ECHA
EUROPEAN CHEMICALS AGENCY

Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

Tetrakis(2,6-dimethylphenyl)-m-phenylene biphosphate

EC number: 432-770-2

CAS number: 139189-30-3

ECHA/RAC/CLH-O-0000002526-74-03/A2

Adopted

30 November 2012

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON TETRAKIS(2,6-DIMETHYLPHENYL)-M-PHENYLENE BIPHOSPHATE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

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

Substance name: Tetrakis(2,6-dimethylphenyl)-m-phenylene biphosphate
EC number: 432-770-2
CAS number: 139189-30-3
Dossier submitter: United Kingdom

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
25/06/2012	Norway		MSCA	1
Comment received				
Considering the present proposal, we agree with the need to revise the harmonised classification & labelling for tetrakis(2,6-dimethylphenyl)-m-phenylene biphosphate. The data as presented in the submitted CLH dossier support the declassification from R53 (according to DSD) or Aquatic Chronic 4, H413 (according to CLP) to no classification for the environment.				
Dossier Submitter's Response				
Thank you for your comment.				
RAC's response				
Noted, please see also response to comments from Germany				

Date	Country	Organisation	Type of Organisation	Comment number
28/06/2012	France		MSCA	2
Comment received				
We agree with the classification proposal.				
Dossier Submitter's Response				
Thank you for your comment.				
RAC's response				
Noted, please see also response to comments from Germany				

CARCINOGENICITY: no comments received
MUTAGENICITY: no comments received
TOXICITY TO REPRODUCTION: no comments received
RESPIRATORY SENSITISATION: no comments received

OTHER HAZARDS AND ENDPOINTS

Aquatic environment

Date	Country	Organisation	Type of Organisation	Comment number
25/06/2012	Belgium		MSCA	3
Comment received				
We support the proposal of the UK CA to remove the classification with Aquatic chronic 4, H314. The substance is poorly soluble in water, shows low potential to bioaccumulate and no toxicity was seen at water solubility levels.				
Dossier Submitter's Response				
Thank you for your comment.				
RAC's response				

Noted, please see also response to comments from Germany

Date	Country	Organisation	Type of Organisation	Comment number
25/06/2012	Germany		MSCA	4

Comment received

p.31 the conclusion on aquatic bioaccumulation:
The estimated log Pow of 11.79 is not reliable because insufficient measured data for log Pow > 9 are within the training dataset of the used QSAR (US EPA KOWWIN v1.67 of EPI Suite v4). As the estimated log Pow is not reliable the BCF estimation based on the unreliable log Pow using the QSAR BCFBAF v 3.2 (of US EPA On-Line EPI Suite™ v4.0) subsequently is not reliable.
The results of the second used QSAR (CAESAR database) is not sufficient reliable because the similartities of the compounds (0.76 – 0.557) identified in the CAESAR database are not high enough (good similarity > 0.85).
The available experimental BCF-values are not reliable because the used test concentrations (1mg/l, 0.1 mg/l) exceed the water solubility of the substance (< 0.1 mg/l). Consequently, the formation of microcrystals can not be ruled out. These microcrystals can not be taken up over gills and may lead to an underestimation of the BCF.
Considering that the estimated log Pow as well as the estimated and measured BCFs are not reliable, the assessment of the bioaccumulation should be based on the measured log Pow of > 6.2. Therefore the substance should be considered as bioaccumulative and the existing classification should not be removed.
Furthermore, it should be mentioned that a log Pow > 10 sufficiently indicate that the BCF of a substance is < 2000. But it does not sufficiently indicate that the BCF of a substance is < 500 (see: Nendza, M. & Müller, M.,2010. Screening for low aquatic bioaccumulation (1): Lipinski's "Rule of five" and molecular size. SAR and QSAR in Environmental Research, 21, 495-512.).

