Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the 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

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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Substance name: peracetic acid ...%
EC number: 201-186-8
CAS number: 79-21-0
Dossier submitter: Finland

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
01.10.2021	Germany		MemberState	1
Comment received				
Peracetic acid (PAA) was evaluated in 2015 (Finland (FI) Rapporteur) in the context of Regulation (EU) No 528/2012. The "DocIIA_Peracetic_acid_PT1-6_Final_CAR_confidential_2015(1)" of the Final CAR is submitted as a confidential annex. 1) The dossier submitter (DS) is requested to include a percentage value (...%) with respect to PAA to which this dossier is concerned or provide an explanation for not doing so. 2) The DS is asked to enhance the explanation/justification provided for using theoretical calculated values (100 % PAA) for classification and ATE derivations. This comment is related to the comment above. Justification: It is noted that the following statement appears in the current dossier "In order to derive a correct classification/ATE value for a mixture containing peracetic acid, a 100 % substance should be classified even if the substance cannot exist in such a high concentration". In the current dossier theoretical calculated values (100 % PAA) have been used for classification and ATE derivations instead of applying acute toxicity estimate calculations to determine the ATE of the mixtures. As this constitutes a conservative approach for hazard assessment purposes, DE CA supports their use in this instance.				
Dossier Submitter's Response				
Thank you for your comments. We are of the opinion that Chemical Identification/ entry's name in Annex VI has to be peracetic acid ...% as concentration of PAA varies. PAA does not exist on its own but it is a reaction product of H2O2 and acetic acid and water.				

The concentration of PAA is typically 5-15 % but depending on the reaction process it can also exist as high as 40 % concentration. Regarding hazard classes for acute toxicity and aquatic environment it is necessary to use a 100 % substance in order to derive correct classifications and ATE values for acute toxicity endpoints. Otherwise it is impossible to derive ATE values for the substance.
RAC's response
RAC agrees with the DS's response.

Date	Country	Organisation	Type of Organisation	Comment number
08.10.2021	Germany		MemberState	2
Comment received				
We do not agree with the assessment of the physical hazard classes Flammable liquids, Organic Peroxides and Oxidising Liquids. Due to the variability of the composition of PAA formulations, the classification could lead to different physical hazard classes and an entry of a harmonised classification in Annex VI is therefore not possible. The entry should be simplified by omitting the classifications for the physical hazards.				
Dossier Submitter's Response				
Thank you for your comment. We agree that the entry will be simplified by omitting the classifications for the physical hazards because of the problematic SID and variation in classifications.				
RAC's response				
The RAC supports the removal of flammable liquids and to keep the classification as Org. Perox. D with the addition of note T.				

Date	Country	Organisation	Type of Organisation	Comment number
07.10.2021	United States of America	Peracetic Acid Registration Group (PAR)	Industry or trade association	3
Comment received				
Section 1.1: The degree of purity (%) is only applicable if peracetic acid is used as an active substance in biocidal products. This purity specification is not applicable when peracetic acid is used for non-biocidal applications. "Specific Conc. Limits, M-factors" but also in the columns for "Classification" and "Labelling". Section 2.1, Table 6: The classification for the hazard class "STOT SE 3 (H335)" should not only be mentioned in the column Section 5 (Identified uses): Peracetic acid has not only biocidal uses but also non-biocidal uses. It has been registered under the REACH regulation with a total tonnage band of greater than 1,000 tonnes. Attachment contains these comments in pdf format. ECHA note – An attachment was submitted with the comment above. Refer to public attachment Peracetic acid - comments on CLH report - Oct 7_final.pdf				

Dossier Submitter's Response
Thank you for your comments. Comment related to the Section 1.1 - Indeed the purity can vary between the substances. Purity in the CLH dossier relates to the substances and studies used in the CLH dossier. Comment related to the Section 2.1 – As the classification for the hazard class "STOT SE 3 (H335) is within the specific concentration limit it is presented only in the column "Specific Conc. Limits, M-factors". Comment related to the Section 5 – Thank you for your comment. It could be added to the CLH dossier that the substance is also registered under the REACH Regulation and is manufactured in and imported to the European Economic Area at ≥ 1 000 to < 10 000 tonnes per annum. The substance is used by consumers and by professional workers (widespread uses) and in formulation and re-packing 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.
RAC's response
Noted.

