Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

L-(+)-lactic acid; (2S)-2-hydroxypropanoic acid

EC Number: 201-196-2
CAS Number: 79-33-4

CLH-O-0000001412-86-191/F

Adopted

9 March 2018

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON L-(+)-LACTIC ACID; (2S)-2-HYDROXYPROPANOIC ACID

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public 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 public 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 public 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.

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Substance name: L-(+)-lactic acid; (2S)-2-hydroxypropanoic acid
EC number: 201-196-2
CAS number: 79-33-4
Dossier submitter: Germany

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
27.04.2017	Switzerland	Philip Morris International	Company-Downstream user	1
Comment received				
PMI supports the proposed classification of L(+)-lactic acid as Skin Irritant Category 2, H315 and Eye Damage Category 1, H318. However, PMI disagrees with the proposed classification of L(+)-lactic acid as irritating to the respiratory tract (STOT SE 3; H335) as this classification is not supported by human data or by "severe respiratory tract irritation" animal studies, hence does not meet the criteria set forth in the CLP regulation. ECHA note – An attachment was submitted with the comment above. Refer to public attachment PMI comments on L-(+)-lactic acid CLH report.pdf				
Dossier Submitter's Response				
Thank you for your comments and for supporting the Skin irrit. 2 and Eye Dam. 1 classifications proposal. • Regarding the STOT SE 3 proposal, as stated in the Guidance on the Application of the CLP Criteria (2015, page 430) at the Classification of Substances for STOT SE: " Although classification in Category 3 is primarily based on human data, **if available**, animal data can be included in the evaluation.These animal data on RTI and NE will generally come from standard **acute inhalation studies**, although it is possible that narcosis could be observed in studies using other routes. Standard acute toxicity tests are often **more useful for Category 3** than for STOT SE Categories 1/2 because overt findings of narcosis and RTI are more often reported in clinical observations." • In the GLP acute inhalation rat study with SY-83 (80-85 % L-(+)-lactic acid in water) (David, 1987), female rats exposed to SY-83 appeared lethargic at one (2/5) and three hours (5/5). The two female rats that were lethargic at one hour also had rapid, shallow breathing and appeared to be gasping at both one and three hours. Even one female rat from the treated group died and was hunched with laboured breathing and gasping one day before death (day 7). Here a body				

weight decrease (-7 %) in the treated females during the first week after exposure was observed. In general, these respiratory pattern effects were transient, but indicative of respiratory tract irritation and adversity for a short duration period after exposure. The histopathological analysis was not conducted in this study possibly due to the reversibility of the effects observed (the animals seemed normal after 24 hours exposure and during the observational period of 14 days).

- Furthermore, other rat acute studies with L-(+)-lactic acid oral administration and one fatal case report (accidental poisoning via duodenum tube in a hospital) showed signs of respiratory system stimulation (e.g. dyspnea, irregular breathing, discoloured lungs and trachea, lacrimation, crusty nose, lethargy and prostration) (Wingard at el., 1983, 1984, Fühner, 1932). The increased work in breathing, stimulation of the receptors of the upper or lower airway, lung parenchyma, or chest wall, and excessive stimulation of the respiratory centre by central and peripheral chemoreceptors can be related to the increase in the circulating L-(+)-lactic acid and oxygen debt as well. That overcomes by deep breathing to oxidise the acid, and the extra oxygen is needed by the liver to finally remove the L-(+)-lactic acid.
- In the definitions and general considerations for STOT SE classification, Annex 1: 3.8.1.4 (Guidance on the Application of the CLP Criteria, 2015, page 428), "Assessment shall be take into consideration not only when significant changes in a single organ or biological system but also generalised changes of a less severe nature involving several organs." That seems the case for the overall studies with L-(+)-lactic acid, where the respiratory system in general is affected via different routes.
- It is clearly indicated in CLP that there are currently no validated animal tests that deal specifically with RTI, but animal studies can be used as part of the weight of evaluation. "For example, animal studies may provide useful information in terms of clinical signs of toxicity (dyspnoea, rhinitis etc.) and histopathology (e.g. hyperaemia, edema, minimal inflammation, thickened mucous layer) which are reversible and may be reflective of the characteristic clinical symptoms described above. Such animal studies can be used as part of weight of evidence evaluation." (Guidance on the Application of the CLP Criteria, 2015, page 433).

