Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

Methyloxirane (Propylene Oxide)

EC number: 200-879-2
CAS number: 75-56-9

CLH-O-0000004152-85-03/F

Adopted

06 June 2014

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ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON PROPYLENE OXIDE; 1,2-EPOXYPROPANE; METHYLOXIRANE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public consultation are made available in this table as submitted by the webform. Please note that some attachments received may have been copied in the table below. The attachments received have been provided in full to the dossier submitter and RAC.

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Substance name: propylene oxide; 1,2-epoxypropane; methyloxirane
CAS number: 75-56-9
EC number: 200-879-2
Dossier submitter: the Netherlands

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
18.10.2013	Germany		MemberState	1
Comment received				
The German CA supports the modification of harmonised classification and labelling for methyloxirane.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Agree				

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2013	France		MemberState	2
Comment received				
FR agrees with the classification proposal.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Agree				

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2013	Belgium		MemberState	3
Comment received				
We would you like to thanks The Netherlands for the CLH report on Methyloxirane We agree with the proposal to replace the Acute toxicity classification via oral and inhalation route for Methyloxirane based on the results of studies : • For oral route : for all studies, LD50 comprise between 382 and 1000 mg/kg bw then the criteria category 4 are fulfilled (>300 and <2000mg/kg). • For inhalation route : for all studies, LC50 comprise between 2.1 and 9.95 mg/l thus the criteria category 3 are fulfilled (>2 and <10mg/l) For the dermal route studies, the both studies do not provide any relevant information to				

support classification (no information on doses, number of animals treated and control animals, reactions to treatment,..). Further, the key study (Smyth et al., 1969) indicate a LD50 (950mg/kg bw) just below the CLP limit, 1000mg/kg, for acute toxicity category 3 and the supportive study (Weil et al., 1963) a LD50(1250mg/kg bw) upper this limit.
Dossier Submitter's Response
Thank you for your support.
RAC's response
Agree

Date	Country	Organisation	Type of Organisation	Comment number
18.10.2013	Germany		MemberState	4
Comment received				
Acute toxicity: inhalation In the key study (Shell Research Ltd. 1977) for acute inhalation toxicity, the LC50 (vapour) was 9.95 mg/l. This value was used for the proposal for the hazard class "Acute Tox. 3" (H331). According to the CLP Regulation, methyloxirane fulfils the criteria for category 3 for acute toxicity hazard categories (2.0 mg/l < ATE ≤ 10.0 mg/l). We support the changing of classification of acute inhalation toxicity from category 4 (H332) to category 3 (H331). Acute toxicity: dermal In the key study (Smyth et al. 1969) for acute dermal toxicity, the LC50 was 950 mg/kg bw. This value was used for the proposal for the hazard class "Acute Tox. 3" (H311). According to the CLP Regulation, methyloxirane fulfils the criteria for category 3 for acute toxicity hazard categories (200 mg/kg bw < ATE ≤ 1000 mg/kg bw) and changing the classification of acute dermal toxicity from category 4 (H312) to category 3 (H311) is supported. Acute toxicity: oral In the key study (Shell Research Ltd. 1968) for acute oral toxicity the LD50 was determined to be between 382 and 587 mg/kg bw. This range was used for the proposal for the hazard class "Acute Tox. 4" (H302). According to the CLP Regulation, methyloxirane fulfils the criteria for category 4 for acute toxicity hazard categories (300 mg/kg bw < ATE ≤ 2 000 mg/kg bw). It is supported that the reference indicating minimum classification (*) for acute toxicity category 4 (H302) is no longer necessary.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Agree				

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2013	France		MemberState	5
Comment received				
Acute oral toxicity: Based on a LD50 determined to be between 382 and 587 mg/kg bw in the key study in rats and a LD50 in mice, rat and guinea pig determined to be between 520 and 950 mg/kg bw,				

and considering the criteria to classify as Acute oral toxicity in category 4: "LD50 comprised between 300 and 2000 mg/kg bw", FR agrees with the classification proposal as Acute oral toxicity in category 4; H302. Acute inhalation toxicity: Based on LC50 (4h) value close to 9.95 mg/kg bw in rats and guinea pigs and between 2.0 and 7.1 mg/kg bw in mice, the classification as Acute inhalation toxicity in Category 3 is appropriate, considering the criteria for classification in category 3, H331: 2.0 < LC50 < 10.0 mg/kg bw. Acute dermal toxicity: Two different LD50 values are available: FR agrees with the lower LD50 value of 950 mg/kg bw from the key study which is more appropriate and allow classifying in category 3, H311 (200 < LD50 < 1000 mg/kg bw).
Dossier Submitter's Response
Thank you for your support.
RAC's response
Agree

OTHER HAZARDS AND ENDPOINTS – Skin Hazard

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2013	Belgium		MemberState	6
Comment received				
We support the removal of the skin irritation classification endpoint based on the results of the studies : • For the key study (Harlan Laboratories Ltd, 2010) based on the OECD guideline 404, the results show a slight erythema in one rabbit fully reversible within 72h and a very slight edema fully reversible within 72h. • Another key study (Harlan Laboratories Ltd, 2010)based on the OECD guideline 431 demonstrate a good tissue viability. • Supportive studies show very slight or no skin reactions. Mean value >2.3 for erythema or for edema in at least 2/3 tested animals or inflammation that persists to the end of the observation period normally 14days on at least 2 animals are not observed in the above mentioned studies and therefore the CLP criteria for skin irritation 2 are not fulfilled.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Agree				

Date	Country	Organisation	Type of Organisation	Comment number
18.10.2013	Germany		MemberState	7
Comment received				
The proposal to remove the classification of methyloxirane as "Skin Irrit. 2; H315" is based on two new studies on skin irritation. The first study is the in vitro EPISKIN test (Harlan				

Laboratories Ltd. 2010). In this test no significant cytotoxicity was seen following methyloxirane treatment, so the test material was considered non-corrosive to the skin. In the second study methyloxirane was also tested in vivo using rabbits (according to OECD 404 and GLP) (Harlan Laboratories Ltd. 2010). Scoring for erythema and oedema showed only minor and transient reactions to treatment which were fully resolved within 48 – 72 h, demonstrating the low skin irritancy of this substance. The German CA supports to remove the classification "Skin Irrit. 2; H315" as well as "Xi; R38" for methyloxirane.
Dossier Submitter's Response
Thank you for your support.
RAC's response
Agree

Date	Country	Organisation	Type of Organisation	Comment number
21.10.2013	France		MemberState	8
Comment received				
Skin irritation: based on the whole studies, the substance is not a skin irritating. The study of BASF (1962) seems not to be reliable and cannot be used to classify this substance.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Agree				