Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

4-tert-butylbenzoic acid

ECHA/RAC/CLH-O-0000001579-64-01/A2

Adopted

21 February 2011

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

[ECHA has compiled the comments received via internet that refer to several hazard classes and entered them under each of the relevant categories/headings as comprehensive as possible. Please note that some of the comments might occur under several headings when splitting the given information is not reasonable.]

Substance name: 4-tert-butylbenzoic acid
CAS number: 98-73-7
EC number: 202-696-3

General comments

Date	Country/ Person/Organisation/ MSCA	Comment	Response	Rapporteur's comment
16/07/2010	France / Elodie Pasquier / MS	The recommendations agreed at the TC C&L regarding the classification of 4-tert-butylbenzoic acid for health effects are supported in absence of any new study since the TC C&L discussions and in agreement with the classification proposed in the CLH report. It is noted that a proposal N; R51-53 was included in the proposal submitted at ECB in March 2007 although this endpoint has not been discussed and concluded by the TC C&L. No information is included in the CLH report on self classification by industry for environment. In case of disagreement, environment should also be included in the proposal for harmonisation of classification to be discussed by the RAC.	At the moment, no data of different self classification by industry are available. Hence, a harmonised classification according to Article 36 (3) CLP Regulation is not justified. After publication of the C&L Inventory the possibility of harmonised classification for environment will be reconsidered.	Noted. It is left up to the submitting MS to decide if they want to propose classification for more than the harmonized effects for the leftovers (i.e. the substances with harmonised classifications already agreed by the Technical Committee for Classification and Labelling but not included in Annex VI of Regulation (EC) No 1272/2008).
19/08/2010	Sweden / MS	Sweden supports the agreement, on the proposed classification and Labelling, taken by the Technical Committee on Classification and Labelling (Directive 67/548/EEC) ('TC C&L') between 2005 and 2007.	Thank you for the support.	Noted.
19/08/2010	UK / Helen McGarry / MS	From the justification on page 27 it appears that a classification for this substance was previously agreed by the TC C&L. It would be helpful to explain that this is a 'transition' substance in a 'Background to the proposal' section at the beginning of the report, and also to state whether the information presented in the report is the same	Thank you for the information which was considered in the report on page 27 (Justification that action is required on a community-wide basis)	Agree with comment from UK that this should be explained early in the report. The report is amended accordingly.

Date	Country/ Person/Organisation/ MSCA	Comment	Response	Rapporteur's comment
		as that considered by the TC C&L in 2007.		

Carcinogenicity

Date	Country/ Person/Organisation/ MSCA	Comment	Response	Rapporteur's comment

Mutagenicity

Date	Country/ Person/Organisation/ MSCA	Comment	Response	Rapporteur's comment

Toxicity to reproduction

Date	Country/ Person/Organisation/ MSCA	Comment	Response	Rapporteur's comment
23/07/2010	Denmark / MS	As the classifications were agreed September 2007 in the TC C&L group, Denmark supports the proposal for the classification. No further data or information is submitted.	Thank you for the support.	Noted.
19/08/2010	UK / Helen McGarry / MS	Page 26. We support the proposed classification of Repr. 1B – H360F / Repr. Cat. 2; R60.	Thank you for the support.	Noted.

Respiratory sensitisation

Date	Country/ Person/Organisation/ MSCA	Comment	Response	Rapporteur's comment

Other hazards and endpoints

Date	Country/ Person/Organisation/ MSCA	Comment	Response	Rapporteur's comment
23/07/2010	Denmark / MS	As the classifications were agreed September 2007 in the TC C&L group, Denmark supports the proposal for the classification. No further data or information is submitted.	Thank you for the support.	Noted.
19/08/2010	UK / Helen McGarry / MS	Page 8. Acute oral toxicity. A consistent set of LD50 values, of between 550 mg/kg and 800 mg/kg, was obtained in rats and mice. We support the proposal to classify as Acute Tox. 4 – H302 / Xn; R22. Page 13. For consistency, should p-tert butyl benzoic acid in the first paragraph read 4-tert butylbenzoic acid? Page 18. Repeated dose toxicity: oral. Since there were deaths in male and female animals from 21 mg/kg/d, 4-tert-butylbenzoic clearly meets the criteria for classification for repeated dose toxicity. The question to consider, then, is which category is the more appropriate. The RMS has selected the renal necrosis and atrophy of the testes (both of which occurred from 6 mg/kg/d) as the critical effects on which classification is based. The testes' effects are covered by the proposed classification for fertility, so for repeated-dose toxicity, the focus should be on the renal necrosis. If the data is available, the inclusion of information on incidences and severity of the kidney effects would be helpful in evaluating the data. The dose of 6 mg/kg/d is below the cut-off for Category 1 in the CLP Regulation and so supports this classification. However, this dose is just above the cut-off of 5 mg/kg/d for T; R48/25, and so if the guidance values of Directive 67/548/EEC are applied strictly, Xn; R48/22 would apply. The statement that 'The same holds true for T; R48/25. 6 mg/kg/d is about 10-fold lower than the critical dose for Xn; R48/22' should therefore be clarified.	now page 7: Registered. now page 12: Amended. now page 17: Repeated dose toxicity: oral. Information on incidences and severity of the kidney effects were added. See the revised CLH-Report on page 11. The reason for classification/labelling was specified (see page 17).	Noted. Noted. Noted. RDT Oral: The seemingly deviating cut-off values between CLP and DSD is now described in the CLH report. In our opinion the data warrant classification as STOT RE-1 (CLP) as well as T; R48/25 (DSD). RDT Inhalation: We do not support this adjusting of the 90-day guidance values to a 10/11 day

