Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the Opinion proposing harmonised classification and labelling at EU level of

Branched hexatriacontane

EC Number: 417-070-7
CAS Number: 151006-62-1

CLH-O-0000001412-86-195/F

Adopted

9 March 2018

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the public consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the public consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties.

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Substance name: branched hexatriacontane
EC number: 417-070-7
CAS number: 151006-62-1
Dossier submitter: United Kingdom

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
18.04.2017	Netherlands	RIVM	National Authority	1
Comment received				
The Dutch CA supports the proposal to remove the current harmonized classification for branched hexatriacontane. In our opinion, there is sufficient evidence that shows that the criteria for 'safety net' classification are no longer met. That said we believe that the case for grouping and read-across could have been more robust and the (Q)SAR results should have been reported in a more transparent way. It would have helped to have the information from the Annex in the main body of the CLH report, since it provides the foundation of the read-across to long-term invertebrates and QSAR prediction of long-term fish. Category definition/Read-across The substance under consideration is a UVCB especially therefore details on the composition or production of the substance are important to consider when assessing the grouping approach. It is mentioned that the hydrogenated materials are saturated with some hydrocarbons with some branching. What is the composition of the branching between the members of the category and the carbon number ranges? Only limited information is given on how the substance is produced and how the members of the category are produced. It is only stated that they are a polymerisation or oligomerisation product of alpha olefins typically ranging from C20 to C60 that may be hydrogenated. Specific details on the polymerisation reaction are not given and also any further preparation or distillation after the polymerisation is not provided. Branched hexatriacontane is stated to contain thousands of more complex branched isomers and more details on the production should be provided to show that its composition is actually comparable to that of the proposed group members. E.g. does the production of the group members also lead to thousands of more complexed branched isomers and could there be different steps in the synthesis causing (different) contaminants in the end product. It is also noted that the original group of PAO (as given on the website: http://www.hopaconsortium.com/substances) contain twelve members that are				

hydrogenated and even more that are not hydrogenated. In the report is stated that branched hexatriacontane falls within the applicability domain of the POA category. Nevertheless, in the report only six members (table 12) of this category are used in the read across, this suggests that a specific category within the category is created without justification. If branched hexatriacontane is assumed to be a member of the PAO category, data from all group members should be used in the read across approach and not data from a selection. If otherwise a selection is made of substances from the PAO category to be used for the read across, what seems logic as the category contains olefins as well as alkanes (hydrolysed olefins), and then this is a new sub-category that should be justified in the report.

(Q)SARs approaches:
Most of the (Q)SAR predictions provided in the CLH report are used as supportive information with the exception for chronic toxicity to fish. We believe that when QSAR data are used for conclusions on the proposed classification, QSAR model reporting format (QMRF) and QSAR prediction reporting format (QPRF) for the QSARs used and generated endpoints should be provided and included in the report. This is not provided for the key study/prediction. These templates are devised to reflect as much as possible the OECD principles for the validation of the model for regulatory purposes and helps establish the adequacy of the prediction in relation to a defined regulatory purpose.

Dossier Submitter's Response

Thank you for the comments, The CLH report cannot be updated at this stage of the process. However, further information to address these points has been provided in this response to comments table and in the attached documents (please see below).

All data available for Polyalpha olefins members from the HOPA category have been included. Table 12 (in the Annex to the CLH report) shows the substances for which data are available and which were used for read-across to the members of the category.

It is noted that the CLH report was prepared by Chevron Phillips Chemicals International N.V. (CPC) and submitted by the UK CA in accordance with Article 37(6) of CLP. CPC note that, with regard to the production and composition, branched hexatriacontane is a highly branched isoparaffinic hydrocarbon (resulting in thousands of complex isomers) produced from 1-dodecene. This substance is produced by: 1) oligomerizing 1-dodecene in the presence of a catalyst under mild temperature and pressure. 2) treatment of the reactor effluent to remove the catalyst residue, 3) fractionation (distillation) and hydrogenation of the resultant oligomers into different fractions to match specific viscosity specifications. The branched C36 alkanes derived from 1-dodecene are separated from the reaction product by continuous distillation under vacuum conditions and then hydrogenated. The isomeric distribution of this substance is consistent with other PAO group members, which have thousands of complex branched isomers as well. Manufactures of PAO group members have similar production processes, catalysts, and feedstocks. Therefore, it is our opinion that contaminants, if present, would also be similar.

