Committee for Risk Assessment
RAC

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

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: **Branched hexatriacontane**

EC Number: **417-070-7**

CAS Number: **151006-62-1**

The proposal was submitted by **the United Kingdom** and received by RAC on **9 February 2017.**

In this opinion, all classification and labelling elements are given in accordance with the CLP Regulation.

PROCESS FOR ADOPTION OF THE OPINION

The United Kingdom has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation/*** on **14 March 2017**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **28 April 2017**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Katalin Gruiz**

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The RAC opinion on the proposed harmonised classification and labelling was adopted on **9 March 2018** by **consensus**.

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard state-ment Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	601-064-00-8	Branched hexatriacontane	417-070-7	151006-62-1	Aquatic Chronic 4	H413		H413			
Dossier submitters proposal		Branched hexatriacontane	417-070-7	151006-62-1	**Remove** Aquatic Chronic 4	**Remove** H413		**Remove** H413			
RAC opinion		Branched hexatriacontane	417-070-7	151006-62-1	**Remove** Aquatic Chronic 4	**Remove** H413		**Remove** H413			
Resulting Annex VI entry if agreed by COM		Branched hexatriacontane	417-070-7	151006-62-1	-	-		-			

GROUNDS FOR ADOPTION OF THE OPINION

ENVIRONMENTAL HAZARD EVALUATION

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

Only hazards to the aquatic environment have been considered in this proposal. The current entry in Annex VI of the CLP Regulation for branched hexatriacontane is Aquatic Chronic 4; H413 – May cause long lasting harmful effects to aquatic life. The proposal of the Dossier Submitter (DS) is to remove this aquatic hazard classification.

Substance composition

Branched hexatriacontane is a branched C36 alkane, i.e. fully saturated and with a molecular weight of 507.97 and the composition:

- Branched hexatriacontane ($C_{36}H_{74}$)   92%–98%, average 95%
- Tetracosane ($C_{24}H_{50}$)   0%–1%, average 0.3%
- Octatetracontane ($C_{48}H_{98}$)   2%–8%, average 4%

Water solubility – unbounded measured results:
<0.482 mg/L at 20°C   EU A.6   Safepharm Laboratories Limited (1995), Klimisch 1
<0.1 mg/L at 20°C   read-across from 1-decene OECD TG 105 (Walker and Mullee, 2006)
<10^{-6} mg/L   No guideline analytical method (Seary, 2000), Klimisch 2

Log Kow – unbounded measured results and one QSAR estimate:
>3.87 at 20°C. OECD TG 107 / EU A.8 , Safepharm Laboratories Limited, (1995), Klimisch 1
>7.64, extrapolated to >8. No guideline, HPLC method (Seary, 2000)
>6.5 at 20°C. OECD TG 117, HPLC Method (Walker and Mullee, 2006)
17.87   QSAR model, KOWWIN v1.68, as part of EPISuite v4.1, US EPA (2012).

The QSAR model could not be validated by the unbounded measured values, so the DS used the unbounded values for classification purposes and the QSAR calculations only as supporting information. QSAR estimations of aquatic toxicity gave the same result for Log Kow >8 and 17.87, so a value of 8 was applied by DS for the estimations.

Koc – QSAR estimates (EPISuite KOCWIN v2.00)
Koc=3,222,800,000,000,000   Log Koc: 15.509, based on Log Kow = 17.87
Koc= 7,041,000,000   Log Koc: 9.8476   MCI method

Degradability – *Not rapidly degradable*

Photodegradation – no data on photodegradation is available.

Hydrolysis or dissociation is not expected, as there are no functional groups in the substance which could be hydrolysed or dissociated.

Ready biodegradability – OECD TG 301B CO_2 evolution test, two negative results
- 19% biodegradation after 28 days (Mead, 2005), GLP, Klimisch 1
- 6% biodegradation after 28 days (Handley and Mead, 1995), GLP, Klimisch 1

The Dossier Submitter conclusion was that the substance is not readily degradable and not rapidly degradable, for classification purposes.

Bioaccumulation potential – No measured data are available, only QSAR estimates:

BCF <10 L/kg. QSAR regression-based model developed by Girling (2007) that used ten substances ranging from C6 to C15. The relationship between carbon number and BCF is described in the model. When the carbon number is greater than 15, the BCF is likely to be below 10. Carbon number of branched hexatriacontane is 36 (24–48), so its BCF is below 10 L/kg.

BCF = 3.162 L/kg => Log BCF = 0.5.

BCFBAF v3.01 within EPISuite v4.11 US EPA (2012) was run using a Log Kow value of 17.87 (a QSAR estimate), resulting in an estimated BCF value of 3.162 L/kg. As the Log Kow value of 17.87 is out of the model dataset range (-6.5–11.26), the use of a Log Kow value of 11.26 results in a BCF of 27.5 L/kg for branched hexatriacontane.