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
01.10.2021	Germany		MemberState	4
Comment received				
Acute Toxicity – oral: 1) DE-CA supports the classification of 100 % PAA with Acute Tox. 3; H301 and the derived oral ATE value of 70 mg/kg bw as proposed by the DS (FI). Justification: The lowest LD50 value reported in the three key studies is found in Anonymous (1985). Here a LD50 of 1400 mg/kg bw for female rats, which corresponds to a LD50 of 70 mg/kg bw for 100 % PAA, is reported. 70 mg/kg bw was identified as the oral ATE, which warrants classification with Acute Tox. 3 according to the CLP criteria. 2) The DS is asked to add a brief explanation to section 10.1.1 as to how and/why the studies by Anonymous (1998b, 1995, 1985) were identified as key studies. Justification: This section would benefit from a description as to the rational by which the key studies were determined. 3) The DS is requested to modify the following statement in paragraph 2 of section 10.1.1. due to exceptions from the given generalisation. "According to the results of all acute oral toxicity studies for peracetic acid concentrations <1 % the oral LD50 is >2000 mg/kg bw and for peracetic acid concentrations of 5.0 - 15.2 % the oral LD50 is from 95.0 to 250 mg/kg bw in males, from 70 to 240 mg/kg bw in females, and from 76.2 to 271 mg/kg bw as combined (male/female)". Justification: a) It is unclear if the LD50 values indicated in this statement refer to the test material utilised in the studies or theoretical calculated values (100 % PAA). b) In the study by Anonymous (1994), conducted with a test preparation containing 0.89				

% PAA, a LD50 of 1663 mg/kg bw (females) is reported, which corresponds to 14.8 mg/kg bw of 100 % PAA. Neither LD50 is >2000 mg/kg bw.
c) In the study by Anonymous (1991e), conducted with a test preparation containing 0.15 % PAA, a LD50 of >7.5 mg/kg bw of 100 % PAA is reported, which could be interpreted as being below 2000 mg/kg bw.
d) In the study by Anonymous (1993a), conducted with a test preparation containing 15 % PAA, a LD50 of >30 mg/kg bw for 100 % PAA (male/female) is reported, which could be interpreted as being below 76.2 mg/kg bw.
e) In the study by Anonymous (1998c), conducted with a test preparation containing 10.85 % PAA, a LD50 of 200-1000 mg/kg bw (male/female) is reported, which corresponds to 21.7-109 mg/kg bw of 100 % PAA. Both LD50s could be interpreted as not conforming to the stated range of 76.2 to 271 mg/kg bw.
f) In the study by Anonymous (1977), which was conducted with a test preparation containing 10 % PAA, an LD50 corresponding to 254 mg/kg bw (males) of 100 % PAA is reported. This LD50 does not conform to the stated range of 95-250 mg/kg bw.