Further information on the QSAR models is provided in the attached QRPF/QMRF's
Attachment 1: ECOSAR QMRF
Attachment 2: KOCWIN QMRF
Attachment 3: KOWWIN QMRF
Attachment 4: BCFBAF QMRF
Attachment 5: SPARC QMRF
Attachment 6: HC5 QMRF
Attachment 7: QPRF Branched hexatriacontane
Attachment 8: HOPA QPRF

RAC's response
RAC agrees with the Member State to remove the current harmonized classification for branched hexatriacontane. Some clarifications in the chemical background information would probably support read-across and the opinion of removal: 1. Hydrolysis of olefins results alcohols, not alkane....Reasoning of the commenter is based on misunderstanding. 2. The statement that PAO category contains olefins and alkanes should be specified: polyalpha-olefins does not contain alkanes, only olefins = alkenes. Hydrogenated polyalpha olefins are not olefins any more but alkanes. 3. Hydrogenated olefins = alkanes: these kinds of substances were selected by DS for the purpose of read across. 4. Sub-categorization means here the selection of hydrogenated substances (alkanes) (in a separate Table on the cited HOPA webpage: http://hopaconsortium.com/substances) with the certain series of carbon chain length which includes the carbon number of branched hexatriacontane (C36 H74). The attached QSAR reporting formats (QMRF / QPRF) are considered by RAC satisfactory.

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
18.04.2017	Netherlands	RIVM	National Authority	2

Comment received
Degradation: Data is provided on degradation tests with the substance considered. The outcome of these tests must be used to conclude if the substance can be considered as rapidly or non-rapidly degradable. To keep the CLH proposal in line with the guideline, the same wording as the guideline should be used. The conclusion of section 5.1.3 should be that the substance is non-rapidly degradable as this is the criterion in the guidance for degradation. Ecotoxicity: In general it is accepted that ecotoxicity of this substance is expected to be low. However, we have the following questions: 1) with regard to the ECOSAR (Q)SAR results reported in Table 14, are the NOEC adjusted values or are these chronic toxicity values (ChV)? and 2) PETROTOX QSAR predictions are provided however, there is no information on the model itself. It would be helpful to provide information on this model.

Dossier Submitter's Response
Thank you for the comments. <u>Response to Degradation:</u> The CLH report cannot be updated at this time. Section 5.1.3 of the CLH report refers to the actual ready biodegradability test reports and the conclusion of the test report is that the substance is not readily biodegradable. A sentence could have been included to say: "On the basis of the available data, branched hexatriacontane is considered not readily biodegradable. As such, the substance is considered to be not rapidly biodegradable under the CLP classification criteria". <u>Response to Ecotoxicity- ECOSAR QSAR results:</u> Table 14 in the Annex to the CLH report shows the ChV values as reported by ECOSAR. The NOEC values were calculated and shown below.

Table 14: Summary of QSAR results on partition coefficient and ecotoxicity properties of poly alpha olefins of C14 and above