Therefore, the DS has the opinion that the effects of L-(+)-lactic acid at the respiratory tract of animals are sufficient to adversely alter human function for a short duration after exposure and, in conclusion, propose a classification as STOT SE 3, H335 - May cause respiratory irritation.

RAC's response

Thank you for your comments. RAC supports the reply provided by the Dossier Submitter, particularly what concerns the interpretation of the CLP criteria. Besides, RAC points out that substances and mixtures with a pH < 2 (concentrated lactic acid has a pH < 2) can be predicted to be irritating or corrosive to skin (CLP 3.2.2.1.2.3. and CLP 3.2.3.2.1.1.) and eyes (CLP 3.3.2.2.4.). Similar effects could be expected on epithelia of the respiratory system. However, due to the limited specific data on this endpoint RAC concluded that a classification for STOT SE 3 might not be justified. On the other hand, RAC assigns EUH071 (corrosive to the respiratory tract) as for the labelling.

Date	Country	Organisation	Type of Organisation	Comment number
07.04.2017	France	Jungbunzlauer SA	Company-Manufacturer	2
Comment received				
See enclosed letter				

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 2017-04-CHL_proposal_Lactic_Acid.pdf

Dossier Submitter's Response

Thank you very much for your comments and please see respective response to comment number 1.

RAC's response

Thank you for your comments. RAC supports the reply provided by the Dossier Submitter, particularly what concerns the interpretation of the CLP criteria. Besides, RAC points out that substances and mixtures with a pH < 2 (concentrated lactic acid has a pH < 2) can be predicted to be irritating or corrosive to skin (CLP 3.2.2.1.2.3. and CLP 3.2.3.2.1.1.) and eyes (CLP 3.3.2.2.4.). Similar effects could be expected on epithelia of the respiratory system. However, due to the limited specific data on this endpoint RAC concluded that a classification for STOT SE 3 might not be justified. On the other hand, RAC assigns EUH071 (corrosive to the respiratory tract) as for the labelling.

Date	Country	Organisation	Type of Organisation	Comment number
28.04.2017	France		MemberState	3

Comment received

The minimum degree of purity of the substance is 95.5% expressed in dry weight according to regulation 2016/2291 (biocidal regulation) and not 92.95% as reported in CLH report.
Moreover, Lactic acid is manufactured as aqueous solution at different concentrations as reported in the biocidal dossier. This should be specified in the substance identity in addition to the minimum degree of purity expressed in dry weight.

Dossier Submitter's Response

Thank you for your comment. It is correct that L(+)-lactic acid is manufactured as aqueous solution at different concentrations. The purity of 92.95 % is no dry weight purity, it is a purity for Lactic acid with the lowest amount of water (see also confidential Annex to CLH Report).
Therefore the given purity and composition is in accordance with the substance definition. Whereas under BPR the water is just calculated out to better compare several manufactured aqueous solutions in the active substance evaluation.
However if needed, we can provide the conf. identity part of the CAR (conf. Doc II A) to the RAC.

RAC's response

Thank you for your comment.

Date	Country	Organisation	Type of Organisation	Comment number
20.04.2017	Germany	IHO INDUSTRIAL ASSOSIATION HYIENE AND SURFACE PROTECTION	Industry or trade association	4

Comment received

IHO is the branch organization of the producers of cleaning and disinfection products for professional application. We are contacting you in the name our companies regarding the classification of lactic acid. Some of our companies have tested different concentrations of

lactic acid in terms of eye effects. They have created in vitro testing data for lactic acid proposing a specific concentration limit of 10% for eye irritation and damage. The in vitro tests were performed according to OECD test no. 437 with lactic acid in a concentration of 10%, 20% and 40%. In order to set a realistic and robust standard, we would purpose to set 10% as a specific concentration limit. This initiative is supported by raw material suppliers.

