Committee for Risk Assessment

RAC

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

Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland | Tel. +358 9 686180 | Fax +358 9 68618210 | echa.europa.eu

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CLH-O-0000001412-86-299/F

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: **Citric acid**

EC Number: **201-069-1**

CAS Number: **77-92-9**

The proposal was submitted by **Belgium** and received by RAC on **30 October 2018.**

In this opinion, all classification and labelling elements are given in accordance with the CLP Regulation.

PROCESS FOR ADOPTION OF THE OPINION

Belgium has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation/*** on **26 November 2018**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **8 February 2019**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: Bert-Ove Lund

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The RAC opinion on the proposed harmonised classification and labelling was adopted on **20 September 2019** by **consensus**.

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	Citric acid	201-069-1	77-92-9	Skin Irrit. 2 Eye Irrit. 2 STOT SE 3	H315 H319 H335	GHS07 Wng	H315 H319 H335			
RAC opinion	TBD	Citric acid	201-069-1	77-92-9	Eye Irrit. 2 STOT SE 3	H319 H335	GHS07 Wng	H319 H335			
Resulting Annex VI entry if agreed by COM	TBD	Citric acid	201-069-1	77-92-9	Eye Irrit. 2 STOT SE 3	H319 H335	GHS07 Wng	H319 H335			

GROUNDS FOR ADOPTION OF THE OPINION

RAC general comment

Citric acid is a biocide and all hazard classes should therefore be assessed; it is also registered under REACH. The substance is a crystalline solid at room temperature, and many of the studies were performed using 100% neat substance. It is highly acidic when dissolved in water, with a pH <2 at concentrations exceeding 2%. Test results may therefore diverge depending on whether the solid neat substance or an acidic solution has been tested.

RAC evaluation of physical hazards

Summary of the Dossier Submitter's proposal

The dossier submitter (DS) asserted that the available data are not sufficient to classify citric acid for explosive properties, flammability, self-reactivity, pyrophoric properties, self-heating, emission of flammable gases, oxidising properties and corrosivity to metals. Classifications for other physical hazards are not applicable.

Comments received during public consultation

No comments were received.

Assessment and comparison with the classification criteria

RAC agrees that based on data, structural considerations or experience of handling the substance, **no classification for any of the physical hazards** is warranted.

HUMAN HEALTH HAZARD EVALUATION

RAC evaluation of acute toxicity

Summary of the Dossier Submitter's proposal

Acute oral toxicity

In the majority of studies, the acute oral LD_{50} is reported as being > 5000 mg/kg bw. The exception was a poorly reported study from 1975, where Test I gave an LD_{50} of 1700 mg/kg bw in rats. However, this value could not be reproduced by the same laboratory in rats of the same strain in an acute oral study (Test II-single) or in a 5-day oral study (Test II-5 days). Given the obvious difference between the results from the first experiment (Test I) and the subsequent experiments (Test II) yielding LD_{50}-values of 2409- 11700 mg/kg bw/day in rats and mice, it seems likely that a technical variable or artefact was the reason for the low value in Test I. The DS suggested a weight of evidence approach in which the isolated lower value is excluded by placing greater weight on the remaining values (LD_{50}>2400 mg/kg bw), which would not warrant classification for acute oral toxicity.

Acute dermal toxicity

A dermal OECD TG 402 test was performed in 2006, where 2000 mg/kg bw crystalline citric acid was applied to the skin of shaved rats. As no signs of toxicity was observed, the DS concluded that no classification is warranted.

Comments received during public consultation

There were no comments.

Assessment and comparison with the classification criteria

Acute oral toxicity

There are three acute oral studies available, with two rather old studies using both rats and mice (1971 and 1975), and a study from 1981 using only mice (cited as OECD, 2001). The citric acid was dissolved in saline (1975), tap water (OECD, 2001) or a not stated vehicle (Yokotani, 1971). Yokotani *et al.* (1971) obtained LD_{50}-values of 11700 mg/kg bw in rats and 5040 mg/kg bw in mice. OECD (2001) reported an LD_{50} of 5400 mg/kg bw in mice. The 1975 study consisted of four sub-studies, which resulted in LD_{50}-values of 1700 mg/kg bw (Test I) and >5000 mg/kg bw (Test II) in rats, and after 5-day oral daily administrations 'LD_{50}'-values of 4696 mg/kg bw/day in rats and 2409 mg/kg bw/day in mice (Test II).

