Agency technical report on the classification and labelling of:

peracetic acid …%

EC Number: 201-186-8
CAS Number: 79-21-0

March 2023

Contents

Brief summary

The conclusion of the Agency technical report is that peracetic acid meets the classification criteria for:

Org. Perox. D; H242 (Heating may cause a fire)

NOT CLASSIFIED for flammable liquids

Acute Tox. 3; H301 (Toxic if swallowed) with an ATE of 80 mg/kg bw

Acute Tox. 2; H310 (Fatal if in contact with skin) with an ATE of 60 mg/kg bw

Acute Tox. 2; H330 (Fatal if inhaled) with an ATE of 0.2 mg/l (dust/mists)

Aquatic Acute 1; H400 (Very toxic to aquatic life) with an Acute M-factor of 10

Aquatic Chronic 1; H410 (Very toxic to aquatic life with long lasting effects) with a Chronic M-factor of 100

The Agency also supports the addition of Note T and the supplementary labelling phrase “EUH071 - corrosive to the respiratory tract”

Is this in agreement with the RAC opinion? **YES**

At the time of publication, this mandatory classification and labelling (MCL) has not been agreed and/or adopted in Great Britain.

This is a targeted technical report which considers the following hazard classes: flammable liquids, organic peroxides, acute toxicity (oral, dermal and inhalation routes) and hazardous to the aquatic environment. These were the only hazards assessed in the EU harmonised classification and labelling (CLH) report and Committee for Risk Assessment (RAC) Opinion.

This substance has an existing MCL which includes Skin Corr. 1A. Skin corrosion is not assessed in this technical report, therefore Skin Corr. 1A should be retained in the GB MCL.

Introduction

Under Article 37 of the GB CLP Regulation[1], the Agency[2] is required to produce a technical report for each substance on which the Committee for Risk Assessment (RAC) of the European Chemicals Agency produces an opinion[3].

This technical report documents an independent scientific assessment, conducted by HSE technical specialists with support from the Environment Agency for the environmental hazard classification, of the classification and labelling of peracetic acid.

Table 1. Information considered in the scientific assessment

Document	Included in assessment
EU CLH report	Yes
Annexes to the EU CLH report	Yes
RAC opinion	Yes
Background document	Yes
Information submitted during the EU public consultation process (RCOM table, including attachments)	Yes
RAC minority opinion(s)	Not Applicable
Other information:	No

This information has been evaluated against the classification and labelling criteria set out in the GB CLP Regulation.

[1]The retained CLP Regulation (EU) No. 1272/2008 as amended for Great Britain

[2] HSE acting in its capacity as the GB CLP Agency

[3] Under Article 37(4) of Regulation (EU) No 1272/2008 on classification, labelling and packaging of substances and mixtures

Overview of current and proposed classification and labelling

Table 2. Current and proposed classification and labelling

	Index No.	International Chemical Identification	EC No.	CAS No.	Classification		Labelling			Specific Concentration Limits, M-factors	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)		
GB MCL List entry	607-094-00-8	peracetic acid … %	201-186-8	79-21-0	Flam. Liq. 3 Org. Perox. D**** Acute Tox. 4 * Acute Tox. 4 * Acute Tox. 4 * Skin Corr. 1A Aquatic Acute 1	H226 H242 H332 H312 H302 H314 H400	GHS02 GHS05 GHS07 GHS09 Dgr	H226 H242 H332 H312 H302 H314 H400		* STOT SE 3; H335: C ≥ 1 %	B, D
EU dossier submitter's proposal	607-094-00-8	peracetic acid … %	201-186-8	79-21-0	**Retain** Org. Perox. D**** Aquatic acute 1 **Add** Aquatic Chronic 2§ **Modify** Acute Tox. 2 Acute Tox. 2 Acute Tox. 3 **Remove** Flam. Liq. 3	**Retain** H242 H400 **Add** H411§ **Modify** H330 H310 H301 **Remove** H226	**Retain** GHS02 GHS09 **Add** GHS06 **Remove** GHS07	**Retain** H242 **Modify** H330 H310 H301 H410 **Remove** H226	**Add** EUH071	**Add** inhalation: ATE = 0.204 mg/L (dusts and mists) dermal: ATE = 56.1 mg/kg bw oral: ATE = 70 mg/kg bw M = 10	
EU RAC opinion	607-094-00-8	peracetic acid …%	201-186-8	79-21-0	**Retain** Org. Perox. D Aquatic Acute 1 **Add** Aquatic Chronic 1 **Modify** Acute Tox. 2 Acute Tox. 2 Acute Tox. 3 **Remove**	**Retain** H242 H400 **Add** H410 **Modify** H330 H310 H301 **Remove**	**Retain** GHS02 GHS09 **Add** GHS06 **Remove** GHS07	**Retain** H242 **Modify** H330 H310 H301 H410 **Remove** H226	**Add** EUH071	**Add** inhalation: ATE = 0.2 mg/L (dusts and mists) dermal: ATE = 60 mg/kg bw oral: ATE = 80 mg/kg bw M = 10 M = 100	**Add** T

	Index No.	International Chemical Identification	EC No.	CAS No.	Classification		Labelling			Specific Concentration Limits, M-factors	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)**		
					Flam. Liq. 3	H226					
Agency technical report conclusion	607-094-00-8	peracetic acid …%	201-186-8	79-21-0	**Retain** Org. Perox. D Aquatic Acute 1 **Add** Aquatic Chronic 1 **Modify** Acute Tox. 2 Acute Tox. 2 Acute Tox. 3 **Remove** Flam. Liq. 3	**Retain** H242 H400 **Add** H410 **Modify** H330 H310 H301 **Remove** H226	**Retain** GHS02 GHS09 **Add** GHS06 **Remove** GHS07	**Retain** H242 **Modify** H330 H310 H301 H410 **Remove** H226	**Add** EUH071	**Add** inhalation: ATE = 0.2 mg/L (dusts and mists) dermal: ATE = 60 mg/kg bw oral: ATE = 80 mg/kg bw M = 10 M = 100	**Add** T
Resulting MCL entry on GB MCL list	607-094-00-8	peracetic acid … %	201-186-8	79-21-0	Org. Perox. D Acute Tox. 2 Acute Tox. 2 Acute Tox. 3 Skin Corr. 1A Aquatic Acute 1 Aquatic Chronic 1	H242 H330 H310 H301 H314 H400 H410	GHS02 GHS06 GHS05 GHS09 Dgr	H242 H330 H310 H301 H314 H410	EUH071	inhalation: ATE = 0,2 mg/L (dusts and mists) dermal: ATE = 60 mg/kg bw oral: ATE = 80 mg/kg bw STOT SE 3; H335: C ≥ 1 % M = 10 M = 100	B, D, T