4) The DS is requested to modify the following statement in paragraph 3 of section 10.1.2. due to exceptions from the given generalisation.
“The results of acute oral toxicity studies performed in rats with formulations containing peracetic acid at concentrations from 5 % to 15 % demonstrated acute oral LD50 values in the range of 314-1859 mg/kg bw (70-93 mg/kg bw for 100 % PAA)”.
Justification:
a) In the key study by Anonymous (1998b), conducted with a test preparation containing 5 % PAA, LD50s of 1922 mg/kg bw (combined) and 1993 mg/kg bw (males) are reported, which correspond to 96.1 and 99.7 mg/kg bw of 100 % PAA. These LD50s do not conform to the ranges stated.
b) In the key study by Anonymous (1985), conducted with a test preparation containing 5 % PAA, a LD50 of 1900 mg/kg bw (males) is reported, which correspond to 95 mg/kg bw of 100 % PAA. These LD50s do not conform to the ranges stated.
c) In the study by Anonymous (1998c), conducted with a test preparation containing 5.6 % PAA, LD50s of 3622 mg/kg bw (combined) 3271 mg/kg bw (males) 4217 mg/kg bw (females) are reported, which correspond to 202.8, 183.2 and 236.2 mg/kg bw of 100 % PAA. These LD50s do not conform to the ranges stated.
d) In the study by Anonymous (1996b), conducted with a test preparation containing 11.69 % PAA, LD50s which correspond to 98.9 (males) and 36.7 (females) mg/kg bw of 100 % PAA are reported. These LD50s do not conform to the stated range.
e) In the study by Anonymous (1993a), conducted with a test preparation containing 15 % PAA, an LD50 of >200 mg/kg bw (combined) is reported, which corresponds to >30 mg/kg bw of 100 % PAA. These LD50s could be interpreted as not conforming to the ranges stated.
f) In the study by Anonymous (1998c), conducted with a test preparation containing 10.85 % PAA, an LD50 of 200-1000 mg/kg bw (combined) is reported, which corresponds to 21.7-109 mg/kg bw of 100 % PAA. These LD50s could be interpreted as not conforming to the ranges stated.
g) In the study by Anonymous (1977), conducted with a test preparation containing 10 % PAA, the LD50s corresponding to 254 (males) and 239 (females) mg/kg bw of 100 % PAA do not conform to the range stated.

5) Some more information might be given why the calculated LD50 values for 100% peracetic acid of Anonymous (1996a) A6.1.1/05 and Anonymous (1984) A6.1.1/05, which were lower than 70 mg/kg bw, were not selected as final LD50 values. Maybe studies with peracetic acid concentrations of less than 5% were excluded and a reasoning for this would be helpful.

6) It is mentioned in chapter 10.1.2 that acetic acid is not taken into account since it is not classified for acute oral toxicity in the C&L inventory. It can be taken from the ECHA-dissemination site, that there are two studies from 1941 (one in rats, one in mice), which applied the sodium salt, which does not reflect the local effect of the acid. One further study from 1951 received a reliability score of 4 (not assignable). Thus, the missing classification for acute oral toxicity should be interpreted with some caution. Acetic acid is classified with Skin Corr. 1A, which implies a very strong local activity that might lead to fatalities after oral administration.

Acute Toxicity – dermal:
1) DE-CA agrees with the classification of 100 % PAA with Acute Tox. 2; H310 as proposed by the DS (FI).
Justification: Classification was based on results in the most sensitive species, which was the rabbit. The lowest LD50 values for the rabbit were reported in the study by Anonymous (1996c). In this study LD50s of 1147 mg/kg bw (combined), 1280 mg/kg bw (males), 1040 mg/kg bw (females) were reported, which correspond to 56.1, 62.6 and 50.9 mg/kg bw of 100 % PAA, respectively. All three LD50 values (for 100 % PAA) warrant classification as Acute Tox. Category 2; H310 according to the CLP criteria.

2) DE-CA does NOT agree with the derived dermal ATE value of 56.1 mg/kg bw as proposed by the DS (FI).
Justification: According to the Guidance on the Application of the CLP Criteria (ECHA 2017) “In general, classification is based on the lowest ATE value available i.e. the lowest ATE in the most sensitive appropriate species tested”. In this regard it is noted that the lowest LD50 reported by Anonymous (1996c) was 50.9 (females) mg/kg bw (100 % AAP). As such, it is the opinion of DE (BfR) that the dermal ATE should be 50.9 mg/kg bw (females).

3) The DS is requested to modify the following statement in paragraph 1 of section 10.2.2. due to exceptions from the given generalisation.
“The acute dermal LD50 of test substance containing 5 – 15 % peracetic acid was between 56.1 and 228.8 mg/kg bw in the rabbit”.
Justification:
a) It is unclear if the LD50 values indicated in this statement refer to the test material utilised in the studies or theoretical calculated values (100 % PAA). 100 % PAA values are however assumed.
b) In the study by Anonymous (1996c), which is identified as a key study, the concentration of PAA in the test material, 4.89 %, is not within the range of 5-15 %. Furthermore, the theoretical calculated LD50 value (100 % PAA) for females, 50.9 mg/kg bw, is not within the range of 56.1-228.8 mg/kg bw.
c) In the study by Anonymous (1996d), conducted with a test preparation containing 11.69 % PAA, the theoretical calculated LD50 value (100 % PAA) for females (232.6 mg/kg bw) is not within the range of 56.1-228.8 mg/kg bw.

