Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

peracetic acid …%

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

CLH-O-0000007133-82-01/F

Adopted

2 June 2022

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

February 2023: latest version, replacing all previous versions

2 June 2022

CLH-O-0000007133-82-01/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: **peracetic acid ...%**

EC Number: **201-186-8**

CAS Number: **79-21-0**

The proposal was submitted by **Finland** and received by RAC on **24 June 2021.**

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

PROCESS FOR ADOPTION OF THE OPINION

Finland 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 **9 August 2021**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **8 October 2021**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Gabriele Aquilina**

Co-Rapporteur, appointed by RAC: **Žilvinas Užomeckas**

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 **2 June 2022** 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	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
Dossier submitters 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	
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** 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 Annex VI entry if agreed by COM	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

GROUNDS FOR ADOPTION OF THE OPINION

RAC general comment

Introduction

Peracetic acid ...% (PAA) is a biocidal active substance with strong bactericidal, fungicidal, and virucidal activity. PAA is mainly used as a bactericide, fungicide or virucide. Moreover, indications of potential efficacy against amoebae and algae have been reported.

The uses belong to the Product Types (PT) 1 – 6, 11 and 12. They are wide-spread and have the following aims:

- PT1: Hand disinfection: the "organism to be protected" is man. The aim of the treatment is to prevent spreading of disease-causing micro-organisms. Hand disinfection products based on PAA are used in hospitals, healthcare areas, as well as in food production and catering environments.
- PT2: Disinfection of textiles during washing process: the "organism to be protected" is man. The aim of the treatment is to control infectious diseases or smell generating micro-organisms in laundry. Treatment of sewage/wastewater including municipal waste water and disinfection of surfaces in industrial, public and health care areas, CIP (Clean-in-Place) in pharmaceutical and cosmetic industry: the "organism to be protected" is man. The aim of the treatments is to control infectious diseases or nuisance (smell generating) organisms.
- PT3: Disinfection of animal houses: the "organisms to be protected" are animals and man (as the consumer of animals). The aim of the treatments is to control infectious diseases.
- PT4: Disinfection in food and feed industry (CIP, dipping of equipment, automated spraying, and manual spraying, foaming): the organisms to be protected are man and animals. The aim of the treatments is to control infectious diseases and to avoid contamination of food or feed. Disinfection of equipment used in animal production (e.g. milking equipment): the "organisms to be protected" are animals and man (as the consumer of animal products such as milk). The aim of the treatments is to control infectious diseases.
- PT5: Disinfection of animal drinking water: the "organisms to be protected" are animals and man (consumption of products of animal origin). The aim of the treatments is to control infectious diseases.
- PT6: In-can preservation in the paper production. The purpose of the treatment is in-can preservation of coating products used in the production of paper.
- PT11: Preservatives for liquid-cooling and processing systems.
- PT12: Slimicides. Used for the prevention or control of slime growth on materials, equipment and structures, used in industrial processes, e.g. on wood and paper pulp, porous sand strata in oil extraction.

Equilibrium PAA products are exclusively applied by professional users except that PAA containing products for hand disinfection are also applied by non-professionals.

The substance is also registered under the REACH Regulation and is manufactured in, or imported to, 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.

The substance is used in the following products: washing & cleaning products, textile treatment products and dyes, paper chemicals and dyes and water treatment chemicals.

Scope of the PAA CLH Report

The PAA solution …% has an entry in Annex VI of CLP and is classified as:

Flam. Liq. 3; H226

Org. Perox. D****; H242

Acute Tox. 4*; H332

Acute Tox. 4*; H312

Acute Tox. 4*; H302

Skin Corr. 1A; H314

Aquatic Acute 1; H400

The entry contains an asterisk (*) in the columns "classification" and "specific concentration limits and M-factors and Acute Toxicity Estimates (ATE)". The asterisk in the column "classification" indicates a minimum classification and the asterisk in the column "Specific concentrations limits, M-factors and Acute Toxicity estimates (ATE)" indicates that the entry had specific concentration limits for acute toxicity under Directive 67/548/EEC.

The dossier submitter (DS) aimed to remove the *(minimum classification) of PAA from the harmonized classification under the Classification, Labelling and Packaging (CLP) Regulation (EC No 1272/2008) and to derive definitive ATE values for a theoretical 100% PAA, which due 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 with equilibrium mixtures of PAA (varying % PAA and other ingredients) to a theoretical 100% PAA for the purpose of classification. This method constitutes a conservative approach for hazard assessment purposes.

Toxicokinetic and bioavailability

A few toxicokinetic studies are available for PAA (see table 11 of CLH dossier). The only *in vivo* study is with dermal exposure; no toxicokinetic data are available for other routes. Based on the physicochemical properties, PAA has a low molecular weight (76.05 g/mol), high water solubility (> 10000 mg/L) and an octanol/water partition coefficient of -0.3. The high water solubility and the low octanol/water partition coefficient may limit absorption via biological membranes. No bioaccumulation is expected for the substance.

Anonymous (1994) studied absorption, distribution and excretion following a single dermal administration of PAA in Sprague-Dawley rats. The study followed the OECD TG 417 (incorporating the TG 427) and the principles of GLP. The test material contained 5.02% PAA, 22.3% H_2O_2, while acetic acid concentration was not specified. Four male rats were given a single application of the test substance to an enclosed area (approx. 4.5 cm^2) of clipped dorsal skin. The treated animals were then placed in metabolism cages and respired air, urine and faeces were analysed for radioactivity up to 72 hours post-treatment. Approximately 36% of the administered dose was recovered as CO_2 in treated animals. There was a lag phase of 1 hour in the formation of CO_2, which may be due to a lower blood flow in skin capillaries and a slower distribution due to formation of micro-emboli resulting from oxygen formation after contact and severe damage to the skin. There was no volatilisation from treated skin since only a small portion of the administered dose (< 1%) was recovered as unchanged PAA. As the skin of the animals was severely damaged due to the corrosive effects of the test solution, the results cannot be used to assess absorption of PAA through intact skin.

In the non-guideline study Anonymous (2003c), the fate of PAA was investigated in blood with samples drawn from one male Wistar rat. The samples were diluted 1000 times with test solutions (containing 15.22% (w/w) PAA and 14.27% (w/w) H_2O_2) in different concentrations (0, 5.4, 10.8

or 21.6 mg/L PAA and 0, 5.1, 10.1 or 20.3 mg/L H_2O_2, respectively) in physiological saline. The solutions were incubated at 37°C and measured for their PAA (or H_2O_2) concentration with the Merck Reflectoquant test systems. Samples were taken immediately before and after addition of blood, at 5, 15, 30, 60, 120 or 240 minutes and after 24 hours. PAA was rapidly degraded in diluted rat blood, with half-lives below five minutes.

The non-guideline study Anonymous (2005c) followed a similar principle: samples were drawn from one male Wistar rat and diluted 1000 times with test solutions (containing 15.1% PAA, 23.0% H_2O_2 and 16.6% acetic acid) of different concentrations (1.0 or 5.0 mg/L PAA) in physiological saline. The solutions were incubated at 37°C and samples were taken immediately after addition of blood and at 5, 15, 30, 60, 120 or 240 minutes. PAA oxidises methyl-p-tolylsulfide (MTS), which was added to each of the samples. The resulting methyl-p- tolylsulfoxide (MTSO) was monitored by HPLC, and the concentration of PAA was calculated. According to the results, PAA was rapidly degraded in blood, with a half-life below five minutes.

Overall, PAA is degraded by catalases found in blood, stomach fluid, saliva and in various organs (CAR, 2015). Most importantly, degradation by catalases in human erythrocytes has been demonstrated. Non-enzymatic degradation to acetic acid and oxygen has been reported at pH values around 7, which is close to physiological pH values both in blood and cells.

RAC evaluation of physical hazards

FLAMMABLE LIQUIDS

Summary of the Dossier Submitter's proposal

The flash point measurements were carried out with the Pensky Martens closed-cup tester (non-equilibrium method). The flash point was measured from the PAA solution: PAA 39.6%, acetic acid 2.0% and H_2O_2 0.34%. The flash point was measured 3 times. Results of 3 different measurements were 61°C, 63°C and 63°C, therefore over the limit value for flammable liquids (≤ 60°C).