Variable/ Organism	Endpoint		≥C14	C14	C16	C18	C20	C22	C24	C30
	ECOSAR	PETROTOX	PETROTOX	ECOSAR	ECOSAR	ECOSAR	ECOSAR	ECOSAR	ECOSAR	ECOSAR
Log Kow			≥7.86	7	8.06	9.04	10.03	11.01	11.99	14.94
Water solubility				0.0139	0.00123	0.0001256	1.26E-05	1.26E-06	1.24E-07	1.16E-10
Fish	96h LC50	LL50	>1000^	0.006	0.000801	0.000123	1.87E-005 *	2.81E-006 *	4.19E-007 *	1.34E-009 *
Daphnid	48h LC50	LL50	>1000^	0.007	0.00111	0.000197*	3.46E-005 *	6.01E-006 *	1.04E-006 *	5.11E-009 *
Green Algae	96h EC50	LL50	>1000^	0.030*	0.007*	0.00199*	0.000536 *	0.000143 *	3.77E-005 *	6.69E-007 *
Fish	ChV			0.000876	0.000125	2.06E-05	3.34E-06	5.36E-07	8.53E-08	3.32E-010 *
Daphnid	ChV			0.00182	0.000335	6.96E-05	1.43E-005 *	2.9E-006 *	5.85E-007 *	4.6E-009 *
Green Algae	ChV			0.026*	0.008*	0.002*	0.00078 *	0.000245 *	7.61E-005 *	2.21E-006 *
Fish	NOEC**	NOEL	>1000	0.001	1.77E-04	2.91E-05	4.72E-06	7.58E-07	1.21E-07	4.70E-10*
Daphnid	NOEC**	NOEL	>1000	0.003	4.74E-04	9.84E-05	2.02E-05*	4.10E-06*	8.27E-07*	6.51E-09*
Green Algae	NOEC**	NOEL	>1000	0.037*	0.011*	2.83E-03*	1.10E-03*	3.46E-04*	1.08E-04*	3.13E-06*

^ LL50 not reached.

* Chemical may not be soluble enough to measure this predicted effect.

** NOEC calculated as ChV multiplied by the square root of 2.

Response to Ecotoxicity-Petrotox:
It is noted that the CLH report was prepared by Chevron Phillips Chemicals International N.V. (CPC) and submitted by the UK CA in accordance with Article 37(6) of CLP. Further information on the applicability of the Petrotox model has been provided by CPC. Please see Attachment 9 : Relevance and applicability of Petrotox for the prediction of chronic ecotoxicity endpoints of polyalpha olefins

RAC's response
RAC agrees with the conclusion to consider the substance as non-rapidly degradable based on the negative ready-biodegradability test results and the lack of hydrolysis or other type of degradation of branched hexatriacontane. RAC has no reason to doubt the correctness of the QSAR models and chemical and ecotox estimates in Tables 13 and 14.

Date	Country	Organisation	Type of Organisation	Comment number
25.04.2017	France		MemberState	3
Comment received				
Page 9: The EC number is functional but the CAS number is inexistent in any of the				

database generally used for risk assessment (PBT profiler, Danish QSAR database, EPIsuite,…) and even in the CAS number registry.
Without proper information on the substance ID it's impossible to run an accurate assessment, that's why we are of the opinion to not modify the actual classification until clarification is made on the substance ID.
Page 12: there is no information on the substance exactly used to perform the read across and to evaluate the log Kow in the Kowin modelisation.
As this value is used later to estimate BCF value and ecotoxicological parameters, it seems to lack appropriate data to validate the proposal to change the classification of this substance.
We recommend to solve these problems and not to change the current classification.

Dossier Submitter's Response

Thank you for the comments.

Response to CAS number:
The existing Annex VI entry is assigned the CAS number 151006-62-1. This CAS number was used in the original notification made under the Notification of New Substances Regulation. Further, the CAS number 151006-62-1 is readily found by signing up to any of the database programs administered by Chemical Abstract Services. Therefore, it is considered that the substance is adequately identified by this CAS number.

Response to Substance used to evaluate the log Kow:

The following SMILE annotation has been used for EPI Suite:
SMILE CC(CCCCCCCCCC)CC(CCCCCCCCCCCC)CCCCCCCCCC

RAC's response

RAC finds the information concerning substance identification satisfactory.

