Committee for Risk Assessment

RAC

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

3 June 2016

CLH-O-0000001412-86-112/F

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: **4-tert-butylphenol**

EC Number: **202-679-0**

CAS Number: **98-54-4**

The proposal was submitted by **Norway** and received by RAC on **26 October 2015.**

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

PROCESS FOR ADOPTION OF THE OPINION

Norway 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 **24 November 2015**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **8 January 2016**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Stephen Dungey**

Co-Rapporteur, appointed by RAC: **Anja Menard Srpčič**

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 **3 June 2016** 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	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	604-090-00-8	4-tert-butylphenol	202-679-0	98-54-4	Repr. 2 Skin Irrit. 2 Eye Dam. 1	H361f H315 H318	GHS08 GHS05 Dgr	H361f H315 H318			
Dossier submitters proposal	604-090-00-8	4-tert-butylphenol	202-679-0	98-54-4	**Add** Aquatic Chronic 1	**Add** H410	**Add** GHS09	**Add** H410		**Add** M=1	
RAC opinion	604-090-00-8	4-tert-butylphenol	202-679-0	98-54-4	**Add** Aquatic Chronic 1	**Add** H410	**Add** GHS09	**Add** H410		**Add** M=1	
Resulting Annex VI entry if agreed by COM	604-090-00-8	4-tert-butylphenol	202-679-0	98-54-4	Repr. 2 Skin Irrit. 2 Eye Dam. 1 Aquatic Chronic 1	H361f H315 H318 H410	GHS08 GHS05 GHS09 Dgr	H361f H315 H318 H410		M=1	

GROUNDS FOR ADOPTION OF THE OPINION

ENVIRONMENTAL HAZARD ASSESSMENT

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

4-*tert*-Butylphenol (ptBP) is currently listed in Annex VI of the CLP Regulation (EC) 1272/2008 but without any classification for environmental hazards. The Dossier Submitter (DS) proposed to classify the substance as Aquatic Chronic 1 - H410 (M=1) based on rapid degradation and a chronic NOEC of 0.01 mg/L in fish.

Degradation

ptBP is stable under visible light irradiation (Xiao *et al.*, 2014). No further information about abiotic degradation is provided by the DS.

Conflicting biodegradability results are available. An inherent MITI II test (MITI, 1992) (equivalent to OECD TG 302C) reported no biodegradation after 14 days in a test system inoculated with 100 mg/L of mixed sludge and 30 mg/L of ptBP. A ready biodegradation study conducted according to OECD TG 301F (Manometric Respirometry Test) (NIVA, 2003b) using non-adapted inoculum from an in-house activated sludge simulation unit indicated 60 % and 42 % degradation after 28 days for 15 and 25 mg/L ptBP, respectively. Failure to meet the 10-day window criterion means that ptBP was not readily biodegradable in this study. However, ptBP is toxic to micro-organisms at concentrations ≥ 25 mg/L, so the slower rates of degradation in these two studies can be ignored. A lag phase was also evident in the Niva (2003b) study, implying that for the lower test concentration of 15 mg/L micro-organisms need an adaptation period in order to be able to degrade ptBP rapidly.

The DS refers to additional studies on ECHA's dissemination page by the REACH Registrants but does not provide any details. For completeness, they are:

- A second ready test conducted according to OECD TG 301B (CO_2 Evolution Test), showing around 60% degradation after 28 days at 5 and 10 mg C/L. Failure to meet the 10-day window criterion indicates that ptBP was not readily biodegradable in this study.
- A third ready test conducted according to OECD TG 301A (Dissolved Organic Carbon (DOC) Die-Away test) used non-adapted inoculum derived from activated sludge from a domestic sewage plant. The DOC removal was found to be 98 % after 28 days at 13 mg/L ptBP (corresponding to 10.4 mg DOC/L). The robust study summary (RSS) states that ptBP was readily biodegradable, meeting the 10-day window criterion, although this cannot be explicitly determined from the information presented. Further details of this study are given under Supplemental Information.

The DS also summarised monitoring evidence from sewage treatment plants (STPs). Scharf and Sattelberger (1999) reported ptBP removal rates of between 3 and 53 % in 17 Austrian STPs. STP monitoring data presented in the EU Risk Assessment Report for ptBP (EC, 2008) under Regulation (EC) 793/93 were also claimed to have indicated 35-45 % degradation of ptBP under

'normal conditions' (although RAC cannot find this information in the original source). Further consideration of these data is given under Supplemental Information.

The DS concluded that the weight of evidence supports characterization of ptBP as »rapidly biodegradable, but not fulfilling the 10 day window criterion«.