Considering that the SADT (Self-Accelerating Decomposition Temperature) is below 60°C and below the flash point, the DS proposed to remove the current harmonised classification (Flam. Liq. 3).

Comments received during consultation

One comment was received during the consultation, suggesting removing the assessment of the physical hazard classes flammable liquids, organic peroxides and oxidising liquids from the CLH dossier. The variability of the composition of PAA formulations could lead to different physical hazard classes, therefore, an entry of a harmonised classification in Annex VI is not possible. The entry should be simplified by omitting the classification for the physical hazards.

The DS agreed to this proposal. However, the RAC decided to retain the assessment of physical hazards, but to remove the classification as flammable liquids on the basis of the available experimental data.

Assessment and comparison with the classification criteria

The Pensky-Martens closed cup method is one of the suitable test methods listed in CLP Annex I, table 2.6.3 for determining the flash point of flammable liquids. For classification purposes it

is recommended to use the mean of at least two test runs. If the experimentally determined flash point is found to be 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 that 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. The composition of the tested solution is PAA 39.6%, acetic acid 2.0% and H_2O_2 0.34%. Therefore, the equilibrium method should have been used.

However, it should also be considered that the flash point for liquid organic peroxides is only relevant in the temperature range where the organic peroxide is thermally stable (Guidance on the Application of the CLP Criteria (CLP guidance) 2.15.4.3.2). Above the 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). PAA currently has a harmonised classification as Flam. Liq. 3; H226, flammable liquid and vapour. Flammable liquid means a liquid having a flash point of not more than 60°C (criteria for flammable liquids category 3: Flash point ≥ 23°C and ≤ 60°C).

Considering that the SADT is below 60°C and below the flash point, the hazard class Flam. Liq. is not applicable. Therefore, in agreement with the DS, RAC suggests removing the current harmonised classification of Flam. Liq. 3.

ORGANIC PEROXIDES

Summary of the Dossier Submitter's proposal

The CLH report refers to the tests for different compositions of PAA, H_2O_2, acetic acid and water performed in accordance with the test series A to H as described in Part II of the UN RTDG, Manual of Tests and Criteria.

The investigated three compositions (PAA 38%, PAA 13.4%, PAA 41.5%, in Anonymous 1997b and Anonymous 1999) would lead to classify as a type F organic peroxide. However, based on previous determinations (see table 10 of the CLH dossier), 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.

Considering the variability of the classification values based on composition, especially in high PAA concentrations, the DS proposed to confirm the current harmonised classification as Org. Perox. D ****.

Comments received during the consultation

As reported in the flammable liquids section, a comment suggesting removing the entry of physical hazards from the harmonised classification in Annex VI was received in PC.

The DS agreed to this proposal. However, RAC decides that the removal of the physical hazard classes and the addition of a note would not be appropriate because the note has to be referred to a specific physical hazard class.

Assessment and comparison with the classification criteria

PAA currently has a harmonised classification as Org. Perox. D ****. The classification of organic peroxides shall be performed in accordance with test series A to H as described in Part II of the UN RTDG, Manual of Tests and Criteria.

According to the criteria specified in the UN RTDG, the investigated three compositions (PAA 38%, PAA 13.4%, PAA 41.5%) should be classified as a type F organic peroxides (table 10 of CLH dossier). However, based on previous determinations 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, it is clear that not only the concentration of PAA influences the classification but the concentrations of acetic acid and H_2O_2 do have a marked influence on the test result.

A list of currently classified organic peroxides is included in the UN RTDG Model regulations, Section 2.5.3.2.4, where PAA with concentration ≤ 43% is classified as organic peroxide type D, E or F.

Considering the variability of the classification values based on composition, especially in high PAA concentrations, in agreement with the DS, RAC proposes to confirm the current harmonised classification as **Org. Perox.** D removing the asterisks and suggests adding note T.

The note T is the following:

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.

EXPLOSIVES

Hazard class not applicable.

The explosive properties do not have to be determined according to the CLP Annex I, Chapter 2.1, because explosive properties are incorporated in the decision logic for organic peroxides.

HUMAN HEALTH HAZARD EVALUATION

RAC evaluation of acute toxicity

ACUTE ORAL TOXICITY

Summary of the Dossier Submitter's proposal

Based on the available data for oral acute toxicity the DS concluded that there is sufficient evidence to remove the minimum classification, since the relevant LD_{50} value is in the range of > 50 and ≤ 300 mg/kg bw.

Acute Tox. 3 is therefore proposed for 100% PAA, with the corresponding hazard statement H301: Toxic if swallowed, with an oral ATE value of 70 mg/kg bw.

Notably, ATE calculated for the test mixture containing different concentrations of both PAA and H_2O_2 would lead to a classification as Acute Tox. 4; H302. Acetic acid is not taken into account since it is not classified for acute oral toxicity in the C&L inventory.

Comments received during consultation

One Member State Competent Authority (MSCA) supported the proposed classification for acute toxicity oral and for derivation of the ATE value as 70 mg/kg bw suggesting some clarifications and editorial amendments.

A second MSCA supported the approach followed by the DS to derive the ATE value and suggested a more stringent classification for this hazard class by including also the studies with reliability 2, whose deviations are considered minor.

Another MSCA pointed out that the approach used to derive the ATE value for acute oral toxicity, where the LD_{50} of the mixture PAA/H_2O_2/AA is derived on the basis of the concentration of PAA only, may lead to a more severe classification, however, in the absence of data on PAA only, such approach is considered acceptable.

One industry or trade association remarked that the derivation of an ATE value is not a mandatory requirement of CLP Regulation. Moreover, the used approach is not scientifically justified and could lead to an over classification. They claimed that the extrapolation approach does not to correctly reflect the mode of action of PAA for acute toxicity. The primary mode of action of PAA is characterized by local irritation/corrosion. Then, in the evaluation of the acute toxicity also the irritant/corrosive properties of the substance should be considered. In the 90-day study, where irritant/corrosion was not present, no systemic effect was reported. The derived ATE value for acute oral toxicity based on the low dosage observed in females, as the more sensitive gender according to the CLH report, was also contested by industry, because the studies do not fully support the conclusion that females are more sensitive than males. Due to the non-consistent gender sensitivities, a combined LD_{50} value (males and females) (i.e. 1700 mg/kg bw corresponds to 85.0 mg/kg bw of a theoretical 100% PAA) for classification purposes was considered more appropriate by industry.

Assessment and comparison with the classification criteria

A total of 18 oral acute toxicity studies were carried out in rats using different test substances containing concentrations of PAA ranging from 0.15 to 35%. In the assessment, 3 studies (Anonymous 1998b; 1995; 1985) were identified as key studies as they were carried out in compliance with OECD TG and GLP principles (Klimisch score 1). The remaining 3 studies (Anonymous 1998c; 1993; 1982) were considered as supportive data by the DS.

Eleven studies were excluded from the evaluation, based on the following criteria: low reliability (Klimisch criteria), absence of vehicle (with consequent excessive concentration of PAA in the tested solution and possible corrosive effects); variable volume administered or not specified; inadequacy of the test item (e.g. exact PAA content not determined or presence of strong mineral acid); inadequacy of the study design to derive a LD_{50} value. In addition, the study by Anonymous (1994) was excluded due inconsistent results observed internally between sexes and with the other studies.

The key studies were performed with test substances containing PAA in concentrations from 5 to 15.2%, which resulted in LD_{50} values between 95 to 99.7 mg/kg bw in males, 70 to 93 mg/kg bw in females, and 85 to 271 mg/kg bw as combined (male/female) for 100% PAA. However, RAC considers the shortcomings observed in the study Anonymous (1993) not sufficient to exclude it from the assessment, thus it was taken into account for the derivation of the ATE. In this study the PAA concentration was 6.11% and the combined LD_{50} was 77.6 mg/kg bw.

