	Kirch (1998a)
68855-56-1	C ₁₂₋₁₆ alcohols	TYPE A (>40% Linear; >95% C12/13/14/15 [range C10-C17]; Even and odd chain lengths present)	0.69	0.212	<1	Palmer and Sherren (2001)
80206-82-2	C ₁₂₋₁₄ alcohols	TYPE A (100% Linear; > 90% C12/14 (C12>14), <10% C16 [range C6–C18]; Even chain lengths present)	4.61	0.282	63 (nominal)	Kirch (1998b)
112-70-9 112-72-1	1-Tridecanol 1-Tetradecanol		0.50 0.20	5.7 0.182	0.5 4	Unilever (1995) Unilever (1995)

4.2.1. Predicting toxicity of complex mixtures

A toxic effect can arise from exposure to a complex mixture if the dissolved concentration of any individual component exceeds its toxic threshold concentration. An effect can also occur if the concentrations of multiple components with a similar mode of action are below their individual toxic threshold concentrations but their combined concentration exceeds the effect threshold concentration for that mode of action.

In the latter case a method for summing the toxic contributions of all the components is needed in order to predict at what level the effect may occur. A 'toxic units' (TU) approach based upon the following expression allows the contribution of all similarly acting components to be summed.

$$\operatorname{Sum} \operatorname{TU} = \sum_{i} \frac{C_{i}}{E(L)C_{50,i}}$$
(16)

where C_i is the concentration of component *i* in solution and $E(L)C_{50,i}$ is the effective or lethal concentration of component *i*.

A toxicity threshold equivalent to an acute EC_{50}/LC_{50} is achieved when the Sum TU is ≥ 1 (Loewe, 1953). A sum less than 1 implies that there are insufficient concentrations of dissolved components for an EC_{50}/LC_{50} response to be mediated.

The approach requires two pieces of information for each component of a mixture i.e. C_i and $E(L)C_{50,i}$. The partitioning and solubility models described above can be used to predict the dissolved concentration of each component at any given loading rate. (Q)SARs that are applicable to single carbon number alcohols have been described above, and these can be used to predict the $E(L)C_{50,i}$ of each component. It is a relatively simple procedure to

combine these two pieces of information using the above expression and to determine a loading rate at which the sum of TUs equals 1, i.e. the loading rate at which a 50% effect on a specified organism would be anticipated.

4.2.2. Comparison of measured and predicted data

The TU approach was used to fill data gaps for fish and *Daphnia* toxicity in the OECD SIAR (2006a), especially for commercial mixtures. When making comparisons it should be noted that the measured data were obtained using a range of test protocols and species and consequently some variability in test results is expected. Even so, the agreement between the measured and predicted toxicity data for the commercial products is good. Table 11 illustrates this for predicted and measured acute *Daphnia* results. In the table, 'types' refer to different commercial grades from different suppliers, which differ in exact composition within the range permitted for the CAS number. These compositions were used on a confidential basis to make the predictions. Predicted results for acute toxicity to fish were similar to the predictions for invertebrates. Full details are presented in the SIAR and its annexes (OECD, 2006a).

The absence of reliable (Q)SARs for algae means that, for the time being, data gaps for effects on this taxonomic group have to be filled by expert judgement and read-across, largely from the *Daphnia* results.

5. Conclusions

Commercial long chain aliphatic alcohols consist of essentially pure and mixed reaction product substances. A substantial amount of physicochemical property data and aquatic ecotoxicology data are available. The predictable nature of relevant physical-chemical properties, aquatic ecotoxicology (Q)SARs and biodegradability relationships fully support a coherent category justification and assessment. Therefore, where gaps in empirical data existed, (Q)SAR or read-across data have been used to fill them, using class-specific (Q)SARs.

These alcohols have been shown in good-quality studies to be rapidly degradable under standard conditions up to C_{18} . Furthermore, evidence suggests that longer chain lengths are also rapidly biodegradable, though bioavailability is limited by very low water solubilities at these longer chain lengths. While log K_{ow} values suggest possible bioaccumulation potential, the available data (from a limited data set) suggest that these substances are not as bioaccumulative as log K_{ow} -based estimation methods would predict. This is supported by the known metabolic potential of these substances.

Biodegradation rates for all chain lengths are high provided that solubility in water is not exceeded. OECD Guideline tests for ready biodegradability typically well exceed the solubility limit for chain lengths C_{12} and above and at low concentrations, degradation is also partially controlled by sorption to suspended solids.

For acute aquatic toxicity, solubility limits the possibility of effects being observed for higher carbon number alcohols (around C_{13-14} and above). However, there might still be concerns about chronic toxicity where the solubility cut-off is different from that for acute toxicity, see Schäfers et al. (2008, this issue). Class and organism-specific acute (Q)SARs have been developed for the purpose of interpretation and ultimately risk assessment.

Many commercial products are multi-component reaction products, and substantial amounts of data are available for these also. A model has been developed and tested, which gives an excellent account of the aquatic ecotoxicity. The availability of this model means that the acute effects of any mixture of alcohols can be predicted, thus avoiding much unnecessary testing of aquatic organisms.

Research needs were clearly identified in the development of this overall effort to understand long chain alcohols in the environment. In an environmental risk assessment context, the particularly rapid rate of alcohol biodegradation clearly reduces the potential dispersion of long chain alcohols into the environment following wastewater treatment. At the same time, ecotoxicity testing is made more are challenging by the same phenomena. The predicted chronic toxicity, assuming typical acute to chronics ratios for non-polar narcotics, could give rise to concern for their hazard. A program was established to understand the chronic toxicity of long chain alcohols in the regions above and below solubility to Daphnia magna based on the physical-chemistry of alcohols reported in this paper and are subsequently reported by Schäfers et al. (2008, this issue). In addition, environmental distribution following wastewater treatment which holistically addresses biodegradation, sorption, and overall exposure was also deemed critical so that potential risks in the environment could be assessed (Belanger et al., 2008, this issue). Research is also needed to integrate metabolism (biodegradation, synthesis of alcohol and relevant pre-cursors, etc.) of alcohol derived from the numerous natural and anthropogenic sources in order to coherently address the relevance of future risk assessments.

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Studies described in this paper that used experimental animals were conducted using methods in accordance with OECD Guidelines, with acceptable deviations in some cases.

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