Dossier Submitter's Response

Thank you for this response. The properties of the substance make reliable quantitative assessment very difficult. It has been noted in the dossier that the measured BCF data are flawed for assessment of the classification as the presence of dispersive agent is considered to affect potential uptake of the substance in the test species, thereby reducing the reliability of the data. It is further noted that existing test methods will not allow for reliable measurement of log Pow above 8 and the limitation of suitable measurement techniques of partition coefficient means that assessment cannot be conducted quantitatively. The measured limit value of 6.2 can be considered suitable as an indicator for further assessment. Nevertheless, for compounds having log Pow greater than 6, a gradual decrease of the BCF is observed and it has been hypothesised within the published literature that a high log Pow is more an effect of solubility than a tendency of the substance to be lipophilic and the substance cannot be considered to be vB.

The reduced reliability of each data endpoint is suitable for quantitative assessment, as noted in ECHA guidance documents Chapter R. 11 and Part C. PBT Assessment. At very high log Kow (>6), a decreasing relationship between the two parameters is typically observed. Given that none of the models have experimental information in this range, more than one model should be used to estimate the Kow value. In order to undertake evaluation of the various endpoint data available an assessment of all the data, albeit with reduced individual reliability, is essential to form a conclusion.

Experimental observation of the relationship between Pow and BCF is that increasingly high Pow values tend to represent ever reducing BCF values. Assessment of the BCF measured above the limit of solubility being extremely low is consistent with and supported by the QSAR assessment available by EPIWIN and CAESAR.
The toxicity of the substance to mammalian species is also very low, achieving limit NOEL values in repeated dose toxicity in rats at the maximum applicable dose of 1000 mg/kg/day, indicating that the substance is not easily absorbed by mammalian species and further suggesting a low uptake of the substance over time. The toxicity of the aquatic species has also been assessed by acute exposure in three species and chronic exposure in Daphnia magna. The substance displays a complete lack of effect in any of these studies at the limit of water solubility achievable in the test systems.

By assessment of each of all of these factors as a whole, quantitative assessment based on a limit value of log Pow is considered not suitable for adequate assessment. The qualitative assessment of all endpoints is considered adequate to determine that the substance is not potentially bioaccumulative and should not be classified B.

RAC's response

RAC noted the limited validity of the methods and results in the experimental and calculated BCFs and concludes that this is not sufficient evidence for disregarding the bioaccumulation potential of the substance. This includes RAC's critique regarding the weakly substantiated read across to one related aryl phosphate, while consideration of further relevant substances of this group would allow a more thorough and sound read across. However, RAC considers the absence of effects in available and foreseeable aquatic toxicity tests as sufficient evidence to warrant the removal of the safety net classification Aquatic Chronic 4.

Date	Country	Organisation	Type of Organisation	Comment number
28/06/2012	Sweden		MSCA	5

Comment received

We agree that based on the data available the substance does not meet the classification criteria for aquatic hazard. The substance has been classified as Chronic IV based on high Log Kow, not readily biodegradability and lack of toxicity data. According to the criteria, the substance is classified in this category "unless other scientific evidence exists showing classification to be unnecessary. Such evidence includes chronic toxicity NOECs > water solubility or > 1 mg/l, or evidence of rapid degradation in the environment".
We find the results from the toxicity studies clearly indicating lack of toxicity in both acute and chronic exposures, which according to our interpretation of the criteria, provides the evidence for no classification.

Dossier Submitter's Response

Thank you for your comment.

RAC's response

Noted, please see also response to comments from Germany

Date	Country	Organisation	Type of Organisation	Comment number
28/06/2012	France		MSCA	6

Comment received

P. 36: Paragraph "Test conditions": Please Indicate the determination limit of the test substance.
P. 37: Paragraph "Results": Typo: Please indicate the line number in front of each line.

Dossier Submitter's Response

Thank you for your comment.
Page 36: The determination limit of the test item in the test solution was 0.000053 mg/L.
Page 37: It is our understanding that we should not update the CLH report following the public consultation. Therefore, we can not include the line numbers on page 37 as requested but can confirm that the numbers refer to lines 3 - the 21-day EC50, 4 – the 21-day LC50 and 5 – the NOEC respectively.

RAC's response

Noted

REFERENCES: None

ATTACHMENTS RECEIVED: None