The most significant clinical signs observed were 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 concentration of 15.2% the

main clinical signs observed were oral and ocular discharges, respiratory distress and abdominal distention.

During necropsy, 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 in the gross necropsy.

High variability of the LD_{50} was observed in the acute oral toxicity studies: the lowest LD_{50} was 5.8 mg/kg bw (Anonymous, 1996a), but also LD_{50} values higher than 200 mg/kg bw were reported (Anonymous, 1977). This variability is probably due to methodological differences in the PAA concentration and volume of the test material solutions applied by gavage. If the stock solution was diluted and a constant volume was administered, the toxicity was lower as compared to studies where undiluted test material was administered or volumes increasing with higher dose levels. For example, LD_{50} was 9.0 mg/kg bw for a product containing 4.89% PAA applied undiluted with volumes ranging from 0.04 to 4.5 mL/kg bw (Anonymous, 1996a), whereas the LD_{50} values ranged from 77.6 to 96.1 mg/kg bw in the other studies conducted with similar products (4.5 - 6.11% PAA), but administered in higher volumes containing lower concentrations of PAA. In the study showing the highest LD_{50} (202.8 mg/kg bw), coconut oil was used as vehicle, whereas water was used in all other studies. Similar differences were seen in the other study conducted by Anonymous (1996b) with a test substance containing 11.7% PAA. It can be concluded that the toxicity is higher when tissue is damaged due to the corrosive properties of PAA at higher concentrations.

Overall, no clear differences in the sensitivity between sexes were observed.

Therefore, RAC agrees that the classification should be based on the lowest value of the combined LD_{50} of 77.6 mg/kg bw, rounded to 80 mg/kg bw (Anonymous, 1993).

***Table**: LD_{50} in key and supportive studies*

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

Comparison with classification criteria

PAA currently has a harmonised classification as Acute Tox. 4*; H302 for the oral route.

Classification for acute oral toxicity under the CLP Regulation is required for substances with an acute oral LD_{50} value of ≤ 2000 mg/kg bw. Category 4 is assigned for substances with an LD_{50} value of > 300 and ≤ 2000 mg/kg bw and category 3 for substances with an LD_{50} value of > 50 and ≤ 300 mg/kg according to the table 3.1.1 of Annex I to the CLP Regulation.

The results of the key and supportive studies for acute oral toxicity performed in rats with formulations containing PAA at concentrations from 5% to 15.2% demonstrated acute oral LD_{50} values in the range of 1270 - 1780 mg/kg bw in females corresponding for 100% PAA to 77.6 -

271 mg/kg bw. In order to derive a correct classification and ATE value for a mixture containing PAA, a 100% substance should be classified even if the substance cannot exist in such a high concentration. Following this criterion, 100% PAA should be classified as Acute Tox. 3; H301 based on the calculated LD_{50} values for PAA in the equilibrium test substance (ATE oral 80 mg/kg bw).

Hydrogen peroxide is classified for acute oral toxicity (Acute Tox. 4*; H302, C ≥ 8%). If ATE_{mix} is calculated for the test substance containing different concentrations of PAA and H_2O_2 using the ATE of 80 mg for PAA and the converted acute toxicity point estimate of 500 (Cat. 4, oral) for H_2O_2, then the formulations used in the key and supportive experimental studies where PAA concentrations were in the range 5 - 15.2%, would be classified as Acute Tox. 4; H302. Acetic acid is not taken into account since it is not classified for acute oral toxicity.

Based on the available data, RAC agrees with the DS that 100% PAA warrants a classification as **Acute Tox. 3**, with the corresponding hazard statement **H301: Toxic if swallowed, with an oral ATE value of 80 mg/kg bw.**

ACUTE DERMAL TOXICITY

Summary of the Dossier Submitter's proposal

Based on the available data, the DS concluded that there is sufficient evidence to remove the asterisk from the classification, since the relevant LD_{50} value is in the range of > 50 and ≤ 200 mg/kg bw based on the CLP classification criteria. Therefore the DS proposed to classify 100% PAA as acute Tox. 2, with the corresponding hazard statement H310: Fatal in contact with skin, and a dermal ATE value of 56 mg/kg bw.

Comments received during consultation

One MSCA agreed with the proposed classification of Acute Tox. 2; H310, but proposed as ATE the lowest dose of LD_{50} of 50.9 mg/kg bw, reported for females instead of 56.1 mg/kg bw, reported for combined (males/females) proposed by the DS.

One comment was provided by the industry, pointing out that the LD_{50} derived from the two key studies are inconsistent. In particular the study performed with PAA 4.89% results, for a theoretical 100% PAA solution, in a LD_{50} of 56.1 mg/kg bw, while in the study performed with a 11.69% PAA results in a LD_{50} value of 228.8 mg/kg bw. Moreover, considering that the mode of action is the corrosion and that substance is already classified for this end-point the classification for dermal acute toxicity could be waived, based on the OECD "Guidance Document on Considerations for Waiving or Bridging of Mammalian Acute Toxicity Tests", ENV/JM/MONO(2016)32. The industry questioned that the proposed classification for dermal acute toxicity is more severe than the classification for oral acute toxicity, which is considered unlikely by the "Guidance Document" mentioned above. Therefore, their suggestion was to maintain the current classification as Acute Tox. 4*; H312 for the dermal route.

Assessment and comparison with the classification criteria

Seven studies are available on the acute dermal toxicity of PAA in the rat and rabbit. Three studies therefrom were selected as key studies. All key studies were carried out in accordance with US-EPA test guidelines and GLP principles as established by OECD. The remaining acute dermal studies in the rat and in the rabbit serve as supportive information on this endpoint.

In the key study Anonymous 1996c (4.89% PAA, 19.72% H_2O_2, 10% acetic acid) conducted in accordance with EPA guideline no. 81-2, undiluted test substance at levels of 500, 1000 and 2020 mg/kg bw were applied to the intact skin of male and female albino rabbits and occlusively covered. After 24 hours, the cover and the test substance were removed and the animals observed for mortality, clinical signs, dermal irritation and body weight development for an observation period of 14 days. A gross necropsy was performed in all animals at study termination. Mortalities occurred at all dose levels during the study. Clinical signs included activity decrease, diarrhoea, lateral recumbency, nasal discharge, ptosis, salivation and star-gazing. These signs were no longer evident in all surviving animals on day 6. Signs of skin irritation included severe erythema, slight to severe oedema, atonia, blanching, bleeding, coriaceousness, desquamation, eschar, fissuring, sloughing and necrosis. There were no significant effects on the body weights. There were no pathological effects in surviving animals revealed by necropsy. Animals that died during the observation 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. The acute dermal LD_{50} in rabbits was 1280 mg/kg bw in males, 1040 mg/kg bw in females and 1147 mg/kg bw as combined (male/female) corresponding to 62.6 mg/kg bw in males, 50.9 mg/kg bw in females and 56.1 mg/kg bw as combined (male/female) of 100% PAA. Females were the most sensitive gender.

In the key study, Anonymous (1996d) (11.69% PAA, 18.05% H_2O_2, 20% acetic acid) conducted in accordance with EPA guideline no. 81-2, undiluted doses at levels of 500, 2020 and 2293 mg/kg bw were applied to the intact skin of male and female albino rabbits and occlusively covered. After 24 hours, the cover and the test substance were removed and the animals observed for mortality, clinical signs, dermal irritation and body weight development for an observation period of 14 days. A gross necropsy was performed in all animals at study termination. No mortality occurred at the 500 mg/kg bw level. The only systemic clinical sign was activity decrease in all dose groups, which was no longer evident in surviving animals by day 4. Signs of skin irritation included atonia, blanching, coriaceousness, oedema, erythema, eschar, necrosis and sloughing, which were seen in all dose groups. Additionally, bleeding was observed in the highest dose group. There was an apparent effect on body weight gain in four surviving animals, three males (two in the lowest, one in the highest dose group) and one female of the lowest dose group. Abnormal necropsy findings occurred only in the animals dying during the study and pertained to the ears, muzzle, anal/genital areas, lungs, heart and major blood vessels. The acute dermal LD_{50} in rabbits was 1957 mg/kg bw (combined), 1912 mg/kg bw (males), 1990 mg/kg bw (females) corresponding to 228.8, 223.5 and 232.6 mg/kg bw of 100% PAA, respectively. Males were the most sensitive gender.