§ proposal changed to Aquatic Chronic 1, M factor = 100, H410 after the commenting period

Background

Active substance in Plant Protection Products: ☐

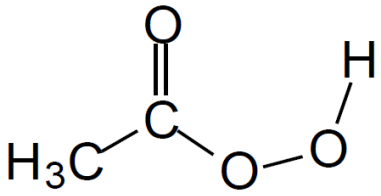
Active substance in Biocidal Products: ☒

Chemical registered under REACH: ☒

The substance is produced by reacting hydrogen peroxide with acetic acid in aqueous solution. In this process, peracetic acid is not obtained as a pure substance but in the form of aqueous solutions containing peracetic acid, acetic acid, hydrogen peroxide and water (Finland, 2015). According to the CLH report, peracetic acid…% (PAA) is a biocidal active substance with strong bactericidal, fungicidal, and virucidal activity (CLH, 2021). The uses belong to the Product Types PT 1 – 5 (disinfectants), 6 & 11 (preservatives) and 12 (slimicides).

PAA is registered under the EU REACH Regulation and is manufactured in, or imported into, the European Economic Area at ≥ 1000 to < 10000 tonnes per annum. The substance is used by consumers and by professional workers (widespread uses) in formulation and repackaging at industrial sites and in manufacturing.

Figure 1. Structure of peracetic acid (taken from ECHA, 2021a)



The current classification of peracetic acid was derived under Directive 67/548/EEC; the classification was then “translated” to give the following classification in Annex VI of the EU CLP Regulation: Flam. Liq. 3 (H226), Org. Perox. D **** (H242), Acute Tox. 4* (H302, H312 and H332), Skin Corr. 1A (H314) and Aquatic Acute 1 (H400), with a specific concentration limit (SCL) of *STOT SE 3; H335: C ≥ 1%. The ‘****’ indicates a physical hazard which needs to be confirmed by testing, and ‘*’ indicates that this is a minimum classification. The dossier submitter (DS – Finnish Safety and Chemicals Agency) prepared a CLH report to reassess the physical hazards covered by the existing

harmonised classification. The DS also sought to address the minimum classifications for acute toxicity and assist classification of mixtures containing PAA, by deriving ATE values for a theoretical 100% PAA, which owing to its high reactivity cannot exist in the pure state. ATE values were derived by linear extrapolation from LD_{50} values obtained from acute toxicity tests on equilibrium mixtures of PAA (varying % PAA and other ingredients). RAC noted that this method constitutes a conservative approach for hazard assessment purposes.

Scientific assessment of the physical, human health and environmental hazard classes

Physical Hazards

Classification agreed by RAC:

Flammable liquids

According to section 2.6.1 of Annex I of CLP, a flammable liquid is one which has a flash point of not more than 60ºC. For PAA, flash point measurements were carried out with the Pensky Martens closed-cup tester (non-equilibrium method) on a solution containing: PAA 39.6%, acetic acid 2.0% and H_2O_2 0.34%. The flash point was measured 3 times, and the following results were obtained: 61ºC, 63ºC and 63°C.

RAC noted that for classification purposes it is recommended to use the mean of two or more test runs, and that if the experimentally determined flash point is within ± 2°C of the threshold limit when using a non-equilibrium method, it is recommended to repeat the determination with an equilibrium method. The arithmetic mean of the three measurements is 62.5°C, which is outside ± 2°C of the threshold limit. Equilibrium methods are also advised if the boiling points of the components of the mixture cover a wide range of temperatures or their concentrations are very different, as was the case here (see above description of the tested PAA solution). Therefore, RAC considered that the equilibrium method should have been used. However, RAC also noted that the flash point for liquid organic peroxides is only relevant in the temperature range where the organic peroxide is thermally stable (ECHA, 2017). Above the Self-Accelerating Decomposition Temperature (SADT) of the organic peroxide, the determination of the flash point is not relevant because decomposition products are evolved. The SADT is 55°C for PAA 38% and 40°C for PAA 41.5% (as reported in table 10 of the CLH dossier). Considering that the SADT is below 60°C and below the flash point, RAC considered that the hazard class flammable liquid is not applicable for this substance. Therefore, in agreement with the DS, RAC concluded that Flam. Liq. 3 should be removed from the existing harmonised classification.

Organic peroxides

The classification of organic peroxides is performed in accordance with test series A to H as described in Part II of the UN RTDG, Manual of Tests and Criteria. Three compositions

of PAA were investigated (PAA 38%, PAA 13.4% and PAA 41.5%). According to the criteria specified in the UN RTDG, the three compositions should be classified as type F organic peroxides. However, previous assessments have indicated that PAA 40.9% is classified as Org. Perox. D, PAA 38.3% is classified as Org. Perox. D and PAA 20.5% is classified as Org. Perox. F. Therefore RAC noted it is not only the concentration of PAA that influences the classification; the concentrations of acetic acid and H_2O_2 also affect the result. Considering the variability of the classification values based on composition, RAC agreed with the DS that the current harmonised classification as Org. Perox. D should be retained and the asterisks removed. RAC also suggested adding note T, which states:

'This substance may be marketed in a form which does not have the physical hazards as indicated by the classification in the entry in Part 3. If the results of the relevant method or methods in accordance with Part 2 of Annex I of this Regulation show that the specific form of substance marketed does not exhibit this physical property or these physical hazards, the substance shall be classified in accordance with the result or results of this test or these tests. Relevant information, including reference to the relevant test method(s) shall be included in the safety data sheet'.