Date	Country	Organisation	Type of Organisation	Comment number
21.04.2017	United Kingdom		MemberState	4

Comment received

In this instance declassification from Aquatic Chronic 4 requires information to show that the substance is not chronic ecotox or, data to demonstrate that the substance is either rapidly degradable or not bioaccumulative.

Ecotoxicity:
Experimental chronic ecotoxicity data using Alkane 4 is not available.

Read-across (RAX) is proposed for chronic ecotoxicity to invertebrates. While we note the value of this approach, we feel that justification of analogues is not clearly made. For example, only predicted physico-chemical data are included so a clear comparison of similarities is not possible.

For chronic toxicity to invertebrates, 2 experimental values using analogues are available with limited details in Table 16. Full details of the studies assessing their reliability and validity are not included. This information is important to support read-across of the study endpoints and should be available in the CLH report.

There are no experimental values for chronic toxicity to fish for any proposed analogues. We are unclear why as we anticipate further analogues covering C15-50 are likely to be

available. To consider the chronic toxicity to fish endpoint, QSAR predictions for Alkane 4 and analogues are presented.

We are unclear if PETROX is applicable for this substance and the purpose of classification. While we are aware that the use of PETROX has been discussed for REACH processes, we do not know the outcome which would be relevant to understand.

For ECOSAR predictions, the CLH report does not include sufficient information to consider if the QSAR training set includes relevant hydrocarbon structures.

At present, we do not consider the proposal provides convincing data to demonstrate Alkane 4 is not chronically ecotoxic.

Bioaccumulation:
As Alkane 4 is not rapidly degradable, consideration of bioaccumulation potential is assessed in relation to declassification.

The measured log Kow for the substance is >8 and a measured BCF is not available. An EPIWIN KOWWIN prediction is 17.87. However, we note that substances in the training set with log Kow >8 do not appear to be representative structures as they all contain benzene rings and frequently chlorine.

The CLH report refers to a paper discussing bioaccumulation potential of Alkane 4 (Girling, 2007). We note that this paper was produced for consideration of vB potential (BCF 5000) only which is different to the bioaccumulation BCF cut off of 500 for classification. We consider there is significant uncertainty regarding the predicted BCF. For example, in the paper, ten C6 to C15 substances were used to develop the model and it is unclear if the relationship between carbon chain length and log BCF declines dramatically after C12 as suggested in the report and Figure 1. This is because the decline is based on a single data point at C15 for a linear hydrocarbon and the relationship may alternatively plateau around C12 resulting in BCFs >500 for C12 and above. Due to this uncertainty we do not consider the paper demonstrates a BCF <500 for the branched hydrocarbon Alkane 4 with C36.

Considering the above comments, we do not consider the current CLH supports declassification. Further data should be considered to support lack of chronic ecotoxicity and bioaccumulation potential.

Dossier Submitter's Response

Response to the read-across chronic toxicity to invertebrates:

The Annex to the CLH Report shows the read-across from the members of the Poly alpha olefins category and explains that the members differ only in carbon chain length. Physico-chemical, fate and ecotoxicity properties of the polyalpha olefins are similar or change in a predictable fashion. Table 17 in the Annex shows a data matrix of the aquatic toxicity by carbon number which demonstrates the lack of toxicity of a range of Poly alpha olefins to aquatic organisms.

Branched hexatriacontane (C36H74, C12 trimer) fits the range of carbon number (C20-60) and oligomer distribution (dimer, trimer, tetramer) of the test materials in the two chronic invertebrate toxicity studies used for read across. The tested substances are also UVCB, with a similar type and extent of branching. Those two studies were conducted on 1-decene homopolymer hydrogenated (CAS 68037-01-4, C30-C60, predominantly C30H62 C10 trimer and C40H82 C10 tetramer with some pentamer and hexamer) and dec-1-ene dimers hydrogenated (CAS 68649-11-6, predominantly C20H42 C10 dimer).