In the key study Anonymous (1994) (0.89% PAA, 7.27% H_2O_2, 10.85% acetic acid) conducted in accordance with EPA guideline no. 81-2, a single dermal dose of 2000 mg/kg bw was applied under an occlusive dressing to the intact skin of five male and five female Wistar rats. Any sign of intoxication occurring during the 14-day observation period was recorded. Gross post-mortem examination was done in all rats at the end of the 14-day observation period. None of the rats died within the 14-day observation period. White and/or red spots were noted on the treated skin after removal of the bandage. These spots got brown and encrusted during the observation period. The skin symptoms subsided after 12 days. No other clinical signs were observed. Transient weight loss was observed in both sexes in the first few days of the study. Thereafter body weight gain appeared to be normal. At autopsy, no treatment related abnormalities were recorded for any of the animals.

The skin of all animals were severely damaged due to the corrosive effects of the applied test substances and therefore the results cannot be used to evaluate absorption of PAA through intact skin. The toxicity of PAA is due to its locally irritating properties. PAA decomposes in H_2O_2 and

acetic acid. After contact with organs and tissues, H_2O_2 will undergo decomposition into water and oxygen. Oxygen bubbles liberated in the blood stream/capillaries may cause reduced blood flow and gas emboli as well as reversible blanching of the exposed tissue area. In acute dermal toxicity studies with 90% H_2O_2 in rabbits, cats, pigs and rats, Hrubetz *et al.* (1951) found that the rabbit appeared to be the most sensitive animal species. High susceptibility of the rabbit to embolism and interspecies differences in the levels of tissue and blood catalases were noted. The authors also proposed that there may be more H_2O_2 available subcutaneously in the rabbit to enter the blood stream and release the oxygen which gives rise to lethal embolic effects. According to the CLP guidance classification should be based on the lowest ATE value available i.e. the lowest ATE in the most sensitive appropriate species tested. If there is information available to inform on species relevance, the studies conducted in the species most relevant for humans should normally be given precedence over the studies in other species. As the mechanism that causes mortality is not completely known and we cannot exclude the relevance for humans, rabbit as used as the most sensitive species.

In rats, the acute dermal LD_{50} values were greater than 60 mg/kg bw for 100% PAA which was the highest dose level tested and which neither caused mortalities nor signs of systemic toxicity.

The acute dermal LD_{50} of test substance containing 4.89 – 11.69% PAA was between 56.1 and 228.8 mg/kg bw in the rabbit (males/females combined). The LD_{50} values derived from the two key studies in rabbit showed clear differences. The compositions of the two tested solutions are reported in the table below.

***Table**: Comparison between the% composition in the two key rabbit studies*

Study	**LD_{50}**	**PAA%**	**H_2O_2%**	**Acetic ac.%**
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 and in the same period of time, with very similar experimental protocols (rabbit strain, treatment conditions, etc.). No relationship between the different composition of the tested solutions and the observed results is apparent. In particular, the percentages of H_2O_2 were very similar and the percentage of acetic acid was higher in the solution that resulted more toxic. Overall, as no evident reason for the different outcomes can be identified and no difference in the sensitivity of the two sexes was reported, the lowest combined LD_{50} value of 56.1 mg/kg bw, rounded to 60 mg/kg bw, is used as ATE dermal values.

Classification for acute dermal toxicity under the CLP Regulation is required for substances with an acute dermal LD_{50} value of ≤ 2000 mg/kg bw. Category 3 is assigned for substances with an LD_{50} value of > 200 and ≤ 1000 mg/kg bw and Category 2 for substances with an LD_{50} value of > 50 and ≤ 200 mg/kg bw according to the table 3.1.1 of Annex I to the CLP Regulation.

In order to derive a correct classification/ATE value for a mixture containing PAA, a 100% substance should be classified even if the substance cannot exist in such a high concentration. Therefore, PAA (100%) should be classified as Acute Tox. 2; H310 based on the calculated LD_{50} values for PAA in the equilibrium test substance.

Based on the results obtained in rabbits, classification of the aforementioned formulations (PAA conc. 4.89 – 11.69%) as Acute Tox. 4 with the hazard statement H312: "Harmful in contact with skin" in accordance with the criteria of the CLP Regulation (reference value 1000 < ATE ≤ 2000 mg/kg bw) is warranted. Neither H_2O_2 nor acetic acid are classified for acute dermal toxicity in Annex VI of the CLP Regulation or in the C&L inventory and therefore they do not have to be taken into account.

Based on the available data, RAC agrees with the DS that 100% PAA warrants a classification as **Acute Tox. Category 2**, with the corresponding hazard statement **H310: Fatal in contact with skin, with a dermal ATE value of 60 mg/kg bw.**

ACUTE INHALATION TOXICITY

Summary of the Dossier Submitter's proposal

Based on the available data, the DS concluded that the relevant LC_{50} value for acute inhalation toxicity of 100% PAA is in the range of > 0.05 and ≤ 0.5 mg/kg bw. Therefore, in accordance with the CLP classification criteria, there is sufficient evidence to remove the asterisk from the classification. Therefore, the DS proposed to classify 100% PAA as Acute Tox. Category 2, with the corresponding hazard statement H330: Fatal if inhaled, and an ATE value of 0.204 mg/L. If the data available indicate that the mechanism of toxicity is corrosivity, then the substance or mixture should also be labelled as EUH071: 'corrosive to the respiratory tract' according to note 1 to table 3.1.3 of CLP Regulation.

Comments received during consultation

One MSCA agreed with the classification of 100% PAA as Acute Tox. 2; H330 and the derived ATE value of 0.204 mg/L (dusts and mists) proposed by the DS. In addition, some editorial revisions were suggested.

No comments were submitted by industry for this hazard class.

Assessment and comparison with the classification criteria

There are several studies where an LC_{50} value has been determined, however only one of these reports was a GLP study performed in line with the OECD TG 403. Many of the studies did not determine an LC_{50} but rather examined the respiratory irritation properties or the influence of PAA on the respiratory rate. There is some variance in the LC_{50} values obtained by different studies. The LC_{50} value used for the comparison with the CLP criteria is 4.080 mg/L (5% PAA) or 0.204 mg/L expressed as 100% PAA. Although this LC_{50} value is not the most conservative value, this study was selected because was conducted according to GLP and OECD TG 403. PAA has a harmonised classification and labelling as Skin Corr. 1A; H314, so it is likely that the mechanism of toxicity is corrosivity.

According to the section 3.1.2 and the table 3.1.1. of the CLP Regulation, if a vapour has an LC_{50} or ATE value of 0.5 or lower, the substance should be classified in category 1. Although the studies often described the test item as vapour, in practise aerosol was created in the experimental settings. That is, small PAA liquid droplets were created, e.g. using a nebulizer, which created PAA mixture suspended in air. Therefore, according to the table 3.1.1., for a mist an ATE of 0.05 - 0.5 mg/L should be classified in category 2 for acute inhalation toxicity. An LC_{50} value of 4.080 mg/L (corresponding to 0.204 mg PAA/L) was used for the comparison with CLP criteria.

According to CLP criteria, a mixture containing 5% PAA should be classified as Acute Tox. 4; H332 (LC_{50} of 4.080 mg/L, assuming 5% concentration). However, in order to derive a correct classification/ATE value for a mixture containing PAA, a 100% substance should be classified even if the substance cannot exist in such a high concentration. In conclusion, based on the presented data, RAC agrees with the DS that 100% PAA warrants a classification as **Acute Tox. 2** with hazard statement **H330: "Fatal if inhaled", and an inhalation ATE value of 0.2 mg/L.**

RAC agrees to the DS proposal to add the labelling "**EUH071 (corrosive to the respiratory tract)".**

ENVIRONMENTAL HAZARD EVALUATION

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

Peracetic acid ...% has harmonised classification regarding environmental hazards as Aquatic Acute 1, H400.

