Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at Community level of

tris(nonylphenyl) phosphite

ECHA/RAC/CLH-O-0000001402-87-01/F

Adopted

26 October 2010

Annankatu 18 | P.O. Box 400 | 00121 Helsinki | Finland
www.echa.eu | Tel.: + 358 9 68.61.80

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

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

Substance Name: ***tris(nonylphenyl)phosphite***

EC Number: ***247-759-6***

CAS Number: ***26523-78-4***

The proposal was submitted by ***France***
and received by RAC on ***09 February 2009***

	Directive 67/548/EEC (criteria)	CLP Regulation (EC) No 1272/2008
Current entry in Annex VI CLP Regulation	No entry (Table 3.2)	No entry (Table 3.2)
Current proposal for consideration by RAC	Xi; R43 R53	Skin Sens. 1 - H317 Aquatic Chronic 4 - H413
Resulting harmonised classification (proposed future entry in Annex VI CLP Regulation)	Xi; R43 R53	Skin Sens. 1 - H317 Aquatic Chronic 4 - H413

PROCESS FOR ADOPTION OF THE OPINION

France 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/consultations/harmonised_cl/harmon_cl_prev_cons_en.asp*** on 22 February 2010. Parties concerned and MSCAs were invited to submit comments and contributions by 08 April 2010.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: ***Hans-Christian Stolzenberg***
Co-rapporteur, appointed by RAC: ***Céu Nunes***

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

The RAC opinion on the proposed harmonised classification and labelling has been reached on ***26 October 2010,*** in accordance with Article 37(4) of the CLP Regulation, giving parties concerned the opportunity to comment. Comments received are compiled in Annex 2.

The RAC Opinion was adopted by ***consensus***.

OPINION OF RAC

The RAC adopted the opinion that ***tris(nonylphenyl)phosphite*** should be classified and labelled as follows:

Classification & Labelling in accordance with the CLP Regulation:	
Classification:	Skin Sens. 1 - H317
	Aquatic Acute 1 - H400
	Aquatic Chronic 1 - H410
Specific concentration limits:	None
M-factors:	None
Notes:	None
Labelling:	GHS07, GHS09, Wng, H317, H410

Classification & labelling in accordance with Directive 67/548/EEC			
Classification:	Xi; R43		
	N; R50/53		
Specific concentration limits:	None		
Notes:	None		
Labelling:	Xi; N	R: 43-50/53	S: 24-37-60-61

SCIENTIFIC GROUNDS FOR THE OPINION

The opinion relates only to those hazard classes that have been reviewed in the proposal for harmonised classification and labelling, as submitted by France.

TNPP is a chemical mainly used as stabiliser in the processing of various plastic and rubber products. TNPP has been assessed as entry on the 4th priority list under Existing Substances Regulation (ESR; Council Regulation (EEC) No 793/93), including consideration of harmonised classification for all endpoints as justified. A classification proposal was submitted and discussed at the Technical Committee on Classification and Labelling of the European Chemicals Bureau (ECB TC C&L) for health endpoints. Classification R43 (may cause sensitization by skin contact) was concluded by the TC C&L for health, summary records of the corresponding meetings being appended to Annex 1. No relevant new data has been identified since TC C&L discussion for health. The proposal for environmental classification was on hold as additional testing had been requested and was on-going, not being completed under ESR.

Reproductive Toxicity

RAC did not further scrutinise the information on reproductive toxicity. The dossier submitter had incorporated selected information just to supply a contingent discussion on the role of nonylphenol (NP) impurities. However, during further processing of the CLH proposal it has been clarified that NP impurities have to be dealt with according to articles 10, 11 of the CLP Regulation, but are not to be covered by the proposal for harmonised classification of TNPP. A potential classification for reproductive toxicity of TNPP was previously discussed at TC C&L (see summary records appended to Annex 1). TC C&L finally concluded no classification justified. Since then, neither the dossier submitter nor the public consultation revealed new information on reproductive toxicity of TNPP to be considered and prepared for the present CLH proposal.