4) It is stated in chapter 10.2.2: „Neither hydrogen peroxide nor acetic acid is 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.“
Has it been clarified, what kind of studies are available for hydrogen peroxide and acetic acid? Maybe the non-classification should be interpreted with some caution.

Acute Toxicity – inhalation:
1) DE-CA agrees with the classification of 100 % PAA with Acute Tox. 2; H330 and the derived ATE value of 0.204 mg/L (dusts and mists) proposed by the DS (FI).

Justification:
Classification and ATE derivation were based on the most reliable study in rats (Anonymous 1994), which utilised a test preparation containing 4.7-5.4 % PAA. In this study an acute inhalation LC50 value of 4.08 mg/L (4 h; male/female) was reported, which corresponds to 0.204 mg/L of 100 % PAA. The ATE value of 0.204 mg/L warrants classification as Acute Tox. Category 2 (dusts and mists); H330 according to the CLP criteria.

2) The DS is asked to add a note to Table 18 similar to that present in Tables 12 and 15 (For example, "Note: this is a theoretical calculated value which does not take into account that both hydrogen peroxide and acetic acid contribute to the acute toxicity observed for the test substance via acute toxicity and/or corrosivity/irritative property"), and indicate in the table (with a *) where this note applies, or provide a justification for not doing so.
Justification: The scientific robustness of this table would benefit from the presence of such a Note and indications within the table where it applies.

3) Some more discussion would be helpful, whether acetic acid or hydrogen peroxide can be excluded as cause for the fatalities.

Dossier Submitter's Response

Acute Toxicity – oral:

1) Thank you for your support.

2) The studies by Anonymous (1998b, 1995, 1985) were identified as key studies as they were GLP studies reliable without restrictions (The Klimisch score 1).

3) Thank you for highlighting the mistake. In the sentence "*According to the results of all acute oral toxicity studies for peracetic acid concentrations <1 % the oral LD50 is >2000 mg/kg bw…"* there is a confusion regarding the acute dermal studies. In the acute dermal studies for peracetic acid concentrations <1 % the dermal LD50 is >2000 mg/kg bw. This is not the case in oral studies and the LD50 values for 100 % peracetic acid are 14.8 mg/kg bw (Anonymous 1994) and >7.5 mg/kg bw (Anonymous 1991e). However we have excluded studies where peracetic acid concentration is <5 % and Anonymous 1996b study (PAA concentration 11,69 %) as the results of the studies do not correlate with higher concentration studies. One reason could be that when no vehicle was used in the studies the deaths were only due to the corrosive properties. In the study (Anonymous 1998) water was used as a vehicle, but the substance included also some strong mineral acid, which was not specified more precisely. Hence we can not know if the acid affects to the results.

Regarding other studies - We have excluded the results that are dose ranging studies (Anonymous 1987 and Anonymous 1998c). Also the studies which can not conclude the LD50 value are excluded, as the results LD50 of >30 mg/kg bw (Anonymous, 1993a) or LD50 of >7.5 mg/kg bw (Anonymous, 1991e) for 100% PAA are not informative to derive LD50 values.

4) We accept the DE's request that the statement could be modified. Given values (70-93 mg/kg bw for 100 % PAA) refer to the key studies' results for females.

5) We have excluded studies where peracetic acid concentration is <5 % and Anonymous 1996b study (PAA concentration 11,69 %) as the results of the studies do not correlate

with higher concentration studies. One reason could be that when no vehicle was used in the studies the deaths occured only due to the corrosive properties.
In the study (Anonymous 1998) water was used as a vehicle, but the substance included also some strong mineral acid, which was not specified more precisely. Hence we can not know if that acid effects to the results.