4 final reports regarding L-(+)-lactic acid (CAS) 79-33-4:

1. Sponsor: Werner & Merz GmbH, Rheinallee 96, D-55120 Mainz
Test Facility: LAUS GmbH, Auf der Schafweide 20, D-67486 Kirrweiler
Test performance: Bovine Corneal Opacity and permeability Assay (BCOP) with Lactic Acid 10 %

2. Sponsor: Ecolab Deutschland GmbH; Reisholzer Werftstr. 38-42, D-40589 Düsseldorf
Test Facility: Harlan Cytotest Cell Research GmbH; in den Leppsteinswiesen 19, D-64380 Rossdorf
Test performance:
I) Bovine Corneal Opacity and permeability Assay (BCOP) with Lactic Acid 10 %
II) Bovine Corneal Opacity and permeability Assay (BCOP with Lactic Acid 20 %)
III) Bovine Corneal Opacity and permeability Assay (BCOP with Lactic Acid 40 %)
Please find more details in attached documents

We submitted our data also to C&L inventory, please use following link:
https://echa.europa.eu/de/information-on-chemicals/cl-inventory-database/-/discli/notification-details/4548/759983
Supporting comments from registrants:
1. Jungbunzlauer International AG, St. Alban-Vorstadt 90, P.O. Box, CH-4002 Basel
2. Prac Biochem BV, Arkelsdijk 46, NL-4206 AC Gornichem
Both confirm that setting 10% as a specific concentration limit for (S)-lactic acid seems correct to us as we do not have any test data contradicting this.

ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Originale.zip

Dossier Submitter's Response

Four new studies on eye irritation where submitted testing different dilutions of lactic acid (10 %, 20 % and 40 %) in deionized water and Bovine corneas incubated in vitro (Bovine cornela opacity and permeability assay) (Sponsor 1: Werner & Merz GmbH, Rheinallee 96, D-55120 Mainz; Sponsor 2: Ecolab Deutschland GmbH; Reisholzer Werftstr. 38-42, D-40589 Düsseldorf). The GLP studies (following OECD 437) with 10 % lactic acid resulted in negative in no eye irritation (Sponsor 1 and 2), but the dilution with 20 % was considered to be a mild eye irritant (Sponsor 2), and the 40 % dilution as severe eye irritant (Sponsor 2).

In the Guidance of the Application of the CLP criteria (2015, page 308,309), setting of specific concentration limits is currently based on human and animal data, especially if dose-response information is available. Because of the physico-chemical properties (pH < 2) of L-(+)-lactic acid, no eye irritation studies in rabbits were performed due to animal welfare considerations and no human data is available. Also in the Guidance (2015), it is stated that: "The possibilities to use **in vitro test methods as a basis for setting SCLs have not yet been explored** and therefore, at the present point in time, it is not possible to provide guidance for the use the in vitro methods for the purpose of setting

SCLs. However, this does not exclude that a method to set SCLs based on in vitro tests could be developed in the future, and these tests may provide a promising option for SCL setting. As SCL should apply to any mixture containing the substance instead of the GCL (that otherwise would apply to the mixture containing the substance). Thus, if the SCL is based on data retrieved from **tests with dilutions of the substance in a specific solvent**, it has to be considered that the derived concentration should be applicable to **all mixtures** for which the SCL should apply." As the DS does not have any other data on the behaviour of the active substance in other different solvents, no information on SCL for lactic acid can be proposed.

RAC's response

Thank you for your comments and thank you for providing the study reports of the four new studies sponsored by industry. RAC is of the opinion that only three concentrations tested in one type of assay, using only one solvent, does not justify the setting of a SCL for the serious eye damage/irritation.

Date	Country	Organisation	Type of Organisation	Comment number
06.04.2017	Netherlands	Corbion (legal entiry = Purac Biochem bv)	Company-Manufacturer	5

Comment received

Corrosion to Metals: in the meantime there are valid data available for this endpoint.
Study Summary (Dec 2015): The corrosive properties of 80% (S)-Lactid acid solution were determined using steel and aluminum specimens according to the UN Manual of Test and Criteria (ST/SG/AC.10/11/Rev5,2009); section 37 Test C.1.
The test item showed a negative corrosion result (uniform) in the test using the steel as well as the aluminum specimen.
The test specimen also showed a negative corrosion result (localized) in the test using the steel as well as the aluminum specimen.
Conclusion: the product has no corrosive properties to metals according to the UN Recommendations on the Transport of Dangerous Goods.
An update of the REACH dossier of (S)-Lactic acid and Lactic acid, including these study results will be made later on.

Dossier Submitter's Response

Thank you very much for your comment and the information on the outcome of the study on corrosive properties.
However, without any knowledge of all test details, test conditions and calculated test results we are not able to confirm your conclusion on non-classification.
Therefore, we would like to ask you to submit the study report from Dec. 2015 of testing the corrosive properties of a 80 % (S)-Lactic acid solution.