Skin sensitisation

According to the guidance on the application of the CLP criteria (CLP guidance), a substance may be classified as skin sensitiser on the basis of a positive test result in one of the animal tests 1) mouse local lymph node assay (LLNA), 2) guinea pig maximisation test (GPMT) and 3) Buehler occluded patch test. The positive result in the maximisation test (more than 30% of animals with a positive reaction in an adjuvant type guinea pig test method) warrants classification with R43 (Skin Sens. 1 – H317 according to the CLP Regulation). The observed dose-response relationship, i.e. 5% intradermal induction and 75% incidence of sensitised guinea pigs, corresponds to a “moderate” potency, which is covered by the generic concentration limit of 1% according to the CLP guidance. Regarding the purity of the tested TNPP grade (> 94%), up to < 5% nonylphenol (NP) might contribute to the test results. However NP is not classified as skin sensitiser and the GPMT with technical TNPP is thus considered sufficiently valid for classification.

Classification for skin sensitisation was previously discussed at TC C&L which finally concluded classification Xi; R43 (see summary records in Appendix I of Annex 1), based on the two tests that are discussed in Annex 1 and their in-depth discussion in the context of the EU RAR. No new relevant data on TNPP have been identified since this recommendation.

During the public consultation, a comment challenged the way how available test results have been used for the final conclusion. However, this comment provided no new data or information; the conclusion as agreed by TC C&L and proposed by the dossier submitter is covered by corresponding CLP guidance.

Environmental hazards

The proposal for harmonised classification (CLH proposal) of the environmental hazards of TNPP is follow-up work from the previous regulatory regime. It was not concluded due to outstanding testing requirements. In addition, TNPP's substance properties cause significant difficulties in testing, assessing and classifying its aquatic toxicity. In absence of the Classification and Labelling Inventory that is not yet available, it is not possible to know what self-classification is applied by manufacturers and importers and if an appropriate classification for environment is applied. Setting a harmonised classification for environment is therefore justified to ensure the application of an appropriate classification.

During the process from initial submission, re-submission after the RAC accordance check, and based on a number of technical comments from its public consultation, the CLH proposal has been subject to quite a few significant revisions, and also changes of the classification proposal for the environment. The submitter's classification proposal R53 (Dir 67/548/EEC) / Aquatic Chronic 4 (CLP Regulation) raised support, argumentation for stricter as well as for no classification during the public consultation. Based on the comments, the dossier submitter again changed the proposal to R50-53 (Dir 67/548/EEC) / Aquatic Acute 1, Aquatic Chronic 1 (CLP Regulation). The present RAC opinion supports this revised proposal, based on a number of further revisions in the dossier (see Annex 1) to strengthen the proposal's justification, to address the technical comments from public consultation (see Annex 2), and to clarify the underlying key considerations.

Available data and information show that TNPP is not rapidly degradable according to the CLP criteria. Experimental key information is lacking to conclude on its bioaccumulation. However, the cut-off value of log Kow $\geq$ 4 set out in the CLP Regulation is exceeded. Due to specific physicochemical properties of TNPP, in particular its very low water solubility and a high octanol-water partitioning quotient, both yet estimated with considerable uncertainties, experimental studies testing TNPP have to be scrutinised very carefully. No ecotoxicological study provides evidence for effects directly exerted by TNPP. The key issue for an adequate classification decision relates to the role of nonylphenol (NP, [Aquatic Acute 1; H400, Aquatic Chronic 1; H410] in Annex VI to the CLP Regulation) as degradation product resulting from TNPP hydrolysis. At the same time, a range of from < 0.1% to < 5 % of NP can occur as impurity in various TNPP grades on the market; however as impurity, NP has to be considered according to articles 10, 11 of the CLP regulation, but not for the harmonised classification proposed in the present document.