Classification proposed by the Agency:

The Agency agrees with RAC's assessment of the data. Flam. Liq. 3; H226 (Flammable liquid and vapour) should be removed from the existing GB MCL list entry.

Org. Perox. D; H242 (Heating may cause a fire) should be retained (asterisks removed). The Agency also supports the addition of Note T.

Health Hazards

Acute Toxicity

Classification agreed by RAC:

Acute toxicity – oral route

Eighteen acute oral toxicity studies (all in rats) were available in the CLH report. The studies were conducted on test materials containing PAA at concentrations ranging from 0.15 to 36.4%. For the purposes of classification, theoretical LD_{50} values for 100% PAA were derived by linear extrapolation from the LD_{50} value obtained in each study (i.e., the LD_{50} relating to the test material - a mixture of peracetic acid, hydrogen peroxide, acetic acid and other substances). The DS identified three key studies (all GLP and OECD TG

compliant; Klimisch 1) and three supportive studies for the assessment of acute oral toxicity (see Table 3). RAC agreed with the DS to exclude the remaining 12 studies from the assessment (based on e.g., low Klimisch score, lack of vehicle, inadequate study design).

Table 3. LD_{50} values calculated for 100% PAA from the results of the key and supportive studies (reproduced from ECHA (2022a))

LD_{50} (mg/kg/bw) for 100 % PAA				
Reference Study type (Klimisch Score)	**Males**	**Females**	**Combined**	**PAA Concentration**
Anonymous (1998b), key (1)	99.7	93	96.1	5%
Anonymous (1995), key (1)	-	-	271	15.2%
Anonymous (1985), key (1)	95	70	85	5%
Anonymous (1998c), supportive (1)	183.2	236.2	202.8	5.6%
Anonymous (1993), supportive (2)	-	-	77.6	6.11%
Anonymous (1982), supportive (2)	153.9	152.3	-	15%

Clinical signs reported in the studies included piloerection, respiratory difficulties, abdominal gripping, abdominal distention, loss of muscle control, squinting eyes, staggered gait, tremors, hypersensitivity to touch, splayed hindlimbs and hypothermia. At the PAA concentration of 15.2% the main clinical signs were oral and ocular discharges, respiratory distress and abdominal distention. Necropsy revealed blanched stomach and intestines, mottled blanched livers, distended stomach with thin linings, darkened red adrenals, white trachea and blood in stomach and intestines were noted. The animals that died during the observation period had severely irritative and corrosive findings at gross necropsy.

When looking at the wider data set (18 studies) RAC noted the high variability in the reported LD_{50} values (5.8 mg/kg bw to >200 mg/kg bw) and considered this was probably due to methodological differences in the PAA production, administration volume and vehicle. RAC concluded that the toxicity is higher when tissue is damaged due to the corrosive properties of PAA at higher concentrations.

RAC acknowledged that 100% PAA could not exist owing to its high reactivity, but agreed with the DS that in order to derive a correct classification and ATE value for a mixture containing PAA, a classification should be derived for the pure substance.

RAC concluded there were no differences in sensitivity between male and female rats, and that classification should be based on the lowest value of the combined $LD_{50,}$ i.e., 77.6 mg/kg bw, rounded to 80 mg/kg bw.

Overall, RAC agreed that 100% PAA warrants classification as **Acute Tox. 3; H301 (Toxic if swallowed), with an oral ATE value of 80 mg/kg bw.**

Acute toxicity – dermal route

Seven studies were available for the assessment of acute dermal toxicity. The DS identified three of these to be key studies (all conducted according to US-EPA test guidelines and GLP); the remaining studies were considered to be supportive.

A summary of the three key studies is provided in Table 4.

Table 4. Summary of key acute dermal toxicity studies (based on information in CLH (2021))

Method, guideline, deviations, (Klimisch Score)	**Species, strain, sex, no./group**	**Test substance, vehicle**	**Dose levels (mg/kg bw)**	**Signs of toxicity**	**LD_{50} value**
Acute dermal toxicity study EPA guideline no. 81-2 GLP Anonymous (1996c) (1)	NZW rabbit, males and females 5/sex/dose No control animals	Proxitane AHC (4.89% PAA, 19.72% hydrogen peroxide, 10% acetic acid) Vehicle: none	500, 1000, 2020	Mortality: 2020 mg/kg bw: 9/10 animals (4 M, 5 F); 1000 mg/kg bw: 2/10 animals (1 M, 1 F); 500 mg/kg bw: 2/10 animals (1 M, 1 F) Clinical signs: activity decrease, diarrhoea, lateral recumbency, nasal discharge, ptosis, salivation and star-gazing (all resolved by day 6). Animals that died during the observation	1147 mg/kg bw (combined), 1280 mg/kg bw (M), 1040 mg/kg bw (F) Correspond to 56.1, 62.6 and 50.9 mg/kg bw of 100% peracetic acid*, respectively.