RAC's response

Thank you for providing the above mentioned study. Based on its outcome, RAC concludes that L-(+)-lactic acid does not require classification for corrosivity to metals.

OTHER HAZARDS AND ENDPOINTS – Skin Hazard

Date	Country	Organisation	Type of Organisation	Comment number
28.04.2017	France		Member State	6

Comment received

Skin irritation: p33

The rabbit study of Van Beek, 1986 is the only reliable in vivo study. Due to the results of this study, a classification Skin Corr 1C – H314 is required. The corrosive properties of the substance are confirmed by the results of the Corrositex assay and the pH value of the substance that is lower than 2 (1.83).

Regarding human data, their quality and relevance should be critically reviewed when using for hazard assessment (according to CLP regulation). As stated in the CLH report, the available human data presented many deficiencies (not conducted according to a guideline, lot/batch number of the test material L-(+)-lactic acid (88 %) not mentioned, test material not specified, purity and stability of the test material not mentioned) and the number of volunteers in the Patch Test experiment is very low. Indeed, only 26 volunteers are involved in the experiment which may be considered not enough to conduct a robust statistical analysis.

Therefore, we consider that a classification Skin Corr 1C – H314 should be applied based on the results on the in vivo rabbit study (Van Beek, 1986).

Dossier Submitter's Response

Thank you very much for your comment, but the humans studies were considered key database for the skin classification proposal based on:

- they represent direct methods of assessing skin irritation hazard to man, by using the **endpoin**t of concern in the **species** of concern;
- from the patch test studies in humans, it is likely that dermal irritation studies in pigs underestimate the irritating potential of L-(+)-lactic acid for human skin while rabbit skin seems to be much more sensitive than human skin;
- ECETOC (2002) reported that existing data indicate that human skin is, in most cases, less sensitive than rabbit skin.

The rabbit study (Van Beek, 1986) can also be used as a key study for the skin classification, but the pH of lactic acid tested was also missing. Therefore, the human patch test and the TER data (*in vitro* human skin transcutaneous electrical resistance) showed only mild to strong erythema and no corrosive reactions (i.e. necrosis through the epidermis and into the dermis, ulcers, bleeding and bloody scabs). Thus, from these studies it was possible to assess the skin irritating potential of L-(+)-lactic acid in humans and to use the results for classification and labelling.
In conclusion, the proposed classification of L-(+)-lactic acid as skin irritation/corrosion. (Category 2: H315, Causes skin irritation) is still maintained.

RAC's response

Thank you for your comments. RAC agrees in principle with the Dossier Submitter that human data should be considered as key information with regard to classification for skin irritation/corrosion. However, in this case it is difficult to ignore the rabbit studies showing corrosion and results from several different *in vitro* skin models showing corrosion also in human skin. RAC thus proposes classification in Category 1C in line with the proposal in the comment.

Date	Country	Organisation	Type of Organisation	Comment number
06.04.2017	Netherlands	Corbion (legal entiry = Purac Biochem bv)	Company-Manufacturer	7

Comment received

see general comment about corrosion to metals

Dossier Submitter's Response
Thank you very much for your comments and please see respective response to comment number 5.
RAC's response
Thank you for providing the above mentioned study. Based on its outcome, RAC concludes that L-(+)-lactic acid does not require classification for corrosivity to metals.

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
28.04.2017	France		MemberState	8
Comment received				
Eye irritation: p35 France agrees with the proposed classification. Nevertheless, Table 20 is erroneous. Indeed, according to OECD 438, no prediction can be made regarding the classification of H60 (2xIII, 1xII) and BF S36 (2xII, 1xI). Respiratory tract irritation : p37 No human data are available to support a classification as STOT SE Cat 3. Furthermore, if the classification as Skin Corr 1C (as we proposed in comment above) is agreed at the RAC level, a classification STOT SE Cat 3 – H335 May cause respiratory irritation, is not necessary. Instead EUH071 would be warranted.				
Dossier Submitter's Response				
Thank you very much for your comments and the supporting classification on Eye Dam. 1. Regarding Table 20 from the CLH report, you are correct about the formulation tested H60 where the combination for the endpoints leads to "no classification"/ or no prediction can be made. Nevertheless, the formulation with HS88 (aqueous solution of 88 % L(+) lactic acid, pH 2) indicated severe to complete corneal opacity and the classification proposal for L-(+)-lactic acid Eye Dam. 1, H318 - Causes serious eye damage is correct. For STOT SE 3. Proposed classification, please see our respective response to comment number 1 and number 6.				
RAC's response				
Thank you for your comments. See also our responses to comments number 1 and 6. RAC supports the proposed additional labelling with EUH071 (corrosive to the respiratory tract).				