Annex 1 provides details of two relevant studies on hydrolysis of TNPP, both basically analysing the formation of NP due to hydrolytic cleavage of the ester-bonds between the phosphorous and NP-moieties of TNPP. In a preliminary study roughly following OECD Test Guideline (TG) 111 at 20°C and pH 7 for 24h, no NP could be detected beyond the limit of detection (LOD) of 23 ng/L. However, the analytical method has apparently not been optimised for the tested TNPP grade with branched NP-chains, and moreover OECD TG 111 suggests conducting a preliminary study at 50°C and three pH levels (4, 7, 9) for 120h to confirm hydrolytic stability. In a second study not referring to a standard method and with no pH and temperature details reported, the tested TNPP grade included 0.75% TIPA which is

added as stabiliser e.g. against hydrolysis. Limited formation of NP resulted in increasing NP concentrations during the first 4 days, then remaining on a constant level of ca. 15 µg/L NP (accounting for ca. 0.1 % hydrolysis) until test termination after 10 days.

In an acute toxicity test with the water flea *Dapnia magna* the test solutions were prepared from a high purity grade (<0.1% free NP) TNPP stock solution, 78 hours subjected to conditions for potential hydrolysis prior to the test. In the highest treatment level (nominal 10.0 mg/L TNPP) 0.3 mg/L NP were detected, of which a maximum of 0.01 mg/L might be attributed to impurities. No NP was detected in lower treatment levels due to the relatively high LOD of 0.2 mg/L NP. The observed effects follow a concentration-response curve with an effect concentration EC50 of 0.3 mg/L TNPP (nominal). This value corresponds to an estimated NP-related EC50 = 0.009 mg/L, which is even lower than results from corresponding *Daphnia* tests with NP, reported in the EU Risk Assessment of NP as part of a comprehensive description of NP aquatic ecotoxicity.

Apart from two further studies providing limited supportive evidence as outlined in Annex 1, all other studies are not useful for classification considerations due to severe limitations as:

- no analytical verifications of TNPP or NP concentrations;
- high limits of detection foreclosing analytical verification of low NP concentrations, yet expected to affect tested organisms;
- either high or unspecified impurity grades of tested TNPP, which foreclose to discern NP as impurity and NP from TNPP hydrolysis;
- insufficient test conditions for hydrolysis (e.g. daily renewal in 21d daphnid study).

Overall, despite the low water solubility and high log Kow of TNPP, formation of NP due to limited hydrolysis has to be expected. Due to low degradation rates, TNPP remains in the environment, mainly adsorbed e.g. to sediment, from where hydrolytic release of NP can also be expected. The key study with water fleas provides sufficient evidence that under environmental conditions the transformation products resulting from applied nominal TNPP concentrations cause adverse, classification relevant ecotoxic effects.

The available data do not allow an adequate description of the apparent bottleneck between undissolved TNPP on one side, and dissolved amounts of TNPP and its major hydrolysis product NP, not to mention other potential transformation products, on the other side. With a view to this lack of key information, RAC dismissed the option to classify TNPP in analogy to its major transformation product NP. RAC concludes that nevertheless TNPP loadings below the corresponding classification criterion of 1 mg/L might be sufficient to result in concentrations of NP and possibly other transformation products, altogether causing classification relevant effects. Thus, combined with persistency, the classification R50-53 (Dir 67/548/EEC) / Aquatic Acute 1, Aquatic Chronic 1 (CLP Regulation) is justified.

RAC has thoroughly discussed several M-Factor options. Based on the available information and its considerable uncertainties, RAC concludes to recommend no harmonised M-Factor (and no SCL). The scientific uncertainty could be significantly reduced by adequate experimental data, carefully taking into account the specific TNPP properties and regulatory needs.

Additional information

The Background Document, attached as Annex 1, gives the detailed scientific grounds for the Opinion.

ANNEXES:

Annex 1 Background Document (BD)[1]

Annex 2 Comments received on the CLH report, response to comments provided by the dossier submitter and rapporteurs' comments (excl. confidential information)

[1] The Background Document (BD) supporting the opinion contains scientific justifications for the CLH proposal. The BD is based on the CLH report prepared by a dossier submitter. The original CLH report may need to be changed as a result of the comments and contributions received during the public consultation(s) and the comments by and discussions in the Committees.