Bioaccumulation

The measured octanol-water partition coefficient (log Kow) of ptBP is in the range 2.4 – 3.3. Freitag *et al.* (1984) studied the bioaccumulation of ptBP in golden orfe (*Leuciscus idus melanotus*) after three days of exposure. The measured bioconcentration factor from this study was 120 L/kg. No information is provided about the time to steady state or lipid content of the fish.

Aquatic toxicity

Aquatic toxicity data are available for all three trophic levels. In the following table, a summary of the relevant information from aquatic toxicity studies is reported (the key endpoint used in long-term hazard classification is highlighted in bold).

Table 1: Summary of relevant information on aquatic toxicity

Method	**Test organism**	**Endpoint**	**Toxicity values in mg a.s./L**	**Reference**
Short-term toxicity to fish				
Standard Methods for the Examination of Water and Wastewater, 16th ed. American Public health Association, Washington DC, 1985	*Pimephales promelas*	96-h EC_{50} (deformities)	5.14	Holcombe *et al.*, 1984
n.a.	*Cyprinus carpio*	96-h LC_{50}	6.9	Barse *et al.*, 2006
Long-term toxicity to fish				
OECD TG 210, extended	*Pimephales promelas*	**128-d NOEC** (growth rate, secondary sexual characteristics and time to hatch)	**0.0096**	Krueger *et al.*, 2008
n.a.	*Cyprinus carpio*	28-d EC_{50} (endocrine disruption, metabolic change)	0.69	Barse *et al.*, 2006
Toxicity to aquatic invertebrates				
DIN 38412, Part II	*Daphnia magna*	48-h EC_{50} (immobilisation)	3.9	Kühn *et al.*, 1989
Toxicity to algae				
OECD TG 201	*Selenastrum capricornutum* (now known as *Raphidocelis* (or *Pseudokirchneriella*) *subcapitata*)	72-h IC_{50} 72-h NOEC (growth inhibition)	14 0.32	NIVA, 2001a
n.a. – data not available				

Two acute and two chronic aquatic toxicity tests on fish are available, the lowest values being obtained in fathead minnow (*Pimephales promelas*). In the acute toxicity study, the 96-h LC_{50} was 5.14 mg a.s./L. The long-term OECD TG 210 (extended) fish toxicity study provided a 128-day NOEC of 0.01 mg/L (nominal), based on growth rate, secondary sexual characteristics and time to hatch. The 128-d LOEC was 0.03 mg/L (nominal). According to the RSS from the registration dossier on ECHA's dissemination page, the NOEC would be 0.0096 mg/L based on mean measured concentrations. The DS reports different measured concentrations, citing 0.002 mg/L for the NOEC (but incorrectly reporting the equivalent nominal concentration as 0.001 mg/L). RAC prefers to use the information from the registration dossier, so the NOEC is taken to be 0.0096 mg/L.

Comments received during public consultation

Four Member State Competent Authorities (MSCAs), one individual and one company commented on the proposed environmental hazard classification. Three MSCAs and the company agreed with the classification proposal, with it also being indicated that the proposed environmental hazard classification was also agreed upon in the REACH consortium.

Two MSCAs asked for clarifications about the degradability conclusion, one of these MSCAs also requested further details about the chronic aquatic toxicity.

One individual proposed classification as Aquatic Chronic 2 based on multiple acute studies available in the CLH report and the fact that the chronic fish study produced a nominal NOEC that is borderline between classification categories (concerns about wide concentration intervals in this study were misplaced because of a typographical error in the original dossier). They were also concerned about the lack of detail in the unpublished chronic fathead minnow study, although the DS pointed out that the information was already included in the REACH registrations with a reliability score of 1 (reliable without restriction).

Assessment and comparison with the classification criteria

Degradation

The DOC Die-Away Test (equivalent to OECD TG 301A) shows degradation of 98 % (DOC decrease) after 28 days and > 70 % within 10 days after the time at which the degradation reached 10 %. ptBP is readily biodegradable based on these results. RAC reviewed the available information for this test (see Supplemental information) and considered it reliable for the purposes of classification. ptBP was significantly degraded (60 % after 28 days) in two additional ready biodegradation tests (OECD TG 301B and OECD TG 301F) but failed to meet the 10-day window (i.e. there was a lag phase). As a result, ready biodegradability cannot be determined from those studies. Nevertheless, these studies indicate that ptBP has the potential to mineralise, with the more extensive degradation measured in the OECD TG 301A study (98% after 28 days) presumably reflecting the presence of competent degraders in this particular test (it is well known that the outcome of ready tests can be limited by compromised microbial diversity (see for example Kowalczyk *et al*., 2015)).

