

Committee for Risk Assessment
RAC

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

Citric acid

EC Number: 201-069-1
CAS Number: 77-92-9

CLH-O-0000001412-86-299/F

Adopted
20 September 2019

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON CITRIC 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: citric acid

EC number: 201-069-1

CAS number: 77-92-9

Dossier submitter: Belgium

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
01.02.2019	Germany		MemberState	1
Comment received				
<p>In the document comprising the confidential annex an index number is given (607-RST-VW-Y) which does not belong to citric acid. Please delete the corresponding information.</p> <p>Moreover in table 1 in section 1.1 of the CLH report in the second row other names (usual name, trade name, abbreviation) are given. Amongst others "Citric Acid Anhydrous" and "Citric Acid Monohydrate" are stated here. If both substances shall be addressed in this re-port, both CAS numbers must be given as well. Please add the CAS number for "Citric Acid Monohydrate" (5949-29-1) in the corresponding sections, if the substance is addressed as well. Otherwise, please amend the given "Other names" accordingly by deleting the names for the monohydrate.</p> <p>Furthermore in table 7 in section 7 of the CLH report amongst others the property "Stability in organic solvents and identity of relevant degradation products" is listed. In the second column the values for the solubility in several solvents are given. Please amend the name of the property using "solubilty in organic solvents" instead.</p>				
Dossier Submitter's Response				
<p>Thank you for your comment :</p> <ul style="list-style-type: none">- Agreed to delete the index number- only citric acid anhydrous is concerned by this CLH report. Therefore, it is proposed to delete mention of Citric acid monohydrate.- Agreed for amending the name of the property.				
RAC's response				
Noted.				

OTHER HAZARDS AND ENDPOINTS – Skin Hazard

Date	Country	Organisation	Type of Organisation	Comment number
23.01.2019	Austria	<confidential>	Company-Manufacturer	2
Comment received				
<p>1. Introduction The harmonised classification proposal for citric acid (EC 201-069-1, CAS 77-92-9) includes classification for skin irritation. This document discusses the proposed classification, concluding that it is not consistent with the data.</p> <p>1.1 The proposal The proposed entry in Annex VI of Regulation (EC) No 1272/2008 (CLP) includes Skin Irrit. 2, H315. This conclusion is based on the pH of citric acid in aqueous solution (as reported in IUCLID 2000 and in a solubility study), supported by:</p> <ol style="list-style-type: none"> 1. OECD SIDS observations on dermatitis in bakers. 2. Use in anti-aging cosmetics as a chemical peel. 3. The difference in results in the Registration dossier between neat substance applied semi-occlusively and a 30% solution applied to scarified skin. <p>2. Response to the proposal</p> <p>2.1 Classification based on pH According to Regulation (EC) No 1272/2008, pH can be used for classification: "In the absence of any other information, a substance is considered as corrosive to skin (Skin Corrosion Category 1) if it has a pH ≤ 2 or a pH ≥ 11,5." In the tiered approach to classification under Regulation (EC) No 1272/2008, emphasis is placed human data followed by animal data, so where data exists pH is not sufficient to classify.</p> <p>2.2 Observations of dermatitis There is no information about what other substances the bakers have been exposed to, so this evidence is not sufficient to classify. The OECD SIDS reports that patch testing of 60 eczema patients with 2.5% citric acid in petrolatum did not produce any irritant or allergic response.</p> <p>2.3 Use as a chemical peel The harmonised classification and labelling (CLH) report references Yates, 1999 for evidence of use of citric acid as a chemical peel. This publication indicates the presence of citric acid in 4 salon or commercial skin-peel products. No toxicity data are included in the paper. Since there is no information on which other substances were present in the products, it is not evidence of use of citric acid as the effective ingredient in skin peel. Therefore we do not consider this is grounds for classification.</p> <p>2.4 Results of animal studies The in vivo skin irritation guideline, OECD TG 404, requires that "care should be taken to avoid abrading the skin, and only animals with healthy, intact skin should be used." The application of a 30% solution of citric acid to scarified skin is not appropriate to use to justify classification for skin irritation and should be discounted from the overall conclusions on classification.</p> <p>In a study conducting according to OECD TG 404 and in compliance with GLP neat citric acid was applied semi-occlusively, with results which do not trigger classification for skin irritation.</p> <p>3. Conclusion Based on the data presented in the CLH report, and the considerations presented above, there is not sufficient evidence for classification of citric acid as irritating to the skin.</p> <p>References Yates R.L and Havery D.C., 1999. Determination of Phenol, Resorcinol, Salicylic Acid and α-Hydroxy Acids in Cosmetic Products and Salon Preparations, Journal of Cosmetic</p>				