The DS proposed to update the current classification for environmental hazards based on the information provided in the biocidal evaluating Competent Authority (eCA) Report (2015) of peracetic acid under Regulation (EU) No. 528/2012. In addition, data for peracetic acid were obtained from the REACH registration dossier and from open literature sources.

Originally, the DS concluded that PAA was "rapidly degradable" and had a low potential for bioaccumulation.

Regarding aquatic acute toxicity, the DS considered that there was available data for all trophic levels. Algae were the most sensitive taxonomic group and green alga *Selenastrum capricornutum* was considered the most sensitive species tested. Therefore, the DS proposed Aquatic Acute 1, with an M-factor of 10 based on the 72-hour E_rC_{50} value of 0.05 mg/L for *Selenastrum capricornutum* (geometric mean measured concentrations).

Regarding aquatic chronic toxicity, DS considered that reliable and valid long-term aquatic toxicity data for PAA were only available for algae. Long-term aquatic toxicity data available in fish and aquatic invertebrate studies were not considered valid for classification purposes due to the analytical deficiencies to monitor PAA concentrations. Therefore 72-hour NOE_rC value of 0.031 mg/L for *Selenastrum capricornutum* based on geometric mean measured concentrations was proposed by DS as the only reliable chronic endpoint.

As adequate chronic toxicity data were available only for one trophic level, the DS indicated that classification of PAA should be derived from the data (acute or chronic) that gives the strictest classification and M-factor. Therefore, the DS proposed Aquatic Chronic 2 based on the 72-hour NOEC value of 0.031 mg/L mentioned above.

During the consultation there were some comments (see section "Comments during consultation") related to the DS conclusion on PAA degradability and to the available chronic studies.

Hence, after the commenting round, the DS agreed that PAA should be considered as not rapidly degradable and that fish appeared to be most sensitive taxonomic group for the chronic toxicity of PAA. Therefore, DS provided alternative approach (please see in section "Additional key elements") regarding the aquatic chronic classification based on recalculated 33-d NOEC value of 0.00069 mg/L for *Danio rerio* from chronic toxicity study with fish.

Overall, after consultation round, the DS concluded that PAA is "not rapidly degradable" and has a low potential for bioaccumulation.

Regarding aquatic acute toxicity, the DS proposed classification as Aquatic Acute 1 with an M-factor of 10, based on the 72-hour E_rC_{50} value of 0.05 mg/L for *Selenastrum capricornutum* based on geometric mean measured concentrations.

Regarding aquatic chronic toxicity DS proposed two options:

Aquatic Chronic 1 with an M-factor of 1, based on the 72-hour NOE_rC value of 0.031 mg/L for *Selenastrum capricornutum* based on geometric mean measured concentrations;

or

Aquatic Chronic 1 with an M-factor of 100, based on the 33-days NOEC value of 0.00069 mg/L for *Danio rerio* based on the initial test concentrations extrapolated from the analytically verified highest test concentration.

The first option (Aquatic Chronic 1, M = 1) was supported by the DS.

Degradation

Based on a ready biodegradability test (OECD TG 301E), degradation of PAA was measured being between 66 to 98% within 14 to 28 days by DOC removal method. However, it was not demonstrated that the degradation passed the 10-d window criteria. Additionally, there were deviations from the TG and deficiencies in study design (e.g., no abiotic control and no analytical verification of PAA concentration in the test solution during the stepwise addition i.e. first 14 days period) nevertheless, the study was considered suitable by the DS for assessing the ready degradability of PAA.

Active sludge respiration inhibition test (OECD TG 209) is not a ready biodegradability test, however DS considered that it provided relevant information on the primary degradation of peracetic acid, which was followed analytically by HPLC. PAA disappeared rapidly with a DT_{50} of < 3 minutes when applied at concentrations < 30 mg/L at pH 7. At higher concentration of 100 mg/L, the degradation in activated sludge respiration inhibition test was slowed down resulting in a DT_{50} of 15 minutes.

Two closed bottle tests (OECD TG 301D) were provided as well. In one test, PAA was determined degrading 33% at the end of the 10-day window (11th day) and 42% at the end of the test (day 28). In the second test, PAA was observed degrading > 70% at the end of the test (day 28). However, DS pointed out that closed bottle tests are not suitable for the assessment of the biodegradation of PAA, as they are based on measurements of the biological oxygen consumption and, therefore, they are not suitable for a reliable biodegradation assessment since PAA itself liberates oxygen upon decomposition and, moreover, produces oxygen also due to the decomposition of hydrogen peroxide.

Overall, the DS concluded that ready biodegradability study results cannot be used for a definite conclusion on the PAA ready biodegradability, however, they can be used as supporting information on the conclusion for rapid degradation of the PAA.

According to a hydrolysis test (OECD TG 111), PAA was found hydrolytically instable with recalculated DT_{50} values of 46.7h (pH 4) and 31.7h (pH 7) at 25°C. The half-lives obtained from the study were recalculated by using first order multi-compartment model (FOMC). Still, the DS pointed out that the hydrolysis was studied only at one temperature, the sterility of the test system was not indicated and it was not stated in the study report whether each sample was taken from a separate vessel as recommended or from a single bulk vessel. Furthermore, only a single sample was taken at each time point instead of the minimum of two replicate samples. In addition, the formation of hydrolysis products was not studied.

Similar results have been derived from another hydrolysis study (EU Method C.7) with DT_{50} value of 31.2h (pH 4) at 25°C and DT_{50} values of 200 min at pH4, 97 min at pH 7 and < 15 min at pH 9 at 50°C. However, this study was considered by the DS only as supportive information as it was conducted with a mixture containing 0.35% PAA and H_2O_2 (no information on acetic acid content available) and only the study summary was available.

Two other non-guideline studies on hydrolytic degradation of PAA indicated acetic acid (CAS 64-19-7) and hydrogen peroxide (CAS 7722-84-1) as hydrolysis products.

Overall, the DS considered that degradation information from the available hydrolysis tests provided sufficient data on PAA of having a half-life of less than 16 days. However, one of the formed hydrolysis products (hydrogen peroxide) fulfils the classification criteria as hazardous for aquatic environment: the lead registrant for REACH registration self-classified hydrogen peroxide as Aquatic Chronic 3, based on a NOEC value of 0.63 mg/L for both aquatic invertebrates and algae.

No studies on photochemical degradation of PAA were available. PAA entering the air was not considered persistent in the atmosphere due to indirect photochemical degradation (DT_{50} value of 3.969 days according to the method of Atkinson). In addition, DT_{50} of 22 minutes has been determined for 25% PAA by using Fourier transfer IR spectroscopy. Therefore, the DS considered that there is no need to investigate the data further.

Several non-guideline studies describing the degradation and decomposition of PAA in different water types and water sources were provided. The studies indicated that dissipation in seawater seems to be very rapid with DT_{50} of 2 min in synthetic seawater. Degradation of PAA was also very rapid under the conditions of effluent water from a sewage treatment plant showing rapid dissipation with DT_{50} < 5 min. Degradation of 95.1% within 1 day in drinking water and from 17% to 91% within 120 minutes in tap water was observed. The lowest degradation measured was 25.6% within 5 days in lake water. Still, the test conditions and characteristics of the test media were not described, therefore the DS considered that only general conclusions can be made from these tests and no reliable half-lives can be calculated from the existing data for fresh water. Nevertheless, the DS assumed that tests showed that dissipation of PAA in tap water or natural waters supported the observations made in hydrolysis studies.

Originally, the DS considered PAA as rapidly degradable based on hydrolysis studies and that formed hydrolysis products (acetic acid and hydrogen peroxide), thus it did not fulfil the classification criteria as hazardous for aquatic environment. However, during consultation period, it was indicated that one of the formed hydrolysis products (hydrogen peroxide) fulfils the classification criteria as hazardous for aquatic environment. Consequently, the DS concluded that degradation information did not provide sufficient data to show that PAA is ultimately degraded to above 70% within 28 days (equivalent to a half-life of less than 16 days) or being transformed to non-classifiable products. In conclusion, PAA was considered by the DS to be not rapidly degradable according to the CLP criteria.

