Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

2-Ethoxyethanol

ECHA/RAC/CLH-O-0000001587-67-01/A2

Adopted

9 March 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: 2-Ethoxyethanol
CAS number: 110-80-5
EC number: 203-804-1

General comments

Date	Country/ Person/Organisation/ MSCA	Comment	Response	Rapporteur's comment
26/08/2010	France / Elodie Pasquier / MSCA	The recommendations agreed at the TC C&L regarding the classification of 2-ethoxyethanol for health effects are supported in absence of any new study since the TC C&L discussions and in agreement with the revision of classification proposed in the CLH report.	This is appreciated.	Noted.
26/08/2010	Sweden / Helena Kramer / MSCA	In absence of any new data Sweden supports the agreement, on the proposed classification and labelling for 2-Ethoxyethanol, taken by the Technical Committee on Classification and Labelling (Directive 67/548/EEC) ('TC C&L').	This is appreciated.	Noted.
04/10/2010	UK / MSCA	We recognise that this is a substance for which the C&L was agreed by the TC C&L in September 2007. As such, the comments submitted below are only observations on the information contained within the proposal.	This is appreciated, too.	Noted.

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
04/10/2010	UK / MSCA	We support the current classification. We have the following observation Effects via lactation: The behavioural developmental toxicity study (Nelson and Brightwell 1984, Nelson et al 1981) reports a marked increase in neonatal mortality and prolonged parturition (dystocia). Is it possible that the prolonged parturition is the underlying cause of the neonatal mortality? If not, should classification for effects via lactation be considered?	The prolonged parturition cannot be ruled out as a cause for the neonatal mortality. An evaluation of the original study report (range-finding, 300-1200 ppm) allows no assessment of effects on lactation, as this was not part of the study design. Cross-fostering of treated pups by untreated dams was mentioned in the introduction to be performed **if** serious maternal toxicity was to be expected and had to be counteracted. As this is not reflected elsewhere in the report (methods, results, discussion), the results do not warrant classification of effects on lactation. The subsequent major behavioural teratology study showed no neonatal mortality at all (100ppm). The corresponding section in the CLH-report has been revised accordingly (tracked	We support the response from the German CA.

Date	Country/ Person/Organisation/ MSCA	Comment	Response	Rapporteur's comment
			changes). The misleading reference to cross-fostering has been deleted.	

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
30/09/2010	Ireland / Health & Safety Authority	The Irish CA is in agreement with the proposal to delete R21, as previously agreed at the TC C&L of September 2007. This amendment is warranted based on the findings of the Union Carbide study demonstrating acute dermal toxicity at doses far exceeding the limit for classification.	This is appreciated.	Noted.
04/10/2010	UK / MSCA	We agree with the proposed classification but have the following observations. Acute Oral Toxicity: How reliable are the LD 50 values in guinea pigs (Smyth et al 1941) and rabbits (Jazyna et al 1988), because these data are much lower than all the other reported values.	Thank you. Smyth et al 1941 and Jazyna et al 1988 have included the rat as a test animal in their studies as well, and the resulting LD_{50} values compare very well to those obtained by all other studies on the rat. Therefore, the values obtained for guinea pig and rabbit are judged to be relevant. There are no data	We support the response from the German CA.

Date	Country/ Person/Organisation/ MSCA	Comment	Response	Rapporteur's comment
			showing that effects in guinea pigs are irrelevant.	
		Acute Inhalation toxicity: The study by Klimisch (1988) appears to be a more reliable study (OECD and GLP compliant) on which to base a classification proposal for acute inhalation toxicity is there any reason why this was not selected. Regardless of which study has been chosen, the classification criteria are based on a 4-hour exposure period. Therefore, we suggest the selected LC 50 values are scaled for a 4-hour exposure period, before comparing them to the classification criteria.	The guideline-conforming study in the Klimisch review reported all (10/10) animals surviving the treatment, which provides no information for classification. Scaling by Habers law according to ten Berge et al 1986 (c^n x t = k; n=2 (OEHHA2008); therefore $c_2 = c_1 \times (t_1/t_2)^{1/n}$ results in an LC_{50} value of 10.4 mg/l in four hours. This warrants Acute $Tox_{inhalation}$ Cat. 4. A second study in mice supports this (Werner et al 1943a), leading to a LC_{50} value of 8.9 mg/l in four hours. The corresponding section in the CLH-report has been revised accordingly (tracked changes).	After scaling both the rat LC_{50} (7.36 mg/l/8h) and the mouse LC_{50} value (6.4-6.7 mg/l/7h) to 10.4 mg/l/4h and 8.5-8.9 mg/l/4h, respectively, the corresponding classification according to the CLP criteria is a borderline case between Acute Tox. 4 – H332 (threshold values 10-20 mg/l/4h) and Acute Tox. 3 – H331 (threshold values 2-10 mg/l/4h). Based on the lowest LC_{50}, which is the one in mice, Acute Tox. 3 – H331 is considered more appropriate than the current (translated) classification as Acute Tox. 4* – H332, and the Annex VI entry is recommended to be changed accordingly.
		Acute Dermal Toxicity We support the proposal to remove the classification for acute dermal toxicity.		Noted

Date	Country/ Person/Organisation/ MSCA	Comment	Response	Rapporteur's comment
		Repeated Dose Toxicity We agree that no classification is required.		Noted

References (already included in the Dossier):

ten Berge WF (1986): Concentration-time mortality response relationship of irritant and systemically acting vapours and gases. Journal of Hazardous Materials 13, 301-309.

OEHHA (2008): Acute RELs and toxicity summaries using the previous version of the Hot Spots Risk Assessment guidelines, Air Toxics Hot Spots Program Technical Support Document for the Derivation of Noncancer Reference Exposure Levels, Appendix D.2, Office of Health Hazard Assessment California, USA

Werner HW, Mitchell JL, Miller JW, von Oettingen WF (1943a): The acute toxicity of vapours of several monoalkyl ethers of ethylene glycol. J Ind Hyg Toxicol 25(4): 157-163