Method, guideline, deviations, (Klimisch Score)	Species, strain, sex, no./group	Test substance, vehicle	Dose levels (mg/kg bw)	Signs of toxicity	LD_{50} value
				period showed wet, matted and/or stained muzzle, urogenital and anal areas, discoloured ears, air in blood vessels, heart and pericardium, fluid in pericardium, discolouration of lungs, mesentery, spleen and thymus. Signs of dermal irritation: well-defined to severe erythema, slight to severe oedema, atonia, blanching, bleeding, coriaceousness, desquamation, eschar, fissuring, sloughing and necrosis.	
Acute dermal toxicity study EPA guideline no. 81-2 GLP Anonymous (1996d) (1)	NZW rabbit, males and females 5/sex/dose No control animals	Proxitane WW12 (11.69% PAA, 18.05% hydrogen peroxide, 20% acetic acid) Vehicle: none	500, 2020 and 2293	Mortality: 2293 mg/kg bw: 9/10 animals (4 M, 5 F); 2020 mg/kg bw: 6/10 animals (3 M, 3 F); 500 mg/kg bw: None Clinical signs: activity decrease (all dose groups), resolved by Day 4 group.	1957 mg/kg bw (combined), 1912 mg/kg bw (males), 1990 mg/kg bw (females) Correspond to 228.8, 223.5 and 232.6 mg/kg bw of 100% peracetic

Method, guideline, deviations, (Klimisch Score)	Species, strain, sex, no./group	Test substance, vehicle	Dose levels (mg/kg bw)	Signs of toxicity	LD_{50} value
				Signs of dermal irritation: light to severe oedema, atonia, blanching, bleeding (only at high dose), desquamation, eschar, sloughing and necrosis were seen in all dose groups.	acid*, respectively.
Acute dermal toxicity study EPA guideline no. 81-2 Anonymous (1994) (1)	Wistar rat, males and females 5/ sex/dose No control animals	Proxitane 0103 (0.89% PAA, 7.27% hydrogen peroxide, 10.85% acetic acid)	2000	No mortality. Clinical signs: white and/or red spots on skin after removal of the bandage.	>2000 mg/kg bw Corresponds to >17.8 mg/kg bw of 100% peracetic acid*.

Deaths were reported in the rabbit studies, but not in the rat study. RAC noted that the skin of the exposed rabbits was severely damaged due to the corrosive effects of the applied test materials, and therefore the results cannot be used to evaluate absorption of PAA through intact skin.

An MoA for the observed lethality has been proposed based on the available TK/ADME data: PAA decomposes forming hydrogen peroxide which on contact with the tissues releases oxygen into the blood stream causing gas emboli. RAC noted that rabbits appear to be the most sensitive species to the formation of fatal embolisms (based on a study by Hrubetz *et al.*(1951)). As the causes of the observed lethality are not completely understood, the relevance of the findings in rabbits to humans cannot be excluded.

RAC noted that the LD_{50} values derived from the two rabbit studies showed clear differences, and compared the compositions to try to establish a cause. The compositions of the two tested solutions are reported in the Table 5.

Table 5. Comparison between the % composition in the two key rabbit studies (reproduced from ECHA, 2022a).

Reference	Combined LD_{50} (100% PAA)	PAA%	H_2O_2%	Acetic acid %
Anonymous (1996b)	56.1	4.89	19.72	10
Anonymous (1996d)	228.8	11.69	18.05	20

The two studies were conducted in the same laboratory within the same year and followed very similar experimental protocols (rabbit strain, treatment conditions, etc.). RAC concluded that no relationship between the different composition of the tested solutions and the observed results was apparent. The percentages of H_2O_2 were very similar and the percentage of acetic acid was higher in the solution that resulted in lower toxicity.

RAC concluded that as no evident reason for the different outcomes could be identified and with no difference in the sensitivity of the two sexes, the lowest combined LD_{50} value of 56.1 mg/kg bw (rounded to 60 mg/kg bw) should be used as the dermal ATE value. This corresponds to classification in Category 2 (i.e., 50 < ATE ≤ 200 mg/kg bw; Table 3.1.1 of Annex I of CLP).

Overall, RAC concluded that PAA (100%) should be classified as Acute Tox. 2; H310 (Fatal in contact with skin) with an ATE value of 60 mg/kg bw.

Acute toxicity – inhalation route

Many of the studies available in the CLH report for the assessment of acute inhalation toxicity did not determine an LC_{50} (i.e., the studies were designed to investigate the respiratory irritation properties or the influence of PAA on the respiratory rate). RAC accepted the identification of a single key study proposed by the DS (the only study which was GLP and OECD TG 403 compliant) from the several studies where an LC_{50} had been determined.

The LC_{50} derived from the key study was 4.080 mg/L (5% PAA) or 0.204 mg/L expressed as 100% PAA. RAC acknowledged that this LC_{50} was not the most conservative from the entire data set but was the most appropriate given the study's GLP and OECD TG compliance. The DS and RAC both recognised that peracetic acid has a harmonised classification and labelling of Skin Corr. 1A, H314, so it is likely that the mechanism of toxicity is corrosivity.

An aerosol of the test substance was created in the study, therefore RAC agreed with the DS that the correct CLP criteria for classification were those for dust/mists and not

vapours. According to the Table 3.1.1., for a dust/mist an ATE of 0.05 - 0.5 mg/L should be classified in category 2 for acute inhalation toxicity. According to Annex II of CLP, where substances are classified for inhalation toxicity and there are data available to indicate that the mechanism of toxicity is corrosivity, then the additional labelling statement "EUH071 – Corrosive to the respiratory tract" should be applied. The DS noted that PAA has a harmonised classification and labelling as Skin Corr. 1A;H314, and therefore considered it likely that the mechanism of toxicity in the acute inhalation toxicity studies was corrosivity.

Overall, RAC agreed with the DS and concluded that 100% PAA warrants a classification of Acute Tox. 2; H330 (Fatal if inhaled) with an ATE value of 0.2 mg/L. RAC agreed to the DS proposal to add the labelling "EUH071 - Corrosive to the respiratory tract".

Classification proposed by the Agency:

The Agency recognises that this is an unusual case. However, after considering all of the available data, and the arguments and counter-arguments presented in the RCOM document, the Agency can support the approach taken by the DS and RAC, i.e., to determine the classification of 100% PAA (even though such a high concentration would not exist in reality, owing to the highly reactive nature of the substance) using liner extrapolation from LD_{50} values obtained in tests on mixtures containing varying amounts of PAA and other substances. The Agency recognises that this is a conservative approach to hazard assessment.