Aquatic Bioaccumulation

As there were no experimental results on BCF values, the bioaccumulation potential for classification purposes was based on the n-octanol/water partition coefficient of PAA. The experimental Log P_{OW} (Partition coefficient (n-octanol/water): Shake Flask Method) ranged between -0.46 and -0.66, whereas the calculated values by using QSAR ranged from -0.23 to -1.20. In addition, the provided calculated BCF value by using program BCFBAF v3.00 was 3.162 L/kg.

Overall, based on the results summarised above, the DS concluded that PAA has a low potential for bioaccumulation.

Aquatic Toxicity

PAA is produced in a reaction of hydrogen peroxide with acetic acid in an aqueous solution. Therefore, classification of PAA was based on ecotoxicity tests on aquatic mixtures of PAA, acetic acid, hydrogen peroxide and water. Hence, the aquatic toxicity results were derived based on PAA content of the test material by extrapolating the toxicity results to peracetic acid content

expressed as mg PAA/L and not based on Test Solution (mg TS/L). DS noted that based on the aquatic toxicity studies with variety of PAA contents (0.35 – 18%) in the CAR (Finland, 2015), no correlation was evident between the aquatic toxicity results and different PAA contents of the test materials used.

Due to the hydrolytical instability of PAA, only studies with analytical monitoring and results based on measured concentrations of the test substance and with a known content of PAA were considered reliable by the DS (Klimisch score 1 & 2).

Results from available acute and chronic studies for all trophic levels of PAA are summarised in the following tables and sections.

Aquatic Acute toxicity

Test method	Test organism	Short-term result (endpoint)	Reference / Test item / Klimisch score
Fish			
U.S. EPA-FIFRA, 40 CFR, Section 158.145 / GLP	*Lepomis macrochirus*	96h LC_{50} = 1.1 mg/L (mm)	Anonymous, 1996a / PAA 5.22% w/w / 2
Aquatic invertebrates			
OECD TG 202 / GLP	*Daphnia magna*	48h EC_{50} = 0.73 mg/L (mm)	Anonymous, 1996b / PAA 5.22% w/w / 2
Algae / other aquatic plants			
OECD TG 201; U.S. EPA-FIFRA 123-2 / GLP	*Selenastrum capricornutum*	72h E_rC_{50} = 0.16 mg/L (initial) 120h E_rC_{50} = 0.18 mg/L (initial) **72h E_rC_{50} = 0.050 mg/L (geom. mean)** 120h E_rC_{50} = 0.052 mg/L (geom. mean)	Anonymous, 1996c / PAA 5.22% w/w / 2

mm = mean measured concentration

In the acute toxicity studies, the PAA concentrations were determined indirectly by measuring the hydrogen peroxide concentrations and converting these into PAA concentrations at the beginning and at the end of the test. The hydrogen peroxide concentrations in the test water samples were determined using a spectrometric method.

In a semi-static (daily renewal) acute toxicity study (similar to OECD TG 203) under GLP with Bluegill sunfish (*Lepomis macrochirus*), a 96h LC_{50} value of 1.1 mg PAA/L was obtained based on mean measured concentrations as measured concentrations of test substance were < 80% of initials during the test. The measurements of pH, dissolved oxygen and temperature were not carried out daily but at 0, 48 and 96 hours deviating from the OECD TG 203. However, these were not considered to have an impact on the outcome of the study as validity criteria of the OECD TG 203 were otherwise met. The study was considered valid and reliable for classification purposes of PAA by the DS.

In the acute toxicity study (OECD TG 202) GLP compliant with aquatic invertebrates (*Daphnia Magna*), a 48h EC_{50} value of 0.73 mg PAA/L was obtained based on mean measured concentrations (analysed indirectly based on hydrogen peroxide concentrations). The study was considered valid and reliable for the classification purposes of PAA by the DS.

In the toxicity study (OECD TG 201) GLP compliant with algae (*Selenastrum capricornutum*), a 72h EC_{50} value of 0.16 mg PAA/L and a 120h EC_{50} value of 0.18 mg PAA/L were obtained based on initial measured concentrations. However, deviations of the test concentrations from the initial measured concentrations were not within the range of ± 20 during the study (only for the highest concentration of 1 mg PAA/L, the concentration of the test item was maintained within the 20% range of the nominal for the whole duration of the test). Thus, the results based on initial

measured concentration were not considered valid for the classification purposes by the DS. Thus, as measured data were available for the start and the end of test, the toxicity values were recalculated by DS based on the geometric mean concentrations. As well, because the concentrations at the end of test were below the analytical detection limit, such concentrations were considered to be half that detection limit by the DS. The obtained EC_{50} values based on the geomean concentrations were 0.050 mg PAA/L for 72 hours and 0.052 mg PAA/L for 120 hours exposures. The biomass in the control cultures increased exponentially by a factor of > 16 within the 72-hour test period, however, no information on coefficient of variation was available. Still the study was considered valid and reliable for the classification purposes by the DS.

Overall, the DS proposed to classify PAA as Aquatic Acute in category 1 based on the 72-hour E_rC_{50} for *Selenastrum capricornutum* of 0.050 mg/L, based on the geometric mean concentrations. As this acute toxicity value falls within the 0.01 < L(E)C50 ≤ 0.1 mg/L range, the acute M-factor proposed by the DS was 10.

Aquatic Chronic toxicity

Test method	Test organism	Long-term result (endpoint)	Reference / Test item/ Klimisch score
Fish			
OECD TG 210 / GLP	*Danio rerio*	33d NOEC = 0.00225 mg/L (nom) **33d NOEC = 0.00069 mg/L (estimated*)**	Anonymous, 2007b / PAA 14.9% w/w / 2 (by eCA) – 3 (by DS)
Aquatic invertebrates			
OECD TG 211 / GLP	*Daphnia magna*	21d NOEC = 0.34 mg/L (nom) 21d NOEC = 0.0121 mg/L (estimated**)	Anonymous, 2000b / PAA 14.8% w/w / 2 (by eCA) – 3 (by DS)
Algae / other aquatic plants			
OECD TG 201 / GLP	*Selenastrum capricornutum*	72h NOEC = 0.061 mg/L (initial) 120h NOEC = 0.12 mg/L (initial) 72h NOEC = 0.031 mg/L (geom. mean) 120h NOEC = 0.043 mg/L (geom. mean)	Anonymous, 1996c / PAA 5.22% w/w / 2

mm: mean measured concentration, nom: nominal concentration
* initial test concentrations extrapolated by the biocidal eCA from the analytically verified highest test concentration concentrations
** recalculated by biocidal eCA using a geomean approach with background correction for supposed PAA concentration in the control samples.

In a flow-through study (OECD TG 210) GLP compliant with Zebrafish (*Danio rerio*), a 33d NOEC value of 0.00225 mg PAA/L based on nominal concentrations for post hatch survival and overall survival was observed. The NOEC value was based on the statistically significant effects seen on the survival at the two highest exposure concentrations, whereas no effects were seen on hatching or growth. PAA concentrations were analytically monitored via LC-MS/MS (by MTSO method), however, due to the low sensitivity of the analytical method, actual concentrations were measured only in the stock solutions (all treatments) and the test vessels of the highest concentration level. During the first 21 days of the study the test concentration in the test solutions could not be verified (measured concentrations of PAA less than Limit of Quantification (LOQ)). As measured concentrations did not remain within 80-120% of the nominal concentrations, the effect concentrations should be determined and expressed relative to the arithmetic mean concentration for flow-through tests. However, the arithmetic mean exposure concentration in the study cannot be determined because the concentrations in test vessels have been analytically determined only at the highest treatment level. The NOEC value of 0.00225 mg

PAA/L based on the nominal concentration was below the analytical LOQ. Thus, the analytical verification of the test concentration of PAA was only possible for the highest test level. This chronic study on fish was originally reported in the biocidal Competent Authority Report (CAR) of PPA. The biocidal evaluating Competent Authority (eCA) originally assigned a reliability score of 2 according to Klimisch approach, however, the DS assigned score 3 and considered the study as not reliable and valid for classification purposes due to lack of analytical verification and/or quantification of the test concentrations of PAA during the test.

