

Committee for Risk Assessment
RAC

Annex 2
Response to comments document (RCOM)
to the Opinion proposing harmonised classification and
labelling at EU level of

**Reaction mass of 1-(2,3-epoxypropoxy)-2,2-bis
((2,3-epoxypropoxy)methyl) butane and
1-(2,3-epoxypropoxy)-2-((2,3-
epoxypropoxy)methyl)-2-hydroxymethyl butane**

EC Number: -
CAS Number: -

CLH-O-0000007002-89-01/F

Adopted
10 June 2021

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON REACTION MASS OF 1-(2,3-EPOXYPROPOXY)-2,2-BIS ((2,3-EPOXYPROPOXY)METHYL) BUTANE AND 1-(2,3-EPOXYPROPOXY)-2-((2,3-EPOXYPROPOXY)METHYL)-2-HYDROXYMETHYL BUTANE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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Substance name: Reaction mass of 1-(2,3-epoxypropoxy)-2,2-bis ((2,3-epoxypropoxy)methyl) butane and 1-(2,3-epoxypropoxy)-2-((2,3-epoxypropoxy)methyl)-2-hydroxymethyl butane

EC number: -

CAS number: -

Dossier submitter: Norway

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
23.06.2020	Germany		MemberState	1
Comment received				
The DE CA supports the proposed classification as Muta. 2 (H341) and Repr. 1B (H360F). No EC-number is mentioned in the CLH report. According to the ECHA dissemination site the EC number of 701-135-4 is assorted.				
Dossier Submitter's Response				
Thank you for your support in the proposed classification. The CAS number has not been provided due to the fact that at the time of the preparation of the CLH report the registrant has not provided the CAS number as part of the substance identity information in the registration dossier. However, in the meantime the CAS number is also given as part of the substance identity information on the ECHA Dissemination page and we support the recommendation to add the CAS (No 30499-70-8) and EC number (No 701-135-4) in the CLH report.				
RAC's response				
Thank you for your comment.				

Date	Country	Organisation	Type of Organisation	Comment number
02.07.2020	France		MemberState	2
Comment received				
In the context of our national priority work for identifying the working plan on classification in 2019, we assessed a substance named: "1,3-Propanediol, 2-ethyl-2-				

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(hydroxymethyl)-, polymer with (chloromethyl)oxirane" (CAS number 30499-70-8; EC number 608-489-8).

<https://echa.europa.eu/fr/substance-information/-/substanceinfo/100.111.042>

After exchanges with ECHA, it was found that it is the same substance as "Reaction mass of 1-(2,3-epoxypropoxy)-2,2-bis ((2,3-epoxypropoxy)methyl) butane and 1-(2,3-epoxypropoxy)-2-((2,3-epoxypropoxy)methyl)-2-hydroxymethyl butane", which is the substance of interest here.

Both consist on the same final UVCB substance obtained by 2 different synthesis ways.

In addition, according to ECHA website, "Reaction mass of 1-(2,3-epoxypropoxy)-2,2-bis ((2,3-epoxypropoxy)methyl) butane and 1-(2,3-epoxypropoxy)-2-((2,3-epoxypropoxy)methyl)-2-hydroxymethyl butane" is associated with EC n°701-135-4 and CAS n°30499-70-8.

Therefore, we are of the opinion that it is important to specify EC/CAS numbers in the classification entry to avoid confusion on the identity of the substance, and consequently possible misclassification.

Dossier Submitter's Response

Many thanks for this note. In fact, this is an important issue which we also noticed at the beginning of our work. As far as we know there has been a substance ID-change during which the EC number was changed from 608-489-8 to 701-135-4 without any changes in the manufacture of the UVCB (we have no information on the details of the ID change). Therefore, both EC numbers were included in the literature searches for the substance. As indicated in our response to Comment No. 1 we support the suggestion to include the CAS number (No 30499-70-8) as well as the EC number (No 701-135-4) in the CLH report.

RAC's response

Thank you for your comment.

MUTAGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
23.06.2020	Germany		MemberState	3
Comment received				
The DE CA supports the proposed classification as Muta. 2 based on positive results obtained in a valid in vivo somatic cell genotoxicity test (Comet Assay, OECD TG 489) supported by positive results from in vitro mutagenicity assays.				
Dossier Submitter's Response				
Thank you for your support in the proposed classification.				
RAC's response				
Thank you for your comment.				