Acute toxicity – oral route

The Agency can agree with RAC's assessment of the data. **PAA (100%) meets the criteria for classification as Acute Tox. 3; H301 (Toxic if swallowed) with an ATE value of 80 mg/kg bw.**

Acute toxicity – dermal route

The Agency can agree with RAC's assessment of the data. **PAA (100%) meets the criteria for classification as Acute Tox. 2; H310 (Fatal in contact with skin) with an ATE value of 60 mg/kg bw.**

Acute toxicity – inhalation route

The Agency can agree with RAC's assessment of the data. **PAA (100%) meets the criteria for classification as Acute Tox. 2; H330 (Fatal if inhaled) with an ATE value of 0.2 mg/L. The Agency also agrees that labelling with "EUH071 (corrosive to the respiratory tract)" is warranted.**

Specific target organ toxicity – single exposure (STOT SE)

Not assessed in the CLH report or RAC Opinion.

Skin corrosion/irritation

Not assessed in the CLH report or RAC Opinion.

Serious eye damage/irritation

Not assessed in the CLH report or RAC Opinion.

Respiratory sensitisation

Not assessed in the CLH report or RAC Opinion.

Skin sensitisation

Not assessed in the CLH report or RAC Opinion.

Specific target organ toxicity – repeated exposure (STOT RE)

Not assessed in the CLH report or RAC Opinion.

Germ cell mutagenicity

Not assessed in the CLH report or RAC Opinion.

Carcinogenicity

Not assessed in the CLH report or RAC Opinion.

Reproductive toxicity

Not assessed in the CLH report or RAC Opinion.

Aspiration hazard

Not assessed in the CLH report or RAC Opinion.

Environmental hazards

Hazardous to the aquatic environment

Classification agreed by RAC:

Rapid degradability of organic substances:

RAC considered that PAA was **not rapidly degradable** for the purpose of hazard classification based on the following data presented in the CLH report (ECHA, 2021) and comments submitted during the public consultation on the CLH proposal (ECHA, 2022a):

- By day 28, 98% dissolved organic carbon (DOC) removal was observed in a ready biodegradability test (non-GLP, OECD TG 301E) which exceeds the hazard classification criterion of 70% after 28 days for tests based on DOC removal. However, it was not possible to demonstrate that the 10-day window was met based on the data points. In response to comments during the public consultation on the CLH proposal, the CLH DS stated that the data was not sufficient to obtain a degradation curve to further understand whether the 10-day window was met. RAC agreed that insufficient information was available to demonstrate that the 10-day window was met.

  The DS for the CLH report also considered the study could not be used to conclude that PAA was readily biodegradable given the study deficiencies and deviations from the test guideline. For example, test solution for the stepwise addition was prepared all at once and there was no abiotic control and no analytical verification of the concentration of PAA in the test solution during the stepwise addition (the first 14 days of the study). Consequently, true biodegradation in the inoculated mineral medium could not be distinguished from potential abiotic degradation in the test solution before its addition to the mineral medium. The observed DOC removal may therefore overestimate the biodegradation of PAA.

- RAC noted that two additional ready biodegradability studies conducted according to OECD TG 301D measuring biological oxygen consumption were available, one using non-adapted inoculum (GLP study) and the other using inoculum pre-adapted to PAA (non-GLP study). After 28 days, 33% degradation was observed in the study with non-adapted inoculum and >70% degradation was observed in the study using pre-adapted inoculum. RAC agreed that these OECD TG 301D studies were not suitable to assess the biodegradation of PAA because the substance liberates oxygen if it degrades abiotically.

- PAA was rapidly hydrolysed (non-GLP, OECD TG 111) at pH 4, 7 and 9 with DT_{50} values extrapolated to 12°C ranging from 10.2 hours to 181.1 hours (7.5 days), which are below the hazard classification criterion of 16 days. Acetic acid (CAS 64-

19-7) and hydrogen peroxide (CAS 7722-84-1) were identified as hydrolysis products of PAA in two other non-GLP, non-guideline studies. A comment was made during the public consultation on the CLH proposal that the lead EU REACH Registrant for hydrogen peroxide includes a self-classification as Aquatic Chronic 3 which was supported by the available data (ECHA, 2022b). RAC agreed that as hydrogen peroxide meets the classification criteria as hazardous to the aquatic environment, hydrolysis studies could not be used to conclude that PAA is rapidly degradable for the purpose of hazard classification.

- Another hydrolysis study (EU Method C.7) included in the CLH report was considered supporting information because only the study summary was available, and the study employed a mixture of 0.35% PAA and hydrogen peroxide with no information on the acetic acid content. DT_{50} values determined from the study were 31.2 hours at pH 4 at 25°C, and 200 minutes at pH 4, 97 minutes at pH 7 and <15 minutes at pH 9 at 50°C.

- Rapid primary degradation was indicated by measured concentrations of PAA in an activated sludge respiration inhibition test (GLP, OECD TG 209) with primary DT_{50} values of <3 minutes at 0.3, 1.0, 3.0, 10 and 30 mg PAA/L and 15 minutes at 100 mg PAA/L. Analytical verification was indirectly based on HPLC analysis of methyl-p-tolylsulfoxide (MTSO) resulting from the oxidation of methyl-p-tolylsulfide (MTS) by PAA (Finland, 2015). Ultimate degradation was not demonstrated in this study and degradation products were not analysed. Therefore, it could not be demonstrated that degradation products formed do not meet the criteria for classification as hazardous to the aquatic environment.

- Four non-GLP, non-guideline studies describing the degradation of PAA in different water types also indicated rapid primary degradation of PAA with:

    - primary degradation DT_{50} values ranging from 2 to 20 minutes in seawater;
    - a primary degradation DT_{50} of <5 minutes for PAA and a primary degradation DT_{50} of 89 minutes for the hydrolysis product hydrogen peroxide at 20°C in sewage treatment plant effluent water;
    - 95.1% primary degradation of PAA within one day in drinking water; and
    - primary degradation of PAA from 17% to 91% within 120 minutes in tap water.