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Science, vol. 50, pp. 315-325
For details please see attachments 1) Response Public Consultation Citric Acid and 2) Jungbunzlauer_Response Public Consultation Citric Acid
ECHA note – An attachment was submitted with the comment above. Refer to public attachment Response Public Consultation Citric Acid.pdf
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Jungbunzlauer_Response Public Consultation Citric Acid.pdf
Dossier Submitter’s Response
Expert judgement was applied based on the available data. Unfortunately, no further data can be provided on the studies from DM. The applied concentration of citric acid has not been specified in OECD TG 404 study and it cannot be excluded that irritation will happen with concentrated solutions that have low pH based on the data on human. Therefore, the position is still supported.
RAC’s response
RAC is also hesitant to support classification based on the data referred to. Although the animal studies are rather poor, they carry more weight than the pH alone in a weight of evidence assessment. Furthermore, as the human data is not conclusive either, due to uncertainties with respect to co-exposure to other chemicals, RAC does not support classification.

Date	Country	Organisation	Type of Organisation	Comment number
01.02.2019	Germany		MemberState	3
Comment received				
The classification of citric acid for Skin Irrit. 2, H315 is supported. As the pH of citric acid in aqueous solutions was reported to be less than 2 and the potential irritant behaviour of citric acid in its use in anti-aging cosmetics, the diluted substance is regarded to be potentially irritating to human skin.				
Dossier Submitter’s Response				
Thank you for your comment and support.				
RAC’s response				
RAC agrees that citric acid is potentially irritating at high concentrations, but does not find sufficient evidence to support classification.				

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
01.02.2019	Germany		MemberState	4
Comment received				
The classification of citric acid for Eye Irrit. 2, H319 is supported. In rabbit tests with 30 % solution the values for conjunctival redness and conjunctival oede-ma (chemosis) fulfil criteria to be classified for Eye Irrit. 2, H319.				
Dossier Submitter’s Response				
Thank you for your comment and support.				
RAC’s response				
RAC agrees and also supports classification for eye irritation.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Single Exposure

Date	Country	Organisation	Type of Organisation	Comment number
01.02.2019	Germany		MemberState	5
Comment received				
<p>The classification of citric acid for STOT SE 3, H335 is supported. In the absence of specific studies, human data on incidences of cough is observed in respiratory sensitization studies. Point a and c of annex 1 3.8.2.2.1 of Regulation (EC) No 1272/2008 are fulfilled.</p>				
Dossier Submitter's Response				
Thank you for your comment and support.				
RAC's response				
RAC agrees that point a and c are fulfilled, and that the cough could be a response to both sensory irritation and cytotoxic irritation. Based on the human data, RAC supports classification.				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
08.02.2019	United Kingdom		MemberState	6
Comment received				
<p>Citric acid (EC: 201-069-1; CAS: 77-92-9) We note that there are data gaps for test item purity and controls validity for some studies including the most sensitive endpoints (McKenzie and Vryenhoef, 2006). It would be useful to present these to confirm study reliability.</p>				
Dossier Submitter's Response				
<p>The test from McKenzie J. and Vryenhoef, H. 2006 was performed with citric acid batch n° S504023. According to the five batch analysis provided in the biocide dossier, this batch has a purity of 99.7%, a water content of 0.036% and an inorganic residue level of 0.188%.</p> <p>According to OECD 201, C3, controls validity criteria are:</p> <p>1° Increase biomass of control during the 0h up to 72h by a factor of 16 at least. The mean cell density in the controls increases during this period from 5.96×10^3 to 3.27×10^5.</p> <p>2° The mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures must not exceed 35%. This value is not expressed specifically in the report. However, based on the raw data, the mean coefficient of variation for section-by-section specific growth rates has been recalculated by the rapporteur and is of 8% for days 0-1, 3% for days 1-2 and 3% for day 2-3</p> <p>3° The coefficient of variation of average specific growth rates during the whole test period in replicate control cultures must not exceed 7% (<i>Desmodesmus subspicatus</i> formerly <i>Scenedesmus subspicatus</i>). This value is 5% in the current test for the control test item.</p> <p>In conclusion, the purity of the test item was not specified but are known via the batch number and suitable as regards to the 5-batch analysis report provided in the biocide dossier. The purity of the test item is 99.7 %.</p>				

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The control validity were not specified in the final report. This is a deviation of the guideline OECD 201, C3 which specified that these informations should be appropriately reported. However, the availability of the raw data allows for recalculation of those parameters. Recalculation shows that the validity criteria for the control were met. This deviation is considered to be not critical in this case. Therefore the test is valid and the result are reliable.

Overall, the score of the study (GLP; OECD guideline 201, C3; quality control,..) can be set to 1 according to klimish classification criteria.

RAC's response

The additional information is noted as well as the confirmation that the study fulfils the criteria for being reliable.

PUBLIC ATTACHMENTS

1. Response Public Consultation Citric Acid.pdf [Please refer to comment No. 2]

CONFIDENTIAL ATTACHMENTS

1. Jungbunzlauer_Response Public Consultation Citric Acid.pdf [Please refer to comment No. 2].