All studies have some shortcomings, hence RAC supports the use of expert judgement and a weight of evidence approach in assessing them. RAC also agrees that the value of 1700 mg/kg bw has little weight, since the follow-up studies in the same rat strain gave an acute LD_{50} value of >5000 mg/kg bw and an 'LD_{50}' value 4696 mg/kg bw/day after 5 daily administrations. RAC thus concludes that the LD_{50} is above 2000 mg/kg and that **no classification for acute oral toxicity is warranted**.

Acute dermal toxicity

One acute dermal study in rats was available (2006), where neat substance at the limit dose (2000 mg/kg bw) was applied to the rat skin. RAC notes that the study deviates from the present OECD TG 402 because the solid substance was not moistened to ensure good contact with the skin. Nevertheless, RAC concludes that, as no signs of toxicity were observed after a 24-hour exposure to the neat substance, citric acid crystals **should not be classified for acute dermal toxicity**.

RAC evaluation of specific target organ toxicity – single exposure (STOT SE)

Summary of the Dossier Submitter's proposal

There were no indications of specific target organ toxicity that would warrant a classification as STOT SE 1 or 2 in the single exposure studies, nor were narcotic effects observed. In the section on respiratory sensitisation, cough was observed in three human studies. In two studies, no relevant effects other than cough were observed. The third study demonstrated that spontaneous, presumably viral, upper respiratory tract infections cause striking increases in bronchial reactivity to inhaled citric acid aerosols in otherwise normal subjects. Therefore, due to the cough, point (a) of annex 1, 3.8.2.2.1 of Regulation (EC) No 1272/2008 was considered to be fulfilled. The cough was expected to appear in the exposed population and not to be an isolated idiosyncratic

reaction triggered only in individuals with hypersensitive airways, as the studies were done on healthy volunteers (criteria c is also fulfilled). However, no objective measurements as electrophysiological responses, biomarkers of inflammation were available (point b). In the absence of other specific data, classification as STOT SE 3; H335 was proposed.

Comments received during public consultation

One comment was received from a Member State that supported the proposed classification based on fulfilling points a) and c) as described above.

Assessment and comparison with the classification criteria

Three studies were conducted where volunteers were exposed to citric acid under controlled conditions.

Winther *et al.* (1970) exposed 10 persons to aerosol (5-25% citric acid) and the only effect observed was cough, but no information on which concentrations had caused the cough or on the dose-response relationship is given in the CLH report or its annex. At each concentration, 5 inhalations of aerosol (with 3 minutes in between them) were performed and the immediate cough response was recorded.

Empey *et al.* (1976) exposed 12 controls to aerosol (0.25-20% citric acid) and the only effect observed was cough, with a median threshold concentration of 3.75% triggering immediate cough after an inhalation of the aerosol. They also observed that 7 other volunteers having a cold were more sensitive to the triggering of cough (2% median threshold) than the controls.

Barros *et al.* (1990) exposed 11 volunteers to increasing concentrations of citric acid (2.5 mg/L up to 640 mg/L, presumably citric acid crystals), and the only effect observed was cough. The cough threshold, measured as a cough immediately following one inhalation, was 21 mg/L at a flow rate of 50 L/min, and an increased cough threshold was noted at higher flow rates. No information was given on variation between the subjects or if the threshold value provided was, e.g., a median value.

Although the studies are very poorly reported, there seems to be a consistent cough response caused by citric acid in all three studies, with the findings of Empey *et al.* (1976) providing the strongest evidence. A cough response was observed when breathing aerosols produced from a 3.75% citric acid solution. RAC agrees that the CLP criteria 3.8.2.2.1. a) cough is observed in humans as a respiratory irritant symptom, and c) the symptoms are observed in normal healthy humans, are met. RAC notes that also criterion e) is met ("…only when more severe organ effects including in the respiratory system are not observed"). The Guidance on the Application of the CLP Criteria v. 5.0, July 2017 ("CLP guidance"), section 3.8.2.3, states that application of STOT SE 3 "is generally limited to local cytotoxic effect" and not to sensory irritation. In the three studies, the cough reaction was observed immediately after a single inhalation of citric acid, but it is not known whether the reaction was caused by a cytotoxic effect or sensory irritation. RAC notes that the low pH (<2) as well as the indications of eye irritation suggest that citric acid may act via a local cytotoxic effect in the airways. However, there are no animal inhalation studies with citric acid to shed light on the potential to cause cytotoxic effects in the respiratory system, and the human studies indicated no effects other than the immediate cough response. Besides not knowing the mode of action (MoA) for the cough reaction, RAC notes that the CLP regulation as such (section 3.8.2.2) does not make this distinction between cytotoxic and sensory irritation. The legal text carries more weight than the guidance, and RAC is thus of the view that the MoA is of little importance as long as effects fulfilling the CLP criteria are observed.