Date	Country/ Person/Organisation/ MSCA	Comment	Response	Rapporteur's comment
		Page 18. The upper limit for CLP Category 1 is ≤ 10 mg/kg/d, not ≤ 20 mg/kg/d, as stated. Page 18. Repeated dose toxicity: inhalation. In the 10/11 day study, severe toxicity was recorded from 0.1 mg/L, including: deaths of 3/16 animals; kidney lesions; lesions of the central nervous system associated with paraplegia. These effects are more severe than the decreased arousal activity at 0.0047 mg/L in the 28-day study on which the proposed classification is based. Whilst it is not ideal to adjust the 90-day guidance values to a 10/11 day study, doing so gives values of approximately 0.16 mg/L (CLP) / 0.2 mg/L (Directive 67/548/EEC) for an 11-day study. Therefore classification for STOT-RE Category 1 / T; R48/23 is supported. Page 18. Repeated-dose toxicity: dermal. The proposed classification is based on the testicular effects observed in a 28-day study. However, such effects are considered to be a specific effect on the reproductive organs and so should be considered for classification under reproductive toxicity rather than repeated dose toxicity. Classification is possibly indicated based on significant toxicity in the 7/13 week study from 70 / 17.5 mg/kg/d: liver cell vacuolation in female rats which was associated with signs of altered renal function, together with indications of altered hepatic function; erythrocytic microcytosis; but it would be helpful to include information on incidences and magnitudes. Also, the argument that, because the criteria for STOT-RE Category 1 are fulfilled, the substance should also be classified as T; R48/24 is not sufficient: under Directive 67/548/EEC, the cut-off guidance value for this classification is ≤ 10 mg/kg/d.	now page 17: Amended. now page 17. Repeated dose toxicity: inhalation. Data from the 10/11 day study were added (see page 17). At the TC NES IV '07 the classification by the dermal route was discussed repeatedly. Whilst some of the values from the dermal toxicity studies showed effects higher than the cut-off value of 10 mg/kg bw/day for classification as T; R48/24, there are effects on reproductive toxicity at levels of 7 mg/kg bw/day. DE considered that taking the database as a whole, a consistent classification between the three routes of exposure is preferred. To this proposal it was agreed at the	study. Data on toxicokinetics, metabolism and distribution of 4-tert-butylbenzoic acid after (oral, dermal and) inhalative uptake in animals and humans are not available. If the substance is efficiently eliminated, using Haber´s rule might be irrelevant. Another point is the quality of the study, which is unpublished (Shell, 1982b). No Klimisch Index is available. In the pre-BD page 15 it is stated one of the findings was white powder on the animals´ haircoat. This may indicate that the substance deposited on the fur during the whole body exposure. The animals could then receive an additional dose from dermal uptake and by grooming/licking the fur. In several trading catalogues the colour of this substance is stated as white. We think this deposition is the main reason for not putting so much weight on this study, but only see it as supportive. RDT dermal: Agree with dossier submitter that a consistent classification

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		Page 19. Repeated dose toxicity: conclusion. The information from oral and inhalation studies, in which serious effects occurred below the cut-off values for category 1 for these exposure routes, supports classification for STOT-RE Category 1. A classification of T; R48/23 is also supported. However, the data and arguments do not fully support a classification of T; R48/24/25 and consideration should be given to whether Xn; R48/21/22 would be more appropriate.	TEC NES without discussion. 4-tert-butybenzoic acid is a 'TC C&L agreed' substance. No further data or relevant information was submitted for 4-tert-butylbenzoic acid since the TC C&L made its recommendations. In order for those substances agreed at TC C&L to be included in Annex VI of the CLP Regulation, they must be processed through the Committee for Risk Assessment (RAC). RAC has informed about the procedure, to support the full utilisation of previous work from TC C&L and to focus its discussion on the impact of any new data has emerged since the TC C&L made its recommendations.	between the three routes of exposure is preferred. RDT conclusion: Agree to keep TC C&L conclusion on RDT classification.