Response to full details of the chronic toxicity to invertebrates studies using analogues assessing their reliability and validity are not included:

The key read across data (Putt 2003a, b) have been used to complete the chronic toxicity to aquatic invertebrates endpoint as no data were available for branched hexatriacontane.

Putt (2003a) is a GLP-compliant semi-static full life-cycle toxicity test with Daphnia magna following OECD 211. The study on 1-decene homopolymer hydrogenated (CAS 68037-01-4) used Water Accommodated Fractions, prepared daily at each renewal period, by fortifying well water (following the US EPA formula for hard water, 148-175 mg/L as CaCO3) and drawing the WAFs off directly into each of the 10 replicates. A control solution was also prepared following the same procedures. The study was conducted as a limit test at a single concentration of 125 mg/L nominal loading rate WAF, though no analytical confirmation of the test media were undertaken due to the low solubility of the substance and the lack of appropriate sensitivity of the analytical method. The results show that following a 21-day exposure, there was no adverse effect observed on survival, growth or reproduction and so the NOELR is 125 mg/L nominal loading rate WAF.

Putt (2003b) is a GLP-compliant, semi-static full life cycle toxicity test with Daphnia magna following OECD 211. The study on dec-1-ene dimers hydrogenated (CAS 68649-11-6) used Water Accommodated Fractions, prepared daily at each renewal period for each of the 10 replicates, by fortifying well water (following the US EPA formula for hard water, 150-180 mg/L as CaCO3). A control solution was also prepared following the same procedures. The study was conducted as a limit test at a single concentration of 125 mg/L nominal loading rate WAF, though no analytical confirmation of the test media were undertaken due to the low solubility of the substance and the lack of appropriate sensitivity of the analytical method. The results show that following a 21-day exposure, there was no adverse effect observed on survival, growth or reproduction and so the NOELR is 125 mg/L nominal loading rate WAF.

The studies were conducted on 1-decene homopolymer hydrogenated (CAS 68037-01-4, predominantly C30H62 and C40H82) and dec-1-ene dimers hydrogenated (CAS 68649-11-6, predominantly C20H42) and read across to branched hexatriacontane (C36H74).

Response to why the CLH report did not include any chronic toxicity to fish experimental endpoints (either for the registered substance or analogues) and that the endpoint relied on QSAR (ECOSAR and PETROX) predictions. It is anticipated experimental data for analogues could be available.

Experimental data for analogues was reported by Girling (2000) (please see attachment 11 – CONFIDENTIAL). The report shows that CONCAWE (1997) reviewed the chronic toxicity to fish (Fathead minnow) of three lubricating base oils with similar chemical structure as branched hexatriacontane. The three base oils tested had carbon numbers in the range of C15 to C50. The experimental data from these base oils was obtained in a test medium of oil in water dispersion (OWD) and results show that there was no effect on reproduction and survival at loading rates >=1000mg/l. It was further mentioned in the Girling (2000) report that extrapolation of results due to chemical similarities between the three base oils and branched hexatriacontane suggests that branched hexatriacontane would not be toxic for reproduction and survival at a loading rate that is considerably in excess of that required to achieve maximum dissolved concentration of its constituents under the test conditions.

Reference

Girling (2000) On the level 2 ecotoxicity testing requirements and environmental risk assessment of alkane 4 (C36 polyalphaolefin, hydrogenated C12 trimer). Expert report. 10 October 2000.

Response to the use of PETROTOX has been discussed for REACH purposes and it would be relevant to understand the outcome.

It is noted that the CLH report was prepared by Chevron Phillips Chemicals International N.V. (CPC) and submitted by the UK CA in accordance with Article 37(6) of CLP. Further information on the applicability of the Petrotox model has been provided by CPC. Please see attachment 9; Relevance and applicability of Petrotox for the prediction of chronic ecotoxicity endpoints of polyalpha olefins.