RAC concludes that cough is triggered in humans, so based on the human data, RAC supports **classification with STOT SE 3 for respiratory tract irritation**.

RAC evaluation of skin corrosion/irritation

Summary of the Dossier Submitter's proposal

According to the DS, the available results indicate that under the current test methods citric acid is not irritating to the skin of animals. The CLP guidance suggests that strong acids with pH < 2 should be classified as Skin Corrosive, Category 1. The substance does not qualify as a strong mineral acid or oxidising substance. Furthermore, indicative studies on citric acid suggest that the substance has the potential to be a skin irritant when moistened, with the potency of the irritation response being determined by the concentration in aqueous solutions. A classification of irritant rather than corrosive was considered appropriate by the DS.

Due to the pH of aqueous solutions of citric acid, the diluted solutions have the potential to be irritant to human skin. Taking into account the evidence presented, the DS concluded that a classification as skin irritant category 2 is warranted.

Comments received during public consultation

One Member State supported the proposed classification mainly based on the low pH of citric acid solutions. One company opposed the classification based on the following:

- (negative) animal data being more important than the pH,
- inconclusive human data regarding its use by bakers and the potential use of citric acid as a chemical peel,
- animal data on abraded skin should not be considered, according to the CLP guidance.

Assessment and comparison with the classification criteria

Seven studies are described in the CLH report, six of them being *in vivo* studies in rabbits.

Two OECD TG 404 studies from 1990, have reliability scores of 1 in the CLH report, but considering identical results they may possibly refer to the same study. In both studies solid citric acid was applied to shaved skin and moistened with water, but the amount of citric acid was 0.5g in one study and unknown in the other. The average erythema score was 0.3 in both studies, and solid citric acid is thus non-irritant according these studies.

Two studies, having reliability scores of 2 in the CLH report, seem to have used 30% (study report, 1984) or 50% citric acid (study report, 1979) dissolved in water for application on intact skin. No irritation was observed on intact skin. Although erythema and oedema were observed on abraded skin in one of the studies, it is clear from the OECD TG 404 that "*care should be taken to avoid abrading the skin, and only animals with healthy, intact skin should be used*".

There are 2 additional rabbit studies, with reliability scores of 4, but since it is not clear how citric acid had been tested, these (negative) studies cannot be used in this assessment.

In the seventh study, a 50% solution of citric acid was applied for 5 minutes on the tongue of dogs resulting in severe ulceration. However, this study cannot be used in relation to classification for skin corrosion/irritation as the relevance of the reaction on the dog tongue in relation to skin irritation is not clear. Furthermore, the study is very poorly reported and it is not clear how the substance was administered.

The DS also used the finding of citric acid in skin peel cosmetics as supporting evidence for an irritating potential of citric acid. RAC notes that the only information comes from one study from 1999 showing citric acid in 4% of the commercial skin peel products analysed, at concentrations of 0.2-4% citric acid. However, it is not known if it is citric acid or other components that cause the skin peeling.

Based on the rabbit studies, neither solid nor dissolved citric acid appear to cause irritation *in vivo* in rabbits. When citric acid is dissolved in water, a pH <2 can be expected at the concentrations used in the 1979 and 1984 studies (50 and 30%, respectively). Nevertheless, no irritation was observed in those *in vivo* studies, suggesting that, in this case, a pH<2 cannot be used as a predictor of skin irritation/corrosion.

As discussed in more detail in the supplemental information section (below), consideration of the acid/alkaline reserve of citric acid does not support corrosivity, and there is no CLP guidance on how to use the information of acid/alkaline reserve in assessing irritation.

Taken together, RAC is of the opinion that the evidence is **not sufficient for classification for skin corrosion/irritation** even though some skin reactions might be expected from concentrated solutions of citric acid.

RAC evaluation of serious eye damage/irritation

Summary of the Dossier Submitter's proposal

In a reliable study performed according to OECD TG 405, a 10 % aqueous solution of citric acid induced moderate to weak conjunctival irritation, which was fully reversed after 7 days. In contrast, a 30 % aqueous solution of citric acid caused well-defined to moderate conjunctival irritation of the rabbit eye (redness not fully resolved in one animal after 14 days) accompanied by discharge and superficial ulceration of conjunctival epithelium. The DS concluded that citric acid had the potential to induce reversible eye irritation and should be classified as Category 2 (irritating to eyes).