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Date	Country	Organisation	Type of Organisation	Comment number
02.07.2020	France		MemberState	4
Comment received				
Based on the positive effects in somatic cells in mammals in vivo (comet assay), supported by positive results from 3 in vitro tests (Ames test, chromosomal aberration study in mammalian cells and gene mutation study in mammalian cells), we agree with the proposal of classification Muta. 2.				
Dossier Submitter's Response				
Thank you for your support in the proposed classification.				
RAC's response				
Thank you for your comment.				

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
23.06.2020	Germany		MemberState	5
Comment received				
The DE CA supports the proposed classification as Repr. 1B (H360F) based on clear evidence from valid experimental studies (OECD TG 422) with rats showing severe effects on male fertility in the absence of relevant systemic toxicity.				
Dossier Submitter's Response				
Thank you for your support in the proposed classification.				
RAC's response				
Thank you for your comment.				

Date	Country	Organisation	Type of Organisation	Comment number
02.07.2020	France		MemberState	6
Comment received				
Data provide clear evidence of an adverse effect on male fertility in the absence of other toxic effects. Although the underlying mode of action is unclear, the data do not allow ruling out the relevance of this effect for humans. Thus, we agree with the proposal of classification in Category 1B, H360F.				
Although no developmental effects were observed in the available studies, only doses without any toxic effects were tested. In the absence of relevant developmental toxicity studies, we agree that no classification can be proposed.				
Dossier Submitter's Response				
Thank you for your support in the proposed classification.				
RAC's response				
Thank you for your comment.				

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Date	Country	Organisation	Type of Organisation	Comment number
03.07.2020	Sweden		MemberState	7
Comment received				
<p>The Swedish CA agrees with the proposed classification as Repr. 1B, H360F for adverse effects on fertility, expressed as impaired male rat fertility in the absence of marked general toxicity.</p> <p>Minor comment on section 10.10.4: We consider that information on the PNDT study performed according to OECD TG 414 in rats that is briefly mentioned in section 10.10.5 and available in Annex I to the CLH-report should have been presented in tabular form (table 15) as well to facilitate a transparent assessment of developmental toxicity.</p>				
Dossier Submitter's Response				
<p>Thank you for your support in the proposed classification and the request for the most transparent presentation possible. We support your proposal for a transparent documentation and assessment and suggest to include a tabular compilation of the OECD 414 study in Table 15 of the CLH report, see Annex I below.</p>				
RAC's response				
Thank you for your comment.				

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Annex I

OECD 414 study to be included in Table 15:

<p>Prenatal Developmental Toxicity Study</p> <p>According to OECD TG 414 Deviations: no GLP: yes</p> <p>Female Wistar Rats- HanTac: WH(24 animals/dose group) RL1 (according to registration dossier)</p> <p>RL3 (according to authors of this document, as the highest dose tested was too low to induce some developmental and/or maternal toxicity (clinical signs or a decrease in body weight) as requested by the guideline)</p>	<p>Reaction mass of 1-(2,3-epoxypropoxy)-2,2-bis((2,3-epoxypropoxy)methyl)butane and 1-(2,3-epoxypropoxy)-2-((2,3-epoxypropoxy)methyl)-2-hydroxymethyl butane (Concentrations of constituents: 58% C15H26O6 and 25% C12H22O5)</p> <p>0, 30, 90, 180 mg /kg bw/d (dose selection “based on the available literature in consultation with the Sponsor” – no further information provided) from GD 5 to GD 19</p> <p>GD 20: females underwent caesarean section, ½ of the fetuses were examined for visceral anomalies and ½ for skeletal anomalies.</p> <p>Application via gavage</p> <p>Vehicle: polyethylene glycol 400</p>	<p><u>Dams</u>: NOAEL: 180 mg/kg bw/d (no maternal toxicity observed up to the highest dose tested; no effects on clinical signs, mortality, body weight and body weight changes, uterine weight and number of corpora lutea, implantations, early resorptions, late resorptions, pre-implantation loss and post implantation loss)</p> <p><u>Offspring</u>: NOAEL: 180 mg/kg bw/d (no toxicity observed up to the highest dose tested; no effects on total number of fetuses, number of alive offspring, sex ratio, litter size and weights, external and skeletal malformations)</p>	<p>Unnamed (2018)</p> <p>(ECHA Dissemination, 2019)</p>
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