Date	Country	Organisation	Type of Organisation	Comment number
20.04.2017	Germany	IHO INDUSTRIAL ASSOSIATION HYIENE AND SURFACE PROTECTION	Industry or trade association	9
Comment received				
1. Sponsor: Werner & Merz GmbH, Rheinallee 96, D-55120 Mainz Test Facility: LAUS GmbH, Auf der Schafweide 20, D-67486 Kirrweiler Test performance: Bovine Corneal Opacity and permeability Assay (BCOP) with Lactic Acid				

10 %

Summary:
One valid experiment was performed.
Bovine corneas were used. They were collected from slaughtered cattle which were between 12 and 60 months old. The test item Lactic acid 10% was brought onto the cornea of a bovine eye which had been incubated with cMEM without phenol red at 32 ± 1 °C for 1 h and whose opacity had been measured. The test item was incubated on the cornea for 10 min. at 32 ± 1 °C. After removal of the test item and 2 h post-incubation, opacity and permeability values were measured.
Physiological sodium chloride solution was used as negative control. The negative control showed no irritating effect on the cornea and the calculated IVIS (in vitro irritancy score) is 0.27.
Dimethylformamide (DMF) undiluted was used as positive control. The positive control showed effects on the cornea and falls within two standard deviations of the current historical mean. The calculated IVIS (in vitro irritancy score) is 28.53.
Under the conditions of this study, the test item Lactic acid 10% showed no effects on the Cornea of the bovine eye. The calculated IVIS (in vitro irritancy score) is 1 .57.
According to OECD Guideline no. 437 (Jul. 2013), a substance with an IVIS < 3 requires no classification for eye irritation or serious eye damage.

2. Sponsor: Ecolab Deutschland GmbH; Reisholzer Werftstr. 38-42, D-40589 Düsseldorf
Test Facility: Harlan Cytotest Cell Research GmbH; in den Leppsteinswiesen 19, D-64380 Rossdorf
Test performance/Title: Bovine Corneal Opacity and permeability Assay (BCOP) with Lactic Acid 10 %

Summary:
This in vitro study was performed to assess the corneal irritation and damage potential of Lactic Acid 10% by means of the BCOP assay using fresh bovine cornea.
After a first opacity measurement of the fresh bovine cornea (to). the neat test item Lactic
Acid 10%, the positive, and the negative controls were applied to cornea and incubated for
10 minutes at 32 ± 2 °C. The posterior chamber contained MEM medium supplemented with sodium bicarbonate and L-glutamine and 1 % fetal calf serum (FCS) (complete medium = cMEM). After the incubation phase the test item, the positive, and the negative controls were each rinsed from the cornea and opacity was measured again (t10).
Further, the corneae were incubated for another 120 minutes at 32 ± 2 °C in complete medium, and opacity was measured a third time (t130).
After the opacity measurements permeability of the corneae was determined while application of 1 ml of a fluorescein solution for 90 minutes at 32 ± 2 °C in a horizontal position. The coming out liquid was measured spectrophotometrically.
With the negative control (0.9% NaCI solution) neither an increase of opacity nor permeability of the cornea could be observed.
The positive control (2-Ethoxyethanol) showed clear opacity and distinctive permeability of the cornea and therefore, is classified as severe eye irritant.
The test item Lactic Acid 10% did not cause any opacity or permeability of the cornea compared with the results of the negative control. The calculated mean in vitro score was 1.16 and therefore, the test item was classified as non-eye irritant.
In conclusion, it can be stated that in this study and under the experimental conditions reported, the test item Lactic Acid 10% is not considered to be an eye irritant.

Please find more details in attached documents ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Originale.zip
Dossier Submitter's Response
Please see respective response on comment number 4.
RAC's response
Thank you for your comments and thank you for providing the study reports of the four new studies sponsored by industry. RAC is of the opinion that only three concentrations tested in one type of assay, using only one solvent, does not justify the setting of a SCL for the endpoint serious eye damage/irritation.