The DS refers to the REACH guidance (Chapter R.7c, ECHA 2014) which also notes that, for PBT assessments, a calculated Log Kow value of 10 or above is taken as an indicator of reduced bioconcentration. As the experimental octanol–water partition coefficient data for branched hexatriacontane are unbounded, they cannot be used for direct comparison to this criterion. However, the QSAR estimated Log Kow of 17.87 is significantly higher than 10, thus, the DS concluded that branched hexatriacontane would have a low potential for bioaccumulation.

Aquatic toxicity – Experimental data

Results	Method	Study author / GLP / reliability
Fish LC$_{50}$ (96 h) >1000 mg/L (nominal WAF)	OECD TG 203 – *Oncorhynchus mykiss*, semi-static, mortality	Handley *et al.*, 1995 GLP, Klimisch 1
Daphnia EC$_{50}$ (48 h) >1000 mg/L (nominal WAF)	OECD TG 202 – *Daphnia magna*, static, mobility	Handley *et al.*, 1995 GLP, Klimisch 1
Algae EC$_{50}$ (96 h) >1000 mg/L (nominal WAF) Algae NOEC (96 h) ⩾1000 mg/L (nominal WAF)	OECD TG 201 – *Pseudokirchneriella subcapitata*, static, growth rate and biomass	Handley *et al.*, 1995 GLP, Klimisch 1

No measured chronic aquatic toxicity data are available for fish and invertebrates, so read-across and QSAR model-based resuls have been used for the hazard assessment of branched hexatriacontane.

Aquatic toxicity – read-across

Experimental data for the analogue 1-decene homopolymer hydrogenated (CAS 68037-01-4) with a carbon number between C16–60 is available, ***read-across*** to branched hexatriacontane is proposed:

Result of hydrogenated 1-decene dimer & homopolymer	Method	Study author / GLP / reliability
Daphnia NOEC (21 d) 125 mg/L (nominal WAF)	OECD TG 211 – *Daphnia magna* survival, growth or reproduction	Putt (2003)

Aquatic toxicity – QSARs

ECOSAR and PETROTOX QSAR predictions were determined for acute and chronic toxicity of poly alpha olefins to fish, invertebrates and algae. The QSAR results for long chain poly alpha olefins predict that, with increasing carbon number and increasing Log Kow values, the aquatic toxicity and the water solubility decrease. The PETROTOX results for poly alpha olefins of C14 and higher and ECOSAR results for poly alpha olefins with Log Kow above 8 predict that no acute or chronic

toxicity would be observed. Additionally, arguments for the use of both ECOSAR and PETROTOX model results, as a basis for accurate, qualitative determination of potential toxicity for branched hexatriacontane have been proposed. All related QMRF and QPRF documentation has also been submitted.

QSAR results	Method and conditions	Conclusion for branched hexatriacontane
Fish NOEC >1000 mg/L	PETROTOX for long chain poly alpha olefins Carbon chain >14 & Log Kow >8	NOEC >1000 mg/L as C36 & Log Kow >8
Fish NOEC > water solubility	ECOSAR for long chain poly alpha olefins Log Kow >8	NOEC >water solubility as Log Kow >8
Daphnia NOEC >1000 mg/L	PETROTOX for long chain poly alpha olefins Carbon chain >14 & Log Kow >8	NOEC >1000 mg/L as C36 & Log Kow >8
Daphnia NOEC > water solubility	ECOSAR for long chain poly alpha olefins Log Kow >8	NOEC >water solubility as Log Kow >8

Based on the results, the DS proposed to remove the classification for hazards to the aquatic environment, as no chronic toxicity NOEC values above water solubility were seen.

Comments received during public consultation

Four comments were submitted.

Two comments were submitted by one Member State (MS) that supported the removal of the environmental classification as Aquatic Chronic 4 stating that sufficient evidence has been provided that the "safety net" classification criteria are no longer met. They have, however, argued that the case for grouping and read-across could have been made in a more robust manner and that the QSAR results could have been presented in a more transparent way. For example, QSAR model reporting (QMRF) and QSAR prediction reporting formats (QPRF) could have been provided. An additional comment referred to the fact that the conclusion of section 5.1.3 of the CLH report should refer to rapid degradation.

The DS responded regarding the similarities between branched hexatriacontane and the substance group used for read-across and addressed the other issues with regards to QSAR modelling.

Another MS was of the view that CAS number is "inexistent" for branched hexatriacontane and constituents in the relevant databases and, thus, the assessment is not possible with, in their opinion, incomplete substance information. The proposal of the MS was not to modify the existing classification until the substance information is clarified.

In response, the DS referred to the existing CLP Annex VI entry and the associated CAS number, which is also found in Chemical Abstract Services databases . The substance is thus, in the opinion of the DS, adequately identified whilst the SMILEs annotation that was used for the computations was also provided.