  A lower level of primary degradation at 25.6% within 5 days in lake water was observed in another non-GLP, non-guideline study. Ultimate degradation was not demonstrated in any of these studies. In addition, degradation products were not analysed and therefore, it could not be demonstrated that degradation products

formed do not meet the criteria for classification as hazardous to the aquatic environment.

RAC also noted that information on the indirect photochemical degradation of PAA in air was available, but this was not considered for the rapid degradability conclusion for the purpose of hazard classification because photodegradation depends on local conditions and the hazard of the degradation products was unknown.

Overall, while significant biodegradation was observed in the OECD TG 301 E ready biodegradability study, there were several study limitations and it was not possible to demonstrate whether the 10-day window was met. The substance underwent rapid hydrolysis to products that meet the classification criteria as hazardous to the aquatic environment. The OECD TG 209 respiration inhibition test and non-standard studies on the degradation of PAA in water indicated rapid primary degradation but ultimate degradation was not demonstrated in any of these studies and degradation products were not analysed. Therefore, it could not be demonstrated that degradation products formed do not meet the criteria for classification as hazardous to the aquatic environment.

Bioaccumulation:

RAC agreed that PAA was **not bioaccumulative** for the purpose of hazard classification based on the following data presented in the CLH report (ECHA, 2021):

- Calculated log K_{OW} values for 100% PAA ranging from -1.20 at pH 9 to -0.23 at pH 5 (ACD/LogDSuite Program, Version 9) which are below the hazard classification criterion of ≥4.

- A calculated BCF value of 3.16 L/kg (BCFBAF v.300) which is well below the hazard classification criterion of ≥500 L/kg.

No experimental BCF values were available. Experimental log K_{OW} values ranging from -0.66 at pH 9 to -0.46 at pH 5 (GLP, OPTTS 830.7550) were included in the CLH report. However, the concentration of PAA used in the test is unknown and the log K_{OW} value of pure PAA cannot be determined in aqueous solution because PAA dissociates to acetic acid and hydrogen peroxide.

Aquatic Toxicity:

Full details on the aquatic toxicity data are presented in the CLH report (ECHA, 2021) and summarised in the RAC Opinion (ECHA, 2022a). As 100% PAA does not exist, the ecotoxicity studies used a mixture of PAA, acetic acid, hydrogen peroxide and water. It was assumed that the ecotoxicity of these solutions was driven mainly by PAA. Toxicity results were derived based on the PAA content of the test material by extrapolating the toxicity results to 100% PAA expressed as PAA/L and not based on test solution mg TS/L.

Aquatic Acute Toxicity

Aquatic acute toxicity data were available for all three trophic levels with the endpoints below.

Acute fish toxicity

Following GLP and U.S. EPA-FIFRA 72-1, which is similar to OECD TG 203, the 96-hour LC_{50} for *Lepomis macrochirus* (Bluegill sunfish) was 1.1 mg PAA/L based on mean measured concentrations analysed indirectly based on hydrogen peroxide concentrations. Validity criteria were met and the study was considered reliable.

Acute invertebrate toxicity

Following GLP and OECD TG 202, the 48-hour $EC_{50(immobilisation)}$ for *Daphnia magna* was 0.73 mg PAA/L based on mean measured concentrations analysed indirectly based on hydrogen peroxide concentrations. Validity criteria were met and the study was considered reliable.

Acute algal toxicity

Following GLP and U.S. EPA-FIFRA 123-2, which is similar to OECD TG 201, the 72-hour E_rC_{50} for *Raphidocelis subcapitata* (cited as former name *Selenastrum capricornutum*) was 0.050 mg PAA/L based on geometric mean measured concentrations analysed indirectly based on hydrogen peroxide concentrations. The validity criterion for an increase in biomass in the controls by a factor of >16 within the 72-hour test period was met. No information on the coefficient of variation for control growth was available for comparison with the other OECD TG 201 validity criteria, however, RAC considered the study was reliable for the purpose of hazard classification.

Aquatic Acute Classification Conclusion

RAC agreed the lowest acute toxicity endpoint was the **72-hour E_rC_{50} of 0.050 mg PAA/L** (geometric mean measured) for *Raphidocelis subcapitata*. As this endpoint falls within the 0.01 mg/L < EC_{50} ≤ 0.1 mg/L range, RAC agreed that PAA should be **classified as Aquatic Acute 1 with an M-factor of 10**.

Aquatic Chronic Toxicity

Aquatic chronic toxicity data were available for all three trophic levels as presented in the CLH report and detailed below. However, not all data were considered reliable for the purpose of hazard classification.

Chronic fish toxicity

The chronic fish toxicity study following GLP and OECD TG 210 was conducted with *Danio rerio* under flow-through conditions. This study resulted in a 33-day NOEC of 0.00225 mg PAA/L (nominal) based on post hatch success and overall survival. Validity criteria were met although analytical measurements of the test concentrations based on PAA were performed only for the highest test concentration (0.0224 mg PAA/L) because the sensitivity of the analytical method was not adequate for the quantification of the lower test concentrations. Analytical verification in the stock solutions showed recovery rates of PAA mainly within the range of 80-120%. However, analytical verification from the test vessels indicated a device issue as fish in the highest treatment were not correctly exposed during the first part of the test, with PAA being below the LOQ (0.00754 mg/L) during the first 21 days. Analytical measurements in the mixing chambers, where the stock solutions were mixed with the respective amount of tap water, showed that PAA was also below the LOQ during the first 15 days of the study.

In response to comments submitted during the public consultation on the CLH proposal, RAC agreed that despite these limitations, this study indicated that fish were the most chronically sensitive trophic group and therefore, the study should not be disregarded. RAC considered that the NOEC based on nominal concentrations underestimated the aquatic chronic toxicity of PAA and that this should not be used for the purpose of hazard classification as measured concentrations were not maintained within 80-120% of the nominal concentrations. Instead, RAC agreed with an alternative approach proposed by the DS for the CLH report to estimate an initial measured NOEC based on the 31% ratio of the geometric mean measured concentration to the nominal concentration in the mixing chamber at the highest nominal 0.0025 mg PAA/L treatment level. The geometric mean measured concentration in the mixing chamber was calculated using half the LOQ for values below the LOQ.