Comments received during public consultation

One Member State supported the proposed classification.

Assessment and comparison with the classification criteria

One OECD TG 405 study in rabbits is available (from 1984). An aqueous solution (0.1 mL, concentration 10% or 30%) of citric acid was administered to 3 rabbits per group, followed by examination at 1, 24, 48, and 72 hours. The condition of the animals was then followed for 14 days.

At 10%, only conjunctival effects were noted, and they were fully reversible by day 7.

A 30% solution caused immediate (1h) conjunctival redness, chemosis, and discharge, followed by ulceration at 24 hours. After 3 days the symptoms started to decrease, but redness remained in one animal until end of study at day 14 (score 1). OECD TG 405 recommends humane killing of test animals when conjunctival ulceration appears, as such lesions generally are not reversible. It is not clear if the ulceration observed in this study was indeed reversible or incorrectly diagnosed. The average score during the 24-72 h examinations were 3 for conjunctival redness and 2.33 for conjunctival oedema (chemosis). Some conjunctival redness (score 1) remained in

one of the three rabbits at the end of the 14-day observation period. However, it is possible and likely that it would have disappeared by day 21 as required by the criteria for substances causing reversible effects on the eyes, and therefore citric acid should be classified for eye irritation.

Thus, RAC supports the DS's proposal to **classify citric acid for eye irritation, Category 2, H319: 'Causes serious eye irritation'**.

RAC evaluation of respiratory sensitisation

Summary of the Dossier Submitter's proposal

According to the DS there was no evidence from the human data available that the substance had the potential to cause respiratory sensitisation. No classification was proposed.

Comments received during public consultation

No comments were received.

Assessment and comparison with the classification criteria

As there are no indications of citric acid being able to elicit respiratory sensitisation, RAC supports the DS proposal for **no classification**.

RAC evaluation of skin sensitisation

Summary of the Dossier Submitter's proposal

There were no publicly available data on the sensitisation properties of citric acid in animals. There were several studies in humans on potential allergenic reactions to the substance via inhalation, in addition to patch testing of the active substance. According to the DS the results of these human studies indicated that there was no conclusive evidence for allergic effects caused by oral exposure or for contact sensitisation from dermal exposure. The DS considered citric acid not to be a skin sensitiser.

Comments received during public consultation

No comments were received.

Assessment and comparison with the classification criteria

There are no animal data available. The only data available is a repeated insult patch test on 197 humans (2002), where the subjects were exposed to patches (for 24 hours) treated with the biocidal product (concentration not known, product used as marketed) for 9 consecutive days followed by a rest period of 10-15 days. A new patch was administered on a previously unexposed site, and observations were recorded 24 and 48 hours after removal of the patch. In one subject, erythema was observed, and consequently, minimal or no effects were recorded in the remaining 196 subjects.

Based on no evidence of sensitisation, RAC supports **no classification**.

RAC evaluation of specific target organ toxicity – repeated exposure (STOT RE)

Summary of the Dossier Submitter's proposal

Of the available reported sub-chronic and chronic oral dietary studies in the rat, rabbit and dog, toxic effects were considered indicative of overloading of the metabolic pathways. The NOAEL for repeat oral dose was 1960 mg/kg bw/day based on the 2-year study in the rat. The adverse effect was based on reduction in bodyweight gain from reduced food consumption, which may have been due to adverse taste in the diet.

The substance is required by all organisms for the functioning of the Krebs cycle. Citric acid is rapidly oxidised to carbon dioxide and water in the citric acid (Krebs) cycle in the cells of all the organs, but especially in those with high concentrations of mitochondria and in well-vascularised organs. There were no adverse effects seen at levels below the limit dose level for non-human studies (1000 mg/kg bw/day). In the absence of toxic effects, classification and labelling for repeated dose effects (STOT RE) was deemed by the DS as not required.

Comments received during public consultation

No comments were received.

Assessment and comparison with the classification criteria

The CLH report describes seven old (1945-1976) non-guideline studies covering rats, mice, rabbits and dogs with dietary exposure to citric acid or sodium citrate. As no effects were seen at exposure levels below the guidance values for classification, RAC supports the proposal for **no classification as STOT RE**.