Furthermore, Petrotox is mentioned in guidance documents from ECHA, including Chapter R.11: PBT/vPvB assessment. Draft version 3.0, March 2017 and Chapter R7.c: Endpoint specific guidance. Draft version 3.0 March 2017. The latter mentions that Petrotox could be used to address individual structures where no experimental data is available.

Response for ECOSAR predictions, the CLH report does not include sufficient information to consider if the QSAR training set

QMRF and QPRF are included for ECOSAR with this response document (Please see attachment 1 and 7).

Response to the uncertainty regarding the argument for the Girling predicted BCF being <500 which is limited to the EPIWIN QSAR predictions as supporting information. However, it is unclear how reliable these predictions are given the training set structures and measured data do not appear to be representative of Alkane 4. In addition, you have not considered the comment about whether the Girling model curve declines or plateaus which is critical to the current BCF prediction. At present, there is large uncertainty around whether it declines instead of plateauing given the decline assumption is based on a single data point which may or may not be an outlier.

In order to address concerns regarding the uncertainty around whether the BCF declines at longer chain lengths greater than C12, further supporting evidence of the decline in BCF values with increasing carbon chain length is provided below.

US EPA
The US EPA (2005) higher olefins category summary concluded that the C6, C7 and C16 to C54 higher olefins category members are not expected to bioaccumulate based on BCF values <250. The reported values show that, up to a carbon chain length of C14, BCF values increase and then BCF values decrease with increased carbon chain length from C15. The calculated BCF values (from EPIWIN v3.10 or 3.11) are summarised in Table 1.

Table 1: Calculated bioconcentration factors (BCF) for C6 to C54 alpha and/or internal olefins

	C6 (i/n*)	C7 (i)	C8 (i)	C9 (i)	C10 (a/i)	C11 (i)	C12 (a/i)	C13 (a/i)	C14 (a/i)	C15 (i)	C16 (i)	C18 (a/i) and C20-54 (a)
BCF	46/ 44	236	659	632	489/ 489	361	313/ 314	748/ 748	1584/ 2030	431	71/ 92	3.2-4.6

(a) alpha olefin
(i) internal olefin
* neohexane

Davi et al (2009) (Please see attachment 10 - CONFIDENTIAL)
Davi et al (2009) modelled BCF values (using BCFBAF) for a range of higher olefins, from C6 to C19, and predictions indicate that C13-C16 olefins exceed the criterion for vB and selected C11, C12 and C14 olefins exceed the B criterion. The model shows that BCF peaks at C14 and subsequently decreases with increasing chain length. From interpretation of the graph, olefins of C8 to C18 have a predicted BCF of ≥500 (the criterion used in the chronic aquatic category 4 classification). The C6, C7 and C19 olefins have a predicted BCF of <500. Therefore, as branched hexatriacontane (C36) has a carbon chain length higher than C19 (the longest chain length covered in the paper), and BCF is demonstrated to decrease with increasing carbon chain length at chain lengths above C14, it is not expected to meet the criteria for bioaccumulation under the chronic aquatic category 4 classification.

Davi et al (2009) also model the bioaccumulation of olefins using the equations developed by Arnot and Gobas (2003), which are included in the upper trophic BCF output from BCFBAF. The BCF predictions were adjusted to a lipid content of 5% (from 10.7%) and default values for particulates and dissolved organic carbon concentrations of 0.5 mg/L that are assumed in the BCFBAF model were also used as conservative defaults in these calculations. The marked influence that fish biotransformation exerts on the predicted BCFs derived from the model is evident as no olefins are shown to exceed the B or vB criteria. The BCF predictions peak at a carbon number of 12 and subsequently decrease with increasing chain length, so that the modelled olefins of C16 to C19 had BCF values of <500 (the criterion used in the chronic aquatic category 4 classification).

