Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

4-tert-butylphenol

EC Number: 202-679-0
CAS Number: 98-54-4

CLH-O-0000001412-86-112/F

Adopted
3 June 2016

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON 4-TERT-BUTYLPHENOL

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: **4-tert-butylphenol**
EC number: **202-679-0**
CAS number: **98-54-4**
Dossier submitter: **Norway**

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
08.01.2016	United Kingdom		Individual	1
Comment received				
The classification proposal is entirely based around the results from the unpublished study by Krueger (p18). This seems to be inappropriate as the results from this study do not appear to be sufficiently reliable for this purpose.				
Dossier Submitter's Response				
The data from this study are available at ECHAs website as a part of the registration dossier. This study (Endocrine effects study with fish (draft OECD ext. ELS test) was required and the protocol discussed under the 793/93 regulation, cfr. Commission regulation 506/2007/EC. Furthermore, the registrant has permitted that we use these data for our proposal.				
RAC's response				
RAC agrees with the Dossier Submitter's view that the Krueger et al. (2008) study available on the ECHA dissemination webpage is appropriate for assessing potential long-term toxicity in the environment. The REACH registrants have given this study a reliability score of 1 (reliable without restriction).				

Date	Country	Organisation	Type of Organisation	Comment number
05.01.2016	Germany		MemberState	2
Comment received				
The German CA supports the Norwegian classification proposal of 4-tert-butylphenol as aquatic chronic 1 with an M-factor of 1. In Part B, section 1.3, table 9 of the CLH report a boiling point of 237.5 °C and a flash point (open cup) of about 115 °C is stated. Please clarify why the boiling point is higher than the flash point. The relative density was determined at 110 °C. The melting point of the solid was stated				

to be about 100 °C. Thus, the density was determined for the melted substance. It would be however favourable to have the density of the substance in its state at 20 °C and 101.3 kPa. This is also valid for the viscosity.

For the water solubility three values were given. All determined at 25 °C. These values differ significantly from each other. Please indicate which of the values is the most reliable one.

Dossier Submitter's Response

Thank you for your support.

We do not fully understand your comment on the flash point versus the boiling point. The data on the boiling point is also published in the registration on ECHAs webpage. The data on the flash point is from Huels and Marl and are not published. A higher boiling point than the flash point is reported for several substances, such as ethanol (flash point 13 °C boiling point 78 °C).

It is correct that the relative density and viscosity are determined for the melted substance. However, we do not have access to other data on these parameters than those from Huels AG Marl (A), 1992.

The key study on the water solubility from registration on ECHAs webpage, as accessed on 3rd February 2016, reports 0.61 g/l. This data is also cited in our proposal and were obtained from the SIDS, SIAP, 2000, the test was performed according to OECD TG 105. We consider this value the most reliable.

RAC's response

RAC notes the additional information provided by the DS, although this does not affect the proposal.

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
08.01.2016	United Kingdom		MemberState	3

Comment received

Please can the authors clarify if the substance is considered rapidly degradable or not rapidly degradable for the purpose of classification. While this would not change the Aquatic Chronic 1 proposal, it has implications for the M-factor.

Please can the authors clarify if endpoints from the Krueger et al. (2008) study are based on nominal or mean measured concentrations. If the former, please can they clarify if measured concentrations were within 20% of nominal values.

We feel the chronic toxicity to invertebrate information should be included or summarised in the CLH report to confirm relative chronic toxicity.

The extended chronic fish study [Krueger et al. (2008)] includes standard endpoints relevant to classification e.g. NOECs for time to hatch and growth rate. We feel standard OECD 210 endpoints using a standard OECD 210 test species, should also be presented for the standard test guideline duration to allow a consistent approach to classification across substances. Based on the information provided in the CLH report, we do not think it is possible to conclude on the relevance of potential endocrine disruption (ED) effects in this study either in relation to population level impacts or the hazard classification of 4-tert butyl phenol (see RAC-35 triadimenol discussion of application of ED data for

classification). In addition, we note it is unclear if the tested species is relevant for the extended duration and ED effects.
Dossier Submitter's Response
Thank you for your comments. The data on degradability are presented in chapter 5.1.2 and discussed in chapter 5.1.3. It is our opinion that the results are conflicting, however we consider the substance rapidly biodegradable without meeting the 10-day window. We have therefore not proposed a higher M-factor. The nominal as well as the measured doses in the Krueger et al. (2008) study are presented in chapter 5.4.1.2 of the proposal. There is no available data on chronic toxicity in invertebrates. The extended chronic fish study [Krueger et al. (2008)] on endocrine effects in fish was required and the protocol discussed under the 793/93 regulation, cfr. Commission regulation 506/2007/EC. OECD 210 test guideline refers to Fathead minnow as one of the fish species recommended for testing. Furthermore, the reported endpoints used for our proposal are covered by the updated OECD testguideline 210, adopted on 26 July 2013; paragraph 34. The most sensitive endpoints from the Krueger-study were reduced growth, reduction in secondary male sex characteristics, and the delay in the time to hatch.
RAC's response
The information and discussion are reflected in the opinion document. RAC agrees with the DS's proposal to consider ptBP as rapidly degradable based on all the available data provided on degradation.