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Single Exposure

Date	Country	Organisation	Type of Organisation	Comment number
27.04.2017	Switzerland	Philip Morris International	Company-Downstream user	10
Comment received				
PMI disagrees with the STOT SE 3, H335 classification for the following reasons: (i) BAuA's conclusion does not meet the criteria for classification established by the CLP regulation. In fact, Annex I, point 3.8.2.2.1, specifies that the classification STOT SE 3 (respiratory tract irritation) should be "based primarily on human data". As the report correctly mentions in section 4.5.3 "No human data available/reported." Animal studies can only be used as part of weight of evidence evaluation. (ii) BAuA based its proposal for CLH classification on only one acute inhalation toxicity study in rats (David, 1987) and they justify their interpretation stating that the "signs of respiratory irritation in rat" reported in the David's study (rapid, shallow, labored breathing, gasping) were transient but indicative for respiratory tract irritation. The CLP regulation states that "there are currently no validated animal tests that deal specifically with RTI [respiratory tract irritation]", however "animal studies may provide useful information in terms of clinical signs of toxicity (dyspnoea, rhinitis etc) and histopathology (e.g. hyperemia, edema, minimal inflammation, thickened mucous layer) which are reversible and may be reflective of the characteristic clinical symptoms described above". CLP regulation sets forth that, in the absence of validated animal tests for RTI, animal data can be used only as part of weight of evidence if severe RTI effects are observed. The "rapid, shallow, labored breathing, gasping" are not considered severe signs for RTI. In addition, the absence of "gross lesions at necropsy" and the lack of histopathological data confirms that no relevant supportive data for the classification as STOT SE 3, H335 are available. PMI was not able to retrieve and review the David study from 1987 as it is not published in a peer reviewed journal nor otherwise publically available. (iii) BAuA claims "For precautionary reasons […] it is considered adequate to propose a classification as respiratory tract irritant STOT SE 3". L-(+)-lactic acid is a registered chemical under REACH for a high tonnage band (100 000 – 1 000 000 tonnes per annum) and it is classified in the REACH dossier as Eye Damage Category 1. The Guidance on the Application of the CLP criteria clarifies that "a				

classification for corrosivity is considered to implicitly cover the potential to cause RTI and so the additional Category 3 is considered to be superfluous". Category 3 would be considered only in case functional or morphological changes occur in the upper respiratory tract (nasal passage, pharynx and larynx) which, as mentioned above, was not reported in any scientific study.

For the above mentioned reasons, PMI disagrees with the proposed classification (STOT SE 3, H335) for L-(+)-lactic acid as the justifications provided by BAuA does not meet the criteria set forth in the CLP regulation.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment PMI comments on L-(+)-lactic acid CLH report.pdf

Dossier Submitter's Response

Thank you very much for your comment and please see our respective response to comment number 1.

RAC's response

Thank you for your comments. RAC supports the reply provided by the Dossier Submitter, particularly what concerns the interpretation of the CLP criteria. Besides, RAC points out that substances and mixtures with a pH < 2 (concentrated lactic acid has a pH < 2) can be predicted to be irritating or corrosive to skin (CLP 3.2.2.1.2.3. and CLP 3.2.3.2.1.1.) and eyes (CLP 3.3.2.2.4.). Similar effects could be expected on epithelia of the respiratory system. However, due to the limited specific data on this endpoint RAC concluded that a classification for STOT SE 3 might not be justified. On the other hand, RAC assigns EUH071 (corrosive to the respiratory tract) as for the labelling.

Date	Country	Organisation	Type of Organisation	Comment number
07.04.2017	France	Jungbunzlauer SA	Company-Manufacturer	11

Comment received

According to the CLP Regulation, Annex I, point 3.8.2.2.1(e), "this special classification (i.e. STOT SE 3, H335) would occur only when more severe organ effects including in the respiratory system are not observed". Also, the classification as respiratory tract irritant STOT SE 3 (H335) risk is already covered by the H315 risk (skin irritation) and H318 risk (causes severe eye damage); and therefore it makes good sense not to add information that does not provide any additional benefit for the protection of users.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 2017-04-CHL_proposal_Lactic_Acid.pdf

Dossier Submitter's Response

Please see our respective response to comment number 1, where the "Definitions and general considerations for STOT SE" classification is exemplified.