This approach resulted in a NOEC of 0.00069 mg PAA/L based on estimated initial measured concentrations (0.00225 × 0.31). The assumption was made that the measured concentrations in the mixing chambers represented the actual initial exposure concentrations in the test vessels which RAC considered reasonable as the test vessels received test solution from the mixing chamber. It was also assumed that the ratio of the nominal concentration to an initial concentration calculated for the highest treatment level (31%) could be applied to all lower treatment levels based on the assumption that PAA degradation was independent of concentration. RAC accepted this assumption given that there was no information on the dependency of PAA degradation on the concentration over the treatment levels in the study.

RAC noted that the analytical data indicated that PAA concentrations in test vessels were lower than PAA concentrations in the mixing chambers, and therefore, the estimated initial measured NOEC of 0.00069 mg PAA/L may not properly represent the intrinsic toxicity of PAA. Taking all information into account however, overall, RAC considered this initial measured NOEC was i) a reliable and conservative estimate of the chronic toxicity of PAA

for the purpose of hazard classification, and ii) a more realistic exposure estimate than nominal concentrations.

Chronic invertebrate toxicity

The chronic invertebrate toxicity study following GLP and OECD TG 211 was conducted with *Daphnia magna* under semi-static conditions. This study resulted in a 21-day NOEC of 0.0121 mg PAA/L for mortality based on geometric mean measured concentrations. Validity criteria were met but the method of analytical verification indirectly based on MTSO resulting from the oxidation of MTS by PAA was invalid because an unknown component in the culture medium was able to produce the reaction from MTS to MTSO. Therefore, RAC agreed that the study was not reliable and should not be used for the purpose of hazard classification.

Chronic algal toxicity

A *Raphidocelis subcapitata* 72-hour NOE_rC of 0.031 mg PAA/L based on geometric mean measured concentrations was available from the above noted study, which was considered relevant and reliable for hazard classification.

Aquatic Chronic Classification Conclusion

RAC agreed the lowest long-term toxicity endpoint was the *Danio rerio* **33-day NOEC of 0.00069 mg PAA/L** (initial measured) based on post hatch success and overall survival. Given RAC considered PAA as a not rapidly degradable substance and since this endpoint falls in the 0.0001 < NOEC ≤ 0.001 mg/L range, RAC considered that PAA should be **classified as Aquatic Chronic 1 with an M-factor of 100.**

In the absence of reliable aquatic chronic toxicity data for all three trophic levels, RAC noted that the surrogate approach based on the acute aquatic invertebrate data would result in a less stringent Aquatic Chronic classification, and therefore was not used.

RAC Opinion:

RAC agreed to classify PAA as:

- **Aquatic Acute 1 (H400) with an M-factor of 10** based on the *Raphidocelis subcapitata* 72-hour E_rC_{50} of 0.05 mg/L.

- **Aquatic Chronic 1 (H410) with an M-factor of 100** based on the *Danio rerio* 33-day NOEC of 0.00069 mg/L for a not rapidly degradable substance.

Classification proposed by the Agency:

The Agency agrees that PAA is not rapidly degradable based on available fate data. In an OECD TG 301E ready biodegradation test, 98% dissolved organic carbon (DOC) removal was observed within 28 days which exceeds the hazard classification criterion of 70% after 28 days. However, insufficient information was available to demonstrate that the 10-day window was met meaning PAA does not meet the rapid degradability criteria. While in a number of other studies, rapid primary degradation was observed in water with DT_{50} values below the hazard classification criterion of 16 days, the Agency agrees that these studies do not demonstrate transformation to non-classifiable products, or ultimate degradation to above 70% within 28 days. The hydrolysis product hydrogen peroxide meets the criteria for classification as Aquatic Chronic 3.

The Agency agrees that PAA is not bioaccumulative for the purpose of hazard classification on the basis of the log Kow values <4 and the calculated fish BCF value <500 L/kg.

Available ecotoxicity studies used a mixture of PAA, acetic acid, hydrogen peroxide and water, as 100% PAA does not exist. RAC derived the ecotoxicity endpoints from these studies based on the PAA content of the test material by extrapolating the toxicity results to 100% PAA (expressed as PAA/L). The Agency acknowledges that there is uncertainty with this approach because acetic acid and hydrogen peroxide are less acutely and chronically ecotoxic than PAA, noting the Aquatic Chronic 3 classification of hydrogen peroxide. According to the biocide assessment report (Finland, 2015), the equilibrium solution is the typical biocidal product placed on the market and the PAA content in existing aqueous equilibrium solutions ranges from <0.1% to >15% (w/w). Nevertheless, the Agency agrees that the approach used by RAC represents a conservative approach and is appropriate as it can be assumed that the ecotoxicity of the test solutions was driven mainly by PAA. Mixture calculations can subsequently be used to derive suitable classifications for solutions containing lower percentages of PAA.

The Agency agrees that the key acute toxicity endpoint is a geometric mean measured 72-hour E_rC_{50} of 0.050 mg PAA/L for *Raphidocelis subcapitata*. On this basis, the Agency agrees with the RAC assessment that PAA meets the classification criteria as **Aquatic Acute 1 (H400) with an Acute M-factor of 10**.