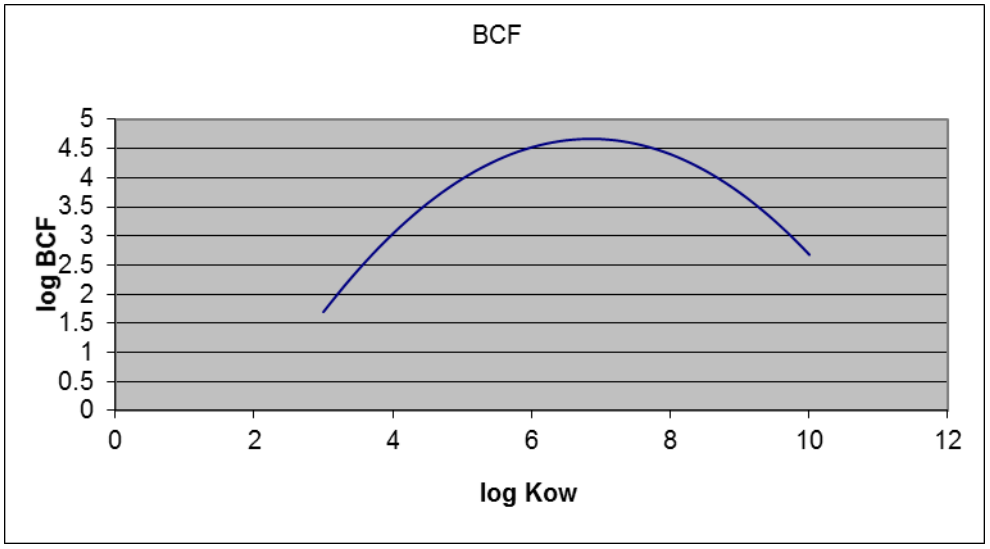
This lack of bioaccumulation for olefins with long chain lengths is supported by experimental data. Davi et al (2009) conclude that, although modelled data appears to under-predict bioaccumulation in the C10-12 range, the models are accurate above and below this range, as evidenced by experimental BCF data. The experimental dietary BCF results for C9 to C16 olefins show a peak in BCF at between C10 to C12 with the BCF decreasing with increasing chain lengths following this.

Girling (2000)
Girling (2000) (Please see attachment 11 - CONFIDENTIAL) reported that the bioconcentration factor (BCF) of branched hexatriacontane cannot be predicted with high accuracy from a measured octanol-water partition coefficient because only limit values for Kow are available (log Kow >3.87 (Safepharm 1995) and >7.64 (Seary 2000)). The predicted Kow value is very high (log Kow 17.87 (KOWWIN v1.68)) and the QSAR for BCF based on Kow is not fully validated at the extreme of Kow. However, Girling (2000) noted it is useful to consider the approach stated in the Technical Guidance Document (TGD). For substance of log Kow >6 and molecular weight <700 (both of which apply to branched hexatriacontane), the following QSAR equation gives an indication of BCF:

$\text{Log } BCF_{fish} = (-0.20 \times \text{log } Kow^2) + (2.74 \times \text{log Kow}) - 4.72$

This equation gives a peak at approximately log Kow of 6.9, which corresponds to a BCF of approximately 45,700 (log BCF of approximately 4.66, see Figure 5.1), but the BCF then decreases with increasing Kow.

Figure 5.1 Plot of log BCF versus log Kow (taken from Girling (2000))



Based on the graph presented in Girling (2000), branched hexatriacontane, with a predicted log Kow of 17.87, would have a very low BCF.

Girling (2000) also reviews other papers relevant to alkanes, as discussed below.

Girling (2000) reported that the result from Vik (1996) is consistent with the TGD prediction. Vik (1996) reviewed toxicity data for synthetic based drilling muds and reported a BCF value in *Mytilus edulis* (mussel) of approximately 126 (reported as log BCF of 2.1) for a C20 PAO synthetic base fluid (log Kow of 11).