The OECD TG 301A study reportedly used an unusually high level of ammonium chloride (NH_4Cl) in the mineral medium. No explanation is provided in the RSS, but although this might be a transcription error, RAC cannot check because the original study report is not available for review. As NH_4Cl is also a nutrient, a high level could have influenced microbial growth, although it is not known whether this would have affected the biodegradability of the substance. There might possibly have been an effect on pH, but this was not measured (the pH was not intentionally

adjusted according to the RSS). The pKa of ptBP is estimated to be above 10 in the REACH registration dossier, indicating that it is not ionised in the normal envirnmental pH range. Changes in pH might therefore affect microbial growth but are unlikely to affect the bioavailability of the substance. For comparison, the pH in the OECD TG 301B and 301F studies was 7.5-7.6 (determined at test termination) and not measured, respectively.

On balance, the influence of the ammonium chloride concentration remains uncertain but is not considered to invalidate the study.

RAC has decided that no firm conclusions regarding biodegradability can be drawn from WWTP (Waste Water Treatment Plant) monitoring studies (see Supplemental information). The results of QSAR modelling performed by RAC are borderline with respect to ready biodegradation (see Supplemental information).

The Guidance on the Application of the CLP Criteria Version 4.1, June 2015, paragraph II.3.5., page 568 gives the following advice: "In general, conflicting results for a substance which has been tested several times with an appropriate biodegradability test could be interpreted by a 'weight of evidence approach'. This implies that if both positive (i.e. higher degradation than the pass level) and negative results have been obtained for a substance in ready biodegradability tests, then the data of the highest quality and the best documentation should be used for determining the ready biodegradability of the substance. However, positive results in ready biodegradability tests could be considered valid, irrespective of negative results, when the scientific quality is good and the test conditions are well documented, i.e. guideline criteria are fulfilled, including the use of non-pre-exposed (non-adapted) inoculum."

Taking into account all available data on degradability (including the result of the DOC Die-Away test) and the CLP guidance, ptBP can be considered as a rapidly degradable substance in the environment.

Bioaccumulation

RAC agrees that ptBP has a low potential to bioaccumulate based on a log K_{ow} value of <4 and measured fish BCF value of 120 L/kg. The measured BCF value is less than the threshold of 500 L/kg in the CLP Regulation.

Aquatic toxicity

Acute*:*

Short-term aquatic toxicity data are available for all three trophic levels, and the L(E)C_{50}s are all above 1 mg/L. The substance therefore **does not require classification for acute aquatic toxicity**.

Chronic*:*

Long-term aquatic toxicity data are available for fish and algae. There are no long-term data for aquatic invertebrates, but the conclusion about rapid degradability and bioaccumulation potential mean that the surrogate method does not need to be applied for this trophic group. The lowest result is a 128-d NOEC of 0.0096 mg/L (mean measured concentration) for the fathead minnow *Pimephales promelas*. As this concentration is below the threshold value of 0.01 mg/L for rapidly degradable substances, RAC concludes that classification as **Aquatic Chronic 1 (H410)** is warrented. As the NOEC value is in the range 0.001 < NOEC ≤ 0.01 mg/L, the chronic **M-factor is 1** for rapidly degradable substances (CLP, Annex I, Table 4.1.3), as proposed by the DS and agreed on by the REACH registrants.

Note: Following the public consultation, RAC became aware of a 28-d semi-static ecotoxicity study with juvenile fish (Pikeperch or Zander *Sander lucioperca*) (Demska-Zakęs. 2005). Significant (irreversible) changes in sex ratio were reported at the lowest test concentration of

0.001 mg/L (nominal). RAC has not evaluated this study, but notes that it supports classification as Aquatic Chronic 1 (see Supplemental Information in the Background Document). If the study were satisfactorily validated, it might influence the M-factor (increasing it by a factor of 10, since it implies a NOEC below 0.001 mg/L).

Additional references

Additional references not included in the CLH report

Demska-Zakęs K. (2005). Effect of select xenobiotics on the development of the fish reproductive system. Dissertations and monographs UWM Olsztyn 103: 1–61 [in Polish].

Hüls AG (1994): EITHER Report No. DDA-59, unpublished OR Report No. SK-94/14, unpublished, as cited in the Reference List for EC (2008).

Kowalczyk A, Martin T J, Price O R, Snape J R, van Egmond R A, Finnegan C J, Schäfer H, Davenport R J & Bending G D (2015). Refinement of biodegradation tests methodologies and the proposed utility of new microbial ecology techniques. Ecotoxicology and Environmental Safety, 111, 9–22.

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 by RAC (excluding confidential information).