The Agency agrees that the long-term toxicity data indicate that fish are the most chronically sensitive trophic group and that relevant effects were observed during the OECD TG 210 study. While this chronic toxicity to fish study has limitations regarding dosing and analytical verification, a clear concentration-response was observed and the results should not be disregarded as this would result in an under representative classification (Aquatic Chronic 1 (H410) with an M-factor of 1 based on the *Raphidocelis subcapitata* 72-hour NOE_rC of 0.031 mg PAA/L (geometric mean measured)). The Agency agrees that a NOEC based on nominal concentrations from this fish study is uncertain given it is below the LOQ and actual concentrations were likely to be lower than the

nominal concentration based on available analytical verification for the highest treatment. The Agency agrees that the estimated initial measured NOEC based on the ratio of the geometric mean measured concentration to the nominal concentration in the mixing chambers at the highest test concentration is a relevant estimated hazard endpoint from this study as it reduces the uncertainty regarding actual concentrations. The Agency also notes that analysis at the highest treatment recorded exposure tank measurements significantly lower than measurements in the mixing chamber. Overall, the Agency agrees that the long-term estimated initial measured 33-day NOEC of 0.00069 mg/L for *Danio rerio* based on post hatch success and overall survival is relevant for hazard classification, resulting in **Aquatic Chronic 1 (H410) with an M-factor of 100** for a not rapidly degradable substance**.**

The EU REACH registration for PAA also includes a *Danio rerio* 33-day NOEC of 0.000094 mg/L based on survival for the same fish study which was calculated based on an estimate that initial concentrations corresponded to 42% of the nominal concentrations (ECHA, 2023). No further details on how these initial measured concentrations were calculated are available. However, the Agency notes that this NOEC is in the same concentration range as the estimated initial measured NOEC of 0.00069 mg/L above.

In the absence of chronic toxicity data for *Lepomis macrochirus* and given there are no reliable chronic toxicity data for aquatic invertebrates, the Agency notes that the surrogate approach with the acute *Lepomis macrochirus* or *Daphnia magna* endpoints would result in a less stringent Aquatic Chronic classification. Therefore, the surrogate approach has not been used.

Other hazards

Hazardous to the ozone layer

No classification proposed and not assessed in the RAC Opinion.

Overall conclusion

The Agency has evaluated the RAC Opinion, its rationale and any additional scientific evidence that may have been made available to HSE against the criteria for classification and labelling in the GB CLP Regulation and technical guidance.

The Agency technical report **agrees** with the classification proposed by RAC for the following hazards:

Org. Perox. D; H242 (Heating may cause a fire)

NOT CLASSIFIED for flammable liquids

Acute Tox. 3; H301 (Toxic if swallowed) with an ATE of 80 mg/kg bw

Acute Tox. 2; H310 (Fatal if in contact with skin) with an ATE of 60 mg/kg bw

Acute Tox. 2; H330 (Fatal if inhaled) with an ATE of 0.2 mg/l (dust/mists)

Aquatic Acute 1; H400 (Very toxic to aquatic life) with an Acute M-factor of 10

Aquatic Chronic 1; H410 (Very toxic to aquatic life with long lasting effects) with a Chronic M-factor of 100

The Agency also supports the addition of Note T and the supplementary labelling phrase “EUH071 - corrosive to the respiratory tract”.

Overall, the conclusion is to **agree** with the RAC opinion.

References

ECHA (2017) Guidance on the application of the CLP criteria. Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, version 5.0, ref: ECHA-17-G-21-EN. Available at https://www.echa.europa.eu/

ECHA (2022b) EU REACH registration dossier for hydrogen peroxide [ONLINE] European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/registration-dossier/-/registered-dossier/15701/1/1 (Accessed January 2023).

ECHA (2023) EU REACH registration dossier for peracetic acid [ONLINE] European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/registration-dossier/-/registered-dossier/14885/6/2/3 (Accessed February 2023).

Finland (2015) Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products Evaluation of active substances Assessment Report Peracetic acid. https://echa.europa.eu. Accessed: 02/2023

For all other references, please see the EU CLH report and the EU RAC opinion (available at: https://echa.europa.eu/registry-of-clh-intentions-until-outcome)

CLH (2021) CLH report (including Annexes): Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2. Substance Name: Peracetic acid…%; Date: 2022; Written by Finnish Safety and Chemicals Agency; Accessed date: 11/2022

ECHA (2022a) Committee for Risk Assessment (RAC) Opinion (including Annexes) proposing harmonised classification and labelling at EU level of peracetic acid …%; Reference CLH-O-0000007133-82-01/F; Date: 02/06/2022, Accessed date: 11/2022

Documents published as part of the EU CLH process: Source: European Chemicals Agency, http://echa.europa.eu/

Glossary of terms used in Agency technical reports

Agency, the	HSE, acting in its capacity as the GB CLP Agency
AR	Applied radioactivity
ATE	Acute toxicity estimate
BCF	Bioconcentration factor
BOD	Biological Oxygen Demand
bw	Body weight
CAR	Competent Authority Report
CAS	Chemical Abstracts Service
CI	Confidence interval
CL	Confidence limits
CLH	Harmonised Classification and Labelling
CLP	Classification, labelling and packaging (of substances and mixtures)
CO_2	Carbon dioxide
COD	Chemical Oxygen Demand
CV	Coefficient of Variation
d	Day
DAR	Draft Assessment Report
DOC	Dissolved Organic Carbon
DS	Dossier Submitter
DT	Dissipation time OR degradation time (also DissT or DegT where apparent)
DT_{50}	Dissipation half-life OR degradation half-life (hours or days), see also above
dw	Dry weight
ECHA	European Chemicals Agency
ECx	x% effect concentration
EFSA	European Food Safety Authority
E_rCx	x% effect concentration based on growth rate
EU	European Union
GLP	Good Laboratory Practice
h	Hours
K_{OC}	Organic carbon-water partition coefficient
K_{OW}	Octanol-water partition coefficient
LC_x	x% lethal effect concentration
MCL	Mandatory Classification and Labelling
M-factor	Multiplying factor
MW	Molecular weight

NOEC	No-observed effect concentration
OECD	Organisation for Economic Co-operation and Development
QSAR	Quantitative structure-activity relationship
RAC	Risk Assessment Committee
RAR	Renewal Assessment Report
RCOM	Response to comments document
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals regulation
SADT	Self-Accelerating Decomposition Temperature
STOT-RE	Specific target organ toxicity – repeated exposure
STOT-SE	Specific target organ toxicity – single exposure
TG	Test Guideline
US EPA	United States Environmental Protection Agency
wt	Weight
wwt	Wet weight

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