In a semi-static study (OECD TG 211) under GLP with aquatic invertebrates (*Daphnia magna*), a 21d NOEC value of 0.34 mg PAA/L based on nominal concentrations was obtained. An attempt of NOEC re-calculation based on geometric mean approach was provided in the CAR, however analytical verification method for PAA was not considered reliable due to the presence of another unknown component and was considered as not acceptable for the classification purposes. The eCA originally assigned a reliability score of 2, however, the DS assigned a score of 3 and considered this study as not reliable and valid for classification purposes due to the invalid analytical method for the verification of PAA concentrations during the test.

In a toxicity study (OECD TG 201) under GLP with algae (*Selenastrum capricornutum*), a 72h NOEC value of 0.061 mg PAA/L and a 120h NOEC value of 0.12 mg PAA/L were obtained based on initial measured concentrations. However, for the same reasons as provided in the ODD section of aquatic acute toxicity for algae, the toxicity values were recalculated by the DS based on the geometric mean concentrations. The obtained NOEC values based on the geomean concentrations were 0.031 mg PAA/L for 72 hours and 0.043 for 120 hours.

For the reasons explained before, the DS originally considered PAA as rapidly degradable and not bioaccumulative, and that reliable and valid long-term aquatic toxicity data for PAA was only available for the algae. Based on this, the initial classification proposal was Aquatic Chronic 2, considering the NOEC of 0.031 mg/L for algae within the range of 0.01 < NOEC ≤ 0.1 mg/L according to table 4.1.0(b)(ii). The so-called "surrogate approach", in accordance with table 4.1.0(b)(iii) was not applied since the substance was considered rapidly degradable and not bioaccumulative.

After the consultation round, the DS re-assessed the rapid degradability of PAA, concluding that the substance should be considered not rapidly degradable. Therefore, DS proposed to classify PAA as Aquatic Chronic in category 1 based on the 72-hour NOEC for *Selenastrum capricornutum* of 0.031 mg/L based on geometric mean. As this chronic toxicity value falls within the 0.01 < NOEC ≤ 0.1 mg/L range, the chronic M-factor proposed by the DS was 1. The same chronic classification was obtained applying the so called "surrogate approach", according to table 4.1.0 (b)(iii) of CLP Regulation, using the lowest acute toxicity data for fish and daphnids (0.1 < EC_{50} = 0.73 ≤ 1 mg/L).

At the same time, after the commenting round, DS re-assessed the reliability of the chronic study on fish and provided the eCA proposal regarding the calculation of the initial concentrations in the test, which would provide a more realistic exposure estimate than using nominal concentrations (please see section "Additional key elements"). Therefore, the DS considered that the re-calculated NOEC of 0.00069 mg PAA/L was the most conservative estimate for chronic toxicity of PAA and considered it a reliable and valid key endpoint for the classification purposes for PAA. Therefore, as an alternative approach, the DS also considered to classify PAA as Aquatic Chronic in category 1 based on the 33-days NOEC for *Danio rerio* of 0.00069 mg/L based on initial test concentrations extrapolated from the analytically verified highest tested level. As the substance was considered not rapidly degradable (after the commenting round) and chronic toxicity value fell within the 0.0001 < NOEC ≤ 0.001 mg/L range, the resulting chronic M-factor was 100.

Comments received during consultation

Two MSCAs and one National Authority (NA) commented and they agreed with the proposed classification as Aquatic Acute 1 (M = 10), however, one MSCA and the NA disagreed with the initially proposed classification as Aquatic Chronic 2.

One MSCA proposed classification as Aquatic Chronic 1 based on the available chronic toxicity study with fish (*Danio rerio*) on the base of the following:

- in the CLH dossier this study got a reliability of 3, while in the CAR in the frame of assessment as biocidal active substance the same study was considered as valid with restrictions (reliability 2) and even the $PNEC_{water}$ is based on the NOEC from the chronic toxicity with fish study.
- arguments for lowering of the reliability of the study to 3 in the CLH dossier is just that the LOQ was very low and therefore analytical monitoring of the test substance concentrations was not performed for all test substance concentrations.
- even the NOEC based on nominal concentrations (0.00225 mg/L) would already trigger a classification as Aquatic Chronic 1.

The second MSCA did not indicate preference regarding to Aquatic Chronic classification, however, pointed out that results from the chronic test with fish suggested that fish were the most sensitive species and an available reliable chronic test on fish would have likely led to a more stringent classification.

The NA disagreed with the DS consideration that PAA should be considered as rapidly degradable based on a weight of evidence:

- asked DS to clarify whether the 10-d window was met in ready biodegradability test OECD TG 301E.
- pointed out that DT_{50} values from the hydrolysis study OECD TG 111 determined at 25 °C should be corrected to 12 °C as the environmentally relevant temperature and indicated that the identified hydrolysis product hydrogen peroxide is classified as hazardous to the aquatic environment, therefore, hydrolysis studies cannot be used alone to conclude that PAA was rapidly degradable for the purpose of hazard classification.
- pointed out that the half-life from the OECD TG 209 study and the non-guideline degradation study in effluent was related to primary degradation and dissipation, with the levels of mineralisation were unknown and ultimate degradation could not be clearly demonstrated. In addition, degradation products were not analysed in these studies, thus it could not be demonstrated that any degradation products do not meet the classification criteria as hazardous to the aquatic environment.

Regarding chronic toxicity, NA pointed out that the chronic toxicity study with fish (*Danio rerio*) and the chronic toxicity study with invertebrates (*Daphnia magna*) should be considered further because the data could have a significant impact on the hazard classification due to the higher sensitivity compared to the current long-term endpoint for algae:

- TG validity criteria for controls were met for both studies although there were limitations with the analytical verification.
- available information indicated that stock solutions used in the flow through systems were broadly in line with nominal concentrations indicating the test systems were dosed with near nominal concentrations.

- although nominal or initial measured concentrations were not ideal, study endpoints based on nominal, initial measured or mean measured concentrations, if possible to calculate, were likely to be more sensitive than the algal NOEC.

In answer to the comments on degradation DS indicated that:

- regarding the ready biodegradability test OECD TG 301E, available data was not sufficient for obtaining the degradation curve to clarify whether the 10-day window was met or not. Taking into account the deviations of the TG and the deficiencies of the study, it could not be used to conclude that PAA is readily biodegradable.
- regarding the DT_{50} values in the hydrolysis study (OECD TG 111), the DS pointed out that the originally corrected values to 12 °C were not presented due to some uncertainties with extrapolation. However, rough hydrolysis temperature correction estimates were available. Therefore, after the temperature correction, the longest half-life was estimated of 181.1 hours (approximately 7.5 days).
- regarding the comment referring to the hydrolysis product, the DS agreed that the hydrolysis of the parent substance (PAA) cannot be considered to reflect environmental degradation as one of its hydrolysis products (hydrogen peroxide) fulfils the criteria for classification as hazardous to the aquatic environment.

Overall, the DS agreed that PAA should be considered as not rapidly degradable for the purpose of hazard classification.

In answer to the chronic toxicity study with fish (*Danio rerio*) DS noted that:

- the assessment as biocidal active substance followed different guidance(s) than the guidance on the application of the CLP criteria.
- reliability of the study was evaluated for the classification purposes. No sufficient evidence was available that the initial measured concentrations have been maintained throughout the test duration and could be used for the derivation of reliable NOEC value for classification purposes.
- CLP guidance was clear that when measured concentrations do not remain within 80-120% of the nominal concentrations, the effect concentrations could not be based on nominal or initial measured concentrations.