RAC evaluation of germ cell mutagenicity

Summary of the Dossier Submitter's proposal

Citric acid was found to be non-mutagenic, with or without metabolic activation, in a bacterial reverse gene mutation study performed using a method similar to OECD TG 471. Citric acid was non-clastogenic without metabolic activation in two *in vitro* chromosome aberration studies performed using CHL cells. Citric acid has been tested according to a method that is similar to OECD TG 473, without activation, and a statistically significant and dose-related increase in the number of cells with aberrations was observed after 24 and 48 hours incubation, including sister chromatid unions which are not usually reported. Insufficient information was provided to analyse the data excluding sister chromatid unions. It was concluded that there may have been potential for citric acid to induce chromosome aberrations in cultured human lymphocytes under the conditions of this study. Citric acid was reported to be non-mutagenic in an *in vivo* rat bone marrow test and not mutagenic or clastogenic in a rat Dominant lethal assay. Taking into consideration the *in vitro* and *in vivo* results, classification was deemed by the DS as not required.

Comments received during public consultation

No comments were received.

Assessment and comparison with the classification criteria

Of the *in vitro* studies, one chromosomal aberration study was positive with a dose-dependent increase especially in sister chromatid unions. The increase was statistically significant and dose-dependent at 24 hours (0.02-0.13-0.19-0.25 chromosome aberrations per cell at 0-50-100-200 µg citric acid/mL), and although statistically significant also at 48 hours, the dose-dependence was less clear at 48 hours. However, as no effects were seen in the two *in vivo* studies (a rat bone marrow chromosome aberration test and a 5 day rat dominant lethal assay at up to 3000 mg/kg bw/day, both of which included an acute study with doses up to 3500 mg/kg bw), and citric acid is an endogenous substance known to be rapidly metabolised, there is no concern for germ cell mutagenicity. Thus, RAC supports the DS proposal for **no classification for germ cell mutagenicity**.

RAC evaluation of carcinogenicity

Summary of the Dossier Submitter's proposal

In the absence of evidence for carcinogenic effects, classification was deemed by the DS to not be required.

Comments received during public consultation

No comments were received.

Assessment and comparison with the classification criteria

There are no proper carcinogenicity studies available. There are no indications of carcinogenicity or precursor effects in the long-term studies available (120 days in dogs at 1380 mg/kg/day, 150 days in rabbits at 2825 mg/kg/day, 14 months in mice at 7500 mg/kg/day, and 2 years or lifetime exposure in rats at ≥1280 and 470 mg/kg/day, respectively). RAC supports **no classification for carcinogenicity**.

RAC evaluation of reproductive toxicity

Summary of the Dossier Submitter's proposal

There is no evidence in the available studies of citric acid causing reproductive effects up to and above the limit dose level in non-human studies (1000 mg/kg bw/day). The DS proposed no classification.

Comments received during public consultation

No comments were received.

Assessment and comparison with the classification criteria

There are two old 2-generation studies available (Bonting and Jansen, 1956; Wright and Hughes, 1976) where rats were exposed to citric acid via the diet (1.2% and 5%, respectively). The

quality of these studies is considered to be poor, with possibly 8 and 6 exposed rats per study, respectively. No effects were reported.

There are three very poorly reported, and possibly poorly conducted, developmental toxicity studies in rats, mice, and rabbits. None fulfil any requirements on reporting on e.g dose levels or number of animals used. Nevertheless, no effects on development were reported.

RAC notes the lack of adequate data for this endpoint and supports no classification.

ENVIRONMENTAL HAZARD EVALUATION

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

Citric acid is a naturally occurring substance which has high water solubility (>500 g/L).

The biodegradation of citric acid was tested in four ready biodegradability tests according to OECD TG 301 A, B, D, and E but not according to GLP, all showing ≥90% biodegradation within the 10d window. Thus, the DS considered citric acid as readily biodegradable and, consequently, as rapidly degradable for classification.

A negative log Pow (<-3.76 according to EC method A8) indicated no bioaccumulation potential. Also, the active substance naturally occurs in all organisms and there is a mechanism for the elimination of the substance via the Kreb's cycle. Therefore, the DS concluded that there is a low potential for bioaccumulation.

Citric acid E(L)C_{50} values for all trophic levels were above 1 mg/L, with the lowest values being caused by a pH-effect of the acid (E_bC_{50} (72h) of 1.9 mg/L for algae and EC_{50} (48h) of 34 mg/L for *Daphnia*), so the acute toxicity to fish, invertebrates and algae is low and the DS concluded that no classification for acute aquatic toxicity was warranted.