RAC's response

Thank you for your comments. RAC supports the reply provided by the Dossier Submitter, particularly what concerns the interpretation of the CLP criteria. Besides, RAC points out that substances and mixtures with a pH < 2 (concentrated lactic acid has a pH < 2) can be predicted to be irritating or corrosive to skin (CLP 3.2.2.1.2.3. and CLP 3.2.3.2.1.1.) and eyes (CLP 3.3.2.2.4.). Similar effects could be expected on epithelia of the respiratory system. However, due to the limited specific data on this endpoint RAC concluded that a classification for STOT SE 3 might not be justified. On the other hand, On the other hand, RAC assigns EUH071 (corrosive to the respiratory tract) as for the labelling.

Date	Country	Organisation	Type of Organisation	Comment number
06.04.2017	Netherlands	Corbion (legal entiry = Purac Biochem bv)	Company-Manufacturer	12

Comment received

1) According to the CLP Regulation, Annex I, point 3.8.2.2.1, classification respiratory irritation, SE3, shall be based primarily on human data; however, there are no data that would demonstrate respiratory irritation caused by L-(+)-lactic acid in humans.
2) According to the CLP Regulation, Annex I, point 3.8.2.2.1(d), there are currently no validated animal tests that deal specifically with RTI. Whereas information from acute and/or repeated dose inhalation toxicity studies may be considered in RTI classification, this should be part of a weight-of-evidence evaluation. Classification applying the precautionary principle (as proposed in the CLH report) would constitute reliance on non-validated animal data alone, which would be in conflict with the provisions of the CLP Regulation.
3) The study cited in the CLH report (David RM 1987, Report No. I - 7083.112) specifies that the symptoms were observed in all animals including the control group at 1–3 hours post-exposure (hunched posture, red stained fur surrounding the eyes (tearing), ruffled fur, ungroomed appearance with soiled fur (stained brown), cf. page 24 CLH report). Therefore, there is no demonstrated relationship between the observed symptoms and exposure to lactic acid. Moreover, the exposure concentration was clearly in excess of the relevant maximum concentration for inhalation toxicity tests (7.94 vs 5 mg/L).
4) Histopathological findings, as requested by the CLP Regulation, Annex I, point 3.8.2.2.1(d) are not available, neither from animals nor from humans. The appropriateness of the classification proposal thus seems questionable.
5) L-(+)-lactic acid is already (voluntarily) classified for skin and eye irritation (H315 and H318). According to the CLP Regulation, Annex I, point 3.8.2.2.1(e), "this special classification (i.e. STOT SE 3, H335) would occur only when more severe organ effects including in the respiratory system are not observed. However, classification as H315 and H318 is based on severe organ effects (e.g. serious eye damage), thus point 3.8.2.2.1(e) prohibits classification for respiratory irritation.

In conclusion, the proposal to classify L-(+)-lactic acid as irritating to the respiratory tract (STOT SE 3) is unjustified, both from a scientific and a regulatory viewpoint, and should be rejected.

Dossier Submitter's Response

Thank you very much for your comment and please see our respective response to comment number 1.

RAC's response

Thank you for your comments. RAC supports the reply provided by the Dossier Submitter, particularly what concerns the interpretation of the CLP criteria. Besides, RAC points out that substances and mixtures with a pH < 2 (concentrated lactic acid has a pH < 2) can be predicted to be irritating or corrosive to skin (CLP 3.2.2.1.2.3. and CLP 3.2.3.2.1.1.) and eyes (CLP 3.3.2.2.4.). Similar effects could be expected on epithelia of the respiratory system. However, due to the limited specific data on this endpoint RAC agreed that a classification for STOT SE 3 might not be justified. On the other hand, On the other hand, RAC assigns EUH071 (corrosive to the respiratory tract) as for the labelling.

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
28.04.2017	France		Member State	13
Comment received				
FRCA supports the proposal not to classify L-(+)-lactic acid for the environment.				
Dossier Submitter's Response				
Thank you very much for your comment.				
RAC's response				
Thank you for your comment.				

PUBLIC ATTACHMENTS
1. PMI comments on L-(+)-lactic acid CLH report.pdf [Please refer to comment No. 1, 10]
2. 2017-04-CHL_proposal_Lactic_Acid.pdf [Please refer to comment No. 2, 11]

CONFIDENTIAL ATTACHMENTS
1. Originale.zip [Please refer to comment No. 4, 9]