Nevertheless, DS agreed that fish seems to be most sensitive taxonomic group for the chronic toxicity of PAA and suggested an alternative approach to derive chronic classification based on the initial test concentrations extrapolated from the analytically verified highest test concentration, if the chronic toxicity study with fish (*Danio rerio*) was considered reliable (see "additional key elements" below). According to this approach, the DS proposed to classify PAA as Aquatic Chronic 1 with an M factor of 100 as the substance was considered not rapidly degradable and the chronic toxicity value fell within the $0.0001 < NOEC \leq 0.001$ mg/L range, according to table 4.1.0(b)(i) and table 4.1.3 of CLP Regulation. Since no chronic toxicity value on aquatic invertebrates is considered reliable, the "surrogate approach", according to table 4.1.0 (b)(iii) of CLP Regulation using the lowest acute toxicity data for daphnids ($0.1 < EC_{50} = 0.73 \leq 1$ mg/L) was considered. However, the most stringent classification was obtained considering the NOEC for fish.

Assessment and comparison with the classification criteria

Degradation

RAC considers that PAA is not demonstrated to be readily biodegradable in a 28-day test for ready biodegradability. The pass level of the test (70% dissolved organic carbon removal or 60% theoretical oxygen demand) was not demonstrated to be achieved within 10 days from the onset of biodegradation. Furthermore, it cannot be confirmed that the formed degradation products do not fulfil the criteria for classification as hazardous to the aquatic environment.

Therefore, RAC considers that, despite some evidence of hydrolysis and some indication of primary degradation and dissipation, PAA is not ultimately degraded to above 70% within 28 days (equivalent to a half-life less than 16 days), or rapidly transformed to non-classifiable products and can be regarded as not rapidly degradable for classification purposes.

Aquatic Bioaccumulation

No experimental results on BCF values are available. The calculated BCF value by use of program BCFBAF v3.00 of 3.16 L/kg is well below the CLP trigger value of ≥ 500. The n-octanol/water partition coefficient estimated by conducting test and calculated by using QSAR of log P_{ow} -0.23 to -1.20 is well below the CLP trigger value of ≥ 4.

Therefore, RAC agrees with the DS that PAA has a low potential for bioaccumulation, according to the CLP criteria.

Aquatic Toxicity

RAC considers that classification of PAA is based on ecotoxicity tests on aquatic mixture of PAA, acetic acid, hydrogen peroxide and water. Therefore, RAC agrees that the aquatic toxicity results are derived based on PAA content of the test material by extrapolating the toxicity results to 100% peracetic acid content expressed as mg PAA/L and not based on test solution mg TS/L.

RAC agrees that in the **acute toxicity studies**, the PAA concentrations are determined indirectly by measuring the hydrogen peroxide concentrations and converting these to PAA concentrations at the beginning and at the end of the test.

RAC notes that there are reliable aquatic acute toxicity data for all trophic levels.

The acute toxicity study (similar to OECD TG 203) under GLP with bluegill sunfish (*Lepomis macrochirus*) is considered reliable and adequate for the classification of PAA by RAC. The obtained 96h LC_{50} value is 1.1 mg PAA/L, based on mean measured concentrations.

The acute toxicity study (OECD TG 202) under GLP with aquatic invertebrates (*Daphnia Magna*) is considered reliable and adequate for the classification of PAA by RAC. The obtained 48h EC_{50} value of 0.73 mg PAA/L is based on mean measured concentrations.

The toxicity study (OECD TG 201) under GLP with algae (*Selenastrum capricornutum*), is considered reliable and adequate for the classification of PAA by RAC. RAC notes that deviation of the test concentrations from the measured initial concentrations are not within the range of ± 20%. OECD TG 201 indicates that "*…if there is evidence that the concentration of the substance being tested has been satisfactorily maintained within ± 20% of the nominal or measured initial concentration throughout the test, analysis of the results can be based on nominal or measured initial values…*". Therefore, RAC agrees that the results based on initial measured concentrations are not considered valid for the classification purposes. CLP Guidance indicates that "*where measured data are available for the start and end of test (as is normal for the acute Daphnia and algal tests), the L(E)C_{50}, for classification purposes, may be calculated based on the geometric mean concentration of the start and end of test. Where concentrations at the end of test are*

below the analytical detection limit, such concentrations shall be considered to be half that detection limit". Therefore, RAC agrees with recalculation of the algae toxicity values based on the geometric mean concentrations using the measured values at the beginning and at the end of the test. RAC acknowledges that biomass in the control cultures increased exponentially by a factor of >16 within the 72-hour test period, however, recognises that there is no information on the OECD TG 201 validity criteria regarding the mean coefficient of variation for section-by-section specific growth rates. Nevertheless, RAC considers that the algae study is valid and reliable for the classification purposes under CLP. Therefore, RAC considers that from the algae study with *Selenastrum capricornutum*, the reliable and valid acute endpoint is the 72-hour E_rC_{50} of 0.05 mg PAA/L, based on geometric measured concentrations.

Based on the available and reliable information, RAC agrees with the DS that PAA warrants acute classification as:

Aquatic Acute 1 based on E_rC_{50} = 0.05 mg/L for *Selenastrum capricornutum.* As this acute toxicity value falls within the 0.01 < $L(E)C_{50}$ ≤ 0.1 mg/L range, the **acute M-factor is 10**.

RAC notes that **chronic data** are available for all trophic levels, however not all the data are considered reliable for classification purposes.

The chronic toxicity study on fish (*Danio rerio*) according to OECD TG 210 indicates that fish are the most sensitive organism in the case of chronic exposure. The aquatic chronic study with fish has an analytical issue (LOQ below quite all tested concentrations) and the fish were not correctly exposed to the substance during the first part of the test (see "Additional key elements"). However, RAC is of opinion that the available chronic toxicity study on fish (*Danio rerio*) according to OECD TG 210 cannot be disregarded and is considered as reliable and valid study for classification purposes (for the reasons explained in detail in section "In depth analyses by RAC"). The obtained toxicity value is a 33-day NOEC of 0.00069 mg PAA/L based on estimated mean concentrations.

The chronic toxicity study (OECD TG 211) under GLP with aquatic invertebrates (*Daphnia Magna*) is considered not reliable for the classification of PAA by RAC due to the uncertainties related to the analytical verification of the test concentrations (invalid analytical method, presence of an unknown component in the culture medium interfering with measurements).

The toxicity study (OECD TG 201) under GLP with algae (*Selenastrum capricornutum*), is considered reliable and adequate for the classification of PAA by RAC. The reliable and valid chronic endpoint is the 72hour NOE_rC of 0.031 mg PAA/L, based on geometric measured concentrations (see above in acute assessment).

According to the CLP criteria, if adequate chronic toxicity data are not available for all trophic levels, the classification shall be assessed according to the criteria given in Table 4.1.0(b)(i) (as the substance has been considered to be not rapidly degradable) and, if for the other trophic level adequate acute toxicity data are available, according to the criteria given in Table 4.1.0(b)(iii) and should be based on the most stringent outcome. In this case, the most stringent classification and M-factor is based on the results of the chronic toxicity value with fish (*Danio rerio*). Therefore, RAC considers that PAA warrants chronic classification as:

Aquatic Chronic 1 based on NOEC =0.00069 mg/L for *Danio rerio*. As this chronic toxicity value falls within the 0.0001 < NOEC ≤ 0.001 mg/L range, the **chronic M-factor is 100.**

Conclusion on classification

Overall PAA is considered not rapidly degradable and does not fulfil the criteria for bioaccumulation.

Based on the available and reliable information, RAC proposes the following classification:

Aquatic Acute 1 based on E_rC_{50} = 0.05 mg/L for *Selenastrum capricornutum.* As this acute toxicity value falls within the 0.01 < $L(E)C_{50}$ ≤ 0.1 mg/L range, the **acute M-factor is 10**.

Aquatic Chronic 1 based on NOEC =0.00069 mg/L for *Danio rerio*. As this chronic toxicity value falls within the 0.0001 < NOEC ≤ 0.001 mg/L range, the **chronic M-factor is 100.**

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).