Chronic toxicity data were not available for all 3 trophic levels, therefore both chronic data and acute data for the other trophic levels are compared with the CLP criteria. The only chronic toxicity data available concern algae, with the lowest NOEC for *Scenedesmus subspicatus* (72h NOEC = 1.4 mg/L) (new name is *Desmodesmus subspicatus)*. However, it should be noted that toxicity is considered to be caused by the initial drop in pH caused by addition of citric acid to water. In addition, citric acid seems to be less toxic towards other algae like *Scenedesmus quadricauda* or *Pavlova lutheri*.

Due to the rapid degradability of the substance and a NOEC above 1 mg/L, the substance does not meet the classification criteria for aquatic chronic toxicity. The lowest EC_{50} value for the other trophic levels (fish and invertebrates) was determined for *Daphnia magna* (most sensitive species with 48h EC_{50} = 34 mg/L). In combination with the rapid degradability and BCF below 500 of citric acid, the chronic classification criteria are not met. Therefore, the DS concluded that classification for chronic aquatic hazards was not warranted.

Comments received during public consultation

One Member State asked for further data on the algae study to confirm the reliability of the study providing the most sensitive endpoints, which the Dossier Submitter did in the RCOM and concluded on a reliability score of 1 for that study.

Assessment and comparison with the classification criteria

Rapid degradability

Based on four reliable ready biodegradability studies indicating that citric acid is biodegraded to a level ≥ 70% after 28d (within the 10d window), RAC agrees with the DS that citric acid is readily biodegradable and, consequently, rapidly degradable for classification.

Bioaccumulation

Based on a log Kow of <-3.76 being below the CLP criterion of 4, together with citric acid being naturally occurring and removed via the Kreb's cycle in organisms, RAC agrees with the DS that citric acid has a low potential for bioaccumulation.

Aquatic toxicity

The key data for each trophic level is summarised in the following table.

***Table**: Key aquatic toxicity studies, all assessed as reliable by RAC*

Species	Method	Endpoint	Toxicity value	Reference
Acute studies				
Fish, *Oncorhynchus mykiss* (rainbow trout)	OECD TG 203, semi-static, GLP	LC_{50} (96 h)	>100 mg/L	Anonymous (2006)
Invertebrate, *Daphnia magna*	OECD TG 202, Static, GLP	EC_{50} (48 h)	34 mg/L	Mead and Hill (2006)
Algea, *Scenedesmus subspicatus,* renamed *Desmodesmus subspicatus*	OECD TG 201, static, GLP	EbC_{50} (72h)	1.9 mg/L	McKenzie and Vryenhoef (2006)
Chronic studies				
Algea, *Scenedesmus subspicatus,* renamed *Desmodesmus subspicatus*	OECD TG 201, static, GLP	NOEC (72h)	1.4 mg/L	McKenzie and Vryenhoef (2006)

An algae study performed according to OECD TG 201 and GLP provides the lowest acute and chronic toxicity values (E_bC_{50} (72h) 1.9 mg/L), seemingly caused by the pH drop caused by the addition of citric acid. Acute toxicity data are also available for invertebrates and fish. As the acute toxicity in three trophic levels is below 1 mg/L, RAC agrees with the DS that classification for acute aquatic toxicity is not warranted.

The only chronic data available is for algae (NOEC (72h) 1.4 mg/L). As this value is above 1 mg/L and citric acid is considered rapidly degradable, it does not meet the criteria for chronic aquatic toxicity classification. The acute toxicity data (above 1 mg/L) for fish and invertebrates, in combination with rapid degradability and a low potential for bioaccumulation, likewise do not lead to classification. Consequently, RAC agrees with the DS that citric acid does not warrant classification for chronic aquatic hazards.

In conclusion, RAC agrees with the DS that **citric acid does not warrant classification for hazards to the aquatic environment.**

Additional references

Scheel *et al*. (2011). Classification and labelling of industrial products with extreme pH by making use of *in vitro* methods for the assessment of skin and eye irritation and corrosion in a weight of evidence approach. Toxicology in vitro, 25, 1435-47.

Young *et al*. (1988) Classification as corrosive or irritant to skin of preparations containing acidic or alkaline substances, without testing on animals. Toxicology in vitro, 2(1), 19-26.

ANNEXES:

Annex 1 The Background Document (BD) gives the detailed scientific grounds for the opinion. The BD is based on the CLH report prepared by the Dossier Submitter; the evaluation performed by RAC is contained in 'RAC boxes'.

Annex 2 Comments received on the CLH report, response to comments provided by the Dossier Submitter and RAC (excluding confidential information).