Another MS commented on the read-across and the QSAR estimations for ecotoxicity and BCF, considering the methods and results too uncertain, arguing that the CLH Report did not support declassification. Different arguments referred to:

(i) Missing a clear justification for analogues used for the aquatic invertebrates read-across and study reliability and validity details
(ii) Missing experimental values for chronic toxicity in fish for the proposed analogues

(iii)   Uncertainty as to whether PETROTOX is applicable for this substance and the purpose of classification

(iv)   Missing information on ECOSAR predictions

(v)   Adequacy issues on the model training set for EPIWIN KOWWIN predictions

(vi)   Doubts related to the hypothesis behind the Girling (2007) conclusion, namely whether the relationship between carbon chain length and log BCF would decline dramatically after C_{12}

In their response, the DS confirmed that Branched hexatriacontane ($C_{36}H_{74}$, C_{12} trimer) fitted in the range of carbon number (C20–60). They also confirmed the oligomer distribution (dimer, trimer, tetramer) of the test materials in the two chronic invertebrate toxicity studies used for read-across and presented a full reliability assessment on the relevant study of Putt (2003). They referred to existing experimental fish toxicity data for analogues as provided during the Public Consultation (confidential data), with the validated studies and read-across for branched hexatriacontane suggesting a NOEC ≥ 1000mg/L, a value considerably above water solubility. Referring to the usability of PETROTOX, the DS mentioned the REACH Guidance where it is stated that Petrotox could be used to address individual structures where no experimental data is available.

Assessment and comparison with the classification criteria

Branched hexatriacontane ($C_{36}H_{74}$) would require classification in case of:

- its bioaccumulative potential being higher than the threshold value of 500 L/kg
    - or
- chronic toxicity occurs below water solubility or 1 mg/L concentration.

If either of these conditions is not met, classification as Aquatic Chronic 4 is not justifiable.

As measured/ experimental data is missing – no measured BCF studies, no fish and invertebrates toxicity results available – the DS presented the available evidence from both argumentation lines:

(i)   BCF being lower that 500 L/kg and

(ii)   no chronic toxicity occurring

Branched hexatriacontane ($C_{36}H_{74}$) has the following properties in the view of RAC:

- ***poorly water soluble*** (<0.482; <0.1; $<10^{-6}$ mg/L);
- ***does not rapidly degrade*** (19% and 6% <<70% within 28 days)
- ***does not exert acute toxicity*** at the limit of solubility (all EC/LC_{50} >1000 mg/L).

BCF

The CLH report includes the results from a QSAR model (BCFBAF v3.01) that estimated the BCF based on a Log Kow value (17.67) that is deemed uncertain. A calculated BCF value (= 3.162 L/kg being << 500 mg/L) has not been used for the current classification purposes.

Additionally, the carbon-number based extrapolation study (Girling, 2007) present in the CLH report also contains uncertainties, as the highest chain length with experimental data was only C15. Thus, the conclusion for a BCF value below 10 L/kg is considered as weak supporting evidence by RAC.

Chronic toxicity

As already noted, the CLP Regulation indicates that, for a substance with the properties and hazard profile of branched hexatriacontane, Aquatic Chronic 4 classification applies, unless other scientific evidence exists such as chronic toxicity NOECs > water solubility or > 1 mg/l showing classification to be unnecessary.

Thus, the CLH report contains:

a) Experimental data on algae: 96h NOEC ≥1000 mg/L (Handley et al., 1995) for branched hexatriacontane;
b) Experimental data on aquatic invertebrates: 21d NOEC = 125 mg/L (Putt, 2003), conducted on the analogues substances 1-decene dimer and homopolymer hydrogenated;
c) Experimental data on fish: no observed effect on reproduction and survival (NOEC ≥ 1000 mg/L), conducted on one light and two heavy paraffinic base oils (confidential data);
d) ECOSAR and PETROTOX model results for all aquatic trophic levels showing chronic NOEC values above water solubility, run for poly alpha olefins (C14 to C60).

RAC is of the opinion that, the overall evidence derived from the read-across and model-based ecotoxicity information is sufficient to predict low chronic aquatic toxicity for branched hexatriacontane.

In conclusion, as noted above, Branched hexatriacontane is poorly soluble, does not rapidly degrade, is not acutely toxic, has no experimentally determined BCF, but its Log Kow is >4. Furthermore, measured data from approproiate analogue substances and QSAR-based NOEC values for three trophic levels show no chronic toxicity. Consequently, the safety net classification is not warranted.

RAC agrees with the proposal of the DS to remove the classification for chronic aquatic hazards to the aquatic environment.

ANNEXES:

Annex 1   The Background Document (BD) gives the detailed scientific grounds for the opinion. The BD is based on the CLH report prepared by the Dossier Submitter; the evaluation performed by RAC is contained in 'RAC boxes'.

Annex 2   Comments received on the CLH report, response to comments provided by the Dossier Submitter and RAC (excluding confidential information).