Date	Country	Organisation	Type of Organisation	Comment number
08.01.2016	United Kingdom		Individual	4
Comment received				
The study summary for the critical study used, the Krueger long term fish study, is light on detail. As an unpublished study it is not possible for an independent reviewer to check the details provided or to seek our more information to check if it supports the conclusions presented. The following points were noted from what was presented in the consultation document: • No indication as to whether the study was carried out to GLP. A guideline study from 2008 ought to be carried out to such standards. • The No effect level as reported falls between the bottom two doses. No effects were seen at 1ug/l and effects reported at 30ug/l. The difference between these two doses is a massive 30x – much greater than the gaps between the other dose levels and greater than would normally be used in a study used for REACH registration purposes. It makes interpolation to determine a 'true' no effect level subject to significant error (see also next point). • The lowest two doses are 1 and 30ug/l respectively. The NOAEC reported is 10ug/l, yet there is no information provided on how this is derived. The statistical method used to derive the NOAEC should be reported along with the uncertainty of the derived value. • The critical effects were reported to be small but statistically significant treatment related effects on growth and secondary sex characteristics. However, no numerical data				

is presented so it is not possible to make an independent assessment of whether these small changes are biologically significant.

The long term study in fish is the only long term study presented. (There is an endocrine disruption fish 28-day study presented, but the doses used were relatively high and the study does not provide any useful contribution towards a discussion on classification.)
However, there are multiple acute studies available – two in fish and one each in daphnia and algae. These consistently show LD/EC50 values in the range 2.5 to 5mg/l.
When discussing the classification of a substance, all relevant data should be taken into account when arriving at a decision rather than focussing on a single study. This is particularly the case if the single study produces a result that is borderline between classification categories. In this case, the Krueger study produced a reported NOEC of 10ug/l, which is borderline between aquatic chronic category 1 and 2 classification.
Bearing in mind that this NOEC has a significant degree of uncertainty involved in its derivation and that it is from a study of much longer duration than standard guideline, it should be used a part of a weight of evidence approach using all other aquatic toxicity data. The four acute studies clearly lead to a conclusion of aquatic chronic 2.
A critique of the overall data available and its reliability should lead to the conclusion that a classification of aquatic chronic 2 is most appropriate.

Dossier Submitter's Response

Thank you for your comments.

As stated in part 5.4.1.2, these data are provided by the registrant. Further details from this study are presented in the registration dossier for this substance which is available on ECHAs webpages. The registrant scores this study with reliability 1 (reliable without restriction). We support this scoring.

The lowest tested dose is 10 ug/l, not 1 ug/l. We apologize for the typing error concerning the doses, as described in part 5.4.1.2 in the proposal under the heading "Doses, vehicle, duration" in the long-term toxicity to fish test.

We present results from two long term fish toxicity in part 5.4.1.2 in the proposal. The study by Barse et al. 2006 has a higher LOEC than the study by Krueger et al.

Data on aquatic toxicity in Daphnia and algae are presented in part 5.4.2 and 5.4.3 of the proposal.

We do not support the suggestion that the studies lead to a conclusion of aquatic chronic 2. We have presented all available aquatic toxicity data and used a weight of evidence approach.

RAC's response

RAC notes the additional explanation provided by the DS. The information and discussion are reflected in the opinion document. RAC is of the opinion that ptBP warrants classification as Aquatic Chronic 1, M=1 as proposed by the DS.

Date	Country	Organisation	Type of Organisation	Comment number
05.01.2016	Finland		MemberState	5
Comment received				
We support the proposed classification for environmental hazards Aquatic Chronic 1 – with M-factor of 1 for 4-tert-butylphenol.				
Dossier Submitter's Response				

Thank you for your support.
RAC's response
RAC agrees with classification as Aquatic Chronic 1, M=1.

Date	Country	Organisation	Type of Organisation	Comment number
04.12.2015	United States	Sasol Germany GmbH	BehalfOfAnOrganisation	6
Comment received				
Sasol Germany GmbH as the lead registrant for 4-tert-butylphenol supports the proposed Aquatic Chronic 1, H410 (M-factor=1) classification. An agreement to use this classification was reached in the REACH registration consortium and the current dossier reflects the classification.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
RAC agrees with classification as Aquatic Chronic 1, M=1.				

Date	Country	Organisation	Type of Organisation	Comment number
11.12.2015	France		MemberState	7
Comment received				
FR MSCA supports the proposal of classification of 4-tert butylphenol as Aquatic Chronic 1, H410. However, a clarification about biodegradation is needed to define accurately M factor. 1. Abiotic biodegradation data are missing to assess the persistent behaviour of the substance 2. Clarifications are needed in section 5.1.2.1.: there are missing data and information about MITI, OECD 301B, OECD 302 C and EU Method C.4.A (Determination of the "Ready" Biodegradability – Dissolved Organic Carbon (DOC) Die-Away Test) tests. 3. There is inconsistency of conclusion on biodegradability of 4-tert butylphenol between section 5.1.3. (considered as rapidly biodegradable) and section 5.5. (not considered as rapidly biodegradable). Please, some clarifications are needed because it will modify the M factor. If substance is considered as rapidly biodegradable, M factor will be 1. Otherwise, it will be 10 in worst case (non-rapidly biodegradable).				
Dossier Submitter's Response				
Thank you for your support. There is no data available to us on abiotic degradation of 4-tert butylphenol. We have no further details on the MITI, OECD 301B, OECD 302 C and EU Method C.4.A (Determination of the "Ready" Biodegradability – Dissolved Organic Carbon (DOC) Die-Away Test) tests, and therefore do not base our proposal on results from these studies. We agree that there are conflicting results on the biodegradation of 4-tert butylphenol, and address this in part 5.1.3 of the proposal. We apologise for the typing error in part 5.5: "(…) ptBP is not considered as rapidly biodegradable without meeting the 10 day window." The word "not" should be deleted from the sentence.				
RAC's response				
Noted. The information and discussion are reflected in the opinion document.				