Girling (2000) notes that Gobas and Morrison (2000) summarise relevant findings influencing the biological uptake of substances, of which Girling (2000) considers the following are applicable to branched hexatriacontane:

- Molecules of internal cross-section >0.95 nm are not bioavailable since they are too large to cross membranes.
- Once ingested, the high log Kow indicates that elimination is likely to be significant via faeces.
- A steady state is unlikely to be achieved in the time-scale of a standard bioconcentration test.
- The substance is likely to bind to any lipid/faecal matter in the water.

Girling (2000) describes that Rausina et al (1996) reported the results of a study in which the use of semi-permeable membrane devices (SPMD) to estimate bioconcentration potential of petroleum additives was investigated. This apparatus mimics membrane behaviour. The conclusions from this study were that uptake is limited when:

- log Kow >6
- water solubility <1 mg/mL
- molecular weight >500 g/mol
- molecular diameter >1 nm

Branched hexatriacontane is expected to have a log Kow >6 (measured log Kow of >3.87 (Safepharm 1995) and >7.64 (Seary 2000), with a predicted log Kow of 17.87,) a water solubility of <1 mg/L (measured water solubility of <0.485 mg/L (Safepharm 1995) and <1

x 10^{-6} mg/L (Seary 2000)) and a molecular weight of >500 g/mol (506 g/mol), though the molecular diameter is currently unknown. On this basis, uptake of branched hexatriacontane would be expected to be limited.

Girling (2000) noted that, of the substances examined by Rausina et al (1996), the one that was most similar to branched hexatriacontane was a poly alpha olefin with a molecular weight of 436 g/mol and a water solubility of <0.001 mg/L. A maximum uptake of <0.001 mg/g into the SPMD was determined for this substance, which indicated that the 14-day BCF would be <1. Girling (2000) concluded that branched hexatriacontane has a higher molecular weight than this substance and therefore would be expected to be less bioavailable, thus the BCF for branched hexatriacontane would be expected to be even lower than that for the poly alpha olefin investigated in this study.

Girling (2000) included a discussion on Tolls et al (1999), which reported studies on the physico-chemical properties and bioconcentration potential of alkanes. Girling (2000) noted that the Tolls et al (1999) report concluded that the environmental fate of these compounds is largely governed by their hydrophobicity, i.e. their tendency to partition from water to surrounding compartments such as sediments or biological tissues. Various alkanes were investigated, the largest being C19 (straight and branched chains). Biotransformation of the accumulated substance was apparent within a 12-day test. The findings support the view that if branched hexatriacontane were taken up, it may be biotransformed by the organism.

Girling (2000) concludes that the literature indicates that bioconcentration of alkanes of high molecular weight is minimal, and may be as low as BCF <1 for branched hexatriacontane. Girling (2000) consider that this is consistent with the analysis of the potential for absorption of branched hexatriacontane by mammals, reported by Illing (2000).

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RAC's response

RAC can see sufficient evidence for non-existence of ecotoxicity for the three trophic levels based on measured and/or calculated EC50 and NOEC data for analogue substances. Experimental data derive from Klimisch 1 (invertebrates) or Klimisch 2 (algae) studies. Chronic fish toxicity data for close analogues exist as confidential information and proves the non-existence of chronic toxicity (Girling, 2000).

The summary overview in Table 17 supports the opinion of DS based on measured and calculated aquatic toxicity data on the series of analogues with growing carbon number from C20 to C60, i.e. that branched hexatriacontane should be classified using a WoE approach as acutely and chronically not ecotoxic.

Concerning bioaccumulation a log Kow above 10 results in a decline in BCF compared to substances with smaller Kow-s. As Kow is in clear correspondence with the carbon chain length in the case of alkanes, RAC's opinion is that alkanes with a carbon chain longer than C20 have very low potential to bioaccumulate.

RAC agrees with the responses and comments of DS that strenghtens the view that alkanes (normal and branched) are the best verified examples for carbon number-based serial characterization (both physico-chemical and biological effects), namely one can better trust in the read-across results and QSAR estimates for alkanes, as in general. RAC opinion is, that the read across and model based values adequately support the proposal of declassification of brached hexatriacontane.