Also a 90-day oral toxicity study supports the findings. The study was performed with a test substance of 5,5 % PPA. In the low-dose group (15/5 mg/kg bw/day corresponds to 0,83/0,28 mg/kg bw of 100% peracetic acid) and mid-dose group (50/15 mg/kg bw/day corresponds to 2,75/0,83 mg/kg bw of 100% peracetic acid) no relevant findings were observed and the overall results demonstrated that following oral administration of peracetic acid by gavage for a period of a total of 92 days, no systemic effects were evident. Findings noted in the stomach and in the GIT can be ascribed to local reactions at the site of first contact after oral dosing by gavage and are related to the known irritating/corrosive properties of peracetic acid and its high reactivity. In the high-dose group (150/100/50 mg/kg bw/day corresponds to 8,25/5,5/2,75 mg/kg bw of 100 % peracetic acid), a total of three males and nine females died or were killed prematurely between day 8 and day 71.

6) Acetic acid concentrations varied between 6,7- 36,3 %. It is true that Acetic acid is classified as Skin Corr. 1A; H314, but the Spesific Concentration limit is ≥ 90 %. For Skin Corr. 1B; H314 the SCL is 25 % ≤ C < 90 % and for Skin Irrit. 2; H315 the SCL is 10 % ≤ C < 25 %. Peracetic acid itself is classified as Skin Corr. 1A; H314.

We also have in the CLH dossier the remark *Note: this is a theoretical calculated value which does not take into account that both hydrogen peroxide and acetic acid contribute to the acute toxicity observed for the test substance via acute toxicity and/or corrosivity/irritative property.

Acute Toxicity – dermal:

1) Thank you for your support.

2) We have two acute dermal studies which can conclude LD50 values (Anonymous 1996c and Anonymous 1996d. In the other study females are the most sensitive gender and in the other study males are the most sensitive gender. As a conclusion we think that according to the results we can not determine which gender is the most sensitive and for that reason we have used the combined ATE value of 56.1 mg/kg bw.

3) We agree that the statement should be modified. 5 % should be amended to 4,89 % and it should be mentioned that the values are the combined values.

4) We agree that this should be interpreted with caution.

Acute Toxicity – inhalation:

Thank you for your comments. We agree with your proposal. We also note that it is unknown what the contribution of hydrogen peroxide and acetic acid is to the mortalities.

RAC's response

Noted.

Date	Country	Organisation	Type of Organisation	Comment number
07.10.2021	United States of America	Peracetic Acid Registration Group (PAR)	Industry or trade association	5

Comment received

Comments on the approach to classify a theoretical 100% substance (section 10.1.2, 10.2.2 and section 10.3.2, comparison with the CLP criteria):

Peracetic acid…% is currently classified in Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation) as Acute Tox. 4* for the oral, dermal and inhalation route. 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 and 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 aims to remove the *(minimum classification) of peracetic acid from the harmonized classification under the Classification, Labelling and Packaging (CLP) Regulation ((EC) No 1272/2008) and to derive definitive ATE values for 100 % peracetic acid, which due to its high reactivity cannot exist in the pure state. For this purpose, ATE values were derived by linear extrapolation from LD50 values obtained from acute toxicity tests with equilibrium mixtures of peracetic acid (varying % peracetic acid and other ingredients) to a theoretical 100% peracetic acid for the purpose of classification.

Accordingly, the dossier submitter's proposal for adaption of the hazard classes acute toxicity – inhalation, dermal and oral - for peracetic % to Acute Tox. 3 oral (H301), Acute Tox. 2 inhalation (H330), and Acute Tox. 2 dermal (H310) is not triggered by actual acute toxicity test data for peracetic acid but is the result of a theoretical calculation approach considering the concentration of peracetic acid only. The potential impact of hydrogen peroxide, for example, which itself is classified into category 4 for acute oral and inhalation toxicity, was not considered by the dossier submitter for the derivation of ATE values with respect to the acute oral and inhalation toxicity of 100 % peracetic acid.

This approach is not a mandatory requirement of the CLP regulation and scientifically not justified for the following reasons:

There is no regulatory requirement that harmonised ATE values have to be established for a substance with a harmonised classification. According to the Guidance on the application of the CLP Criteria Version 5.0 – July 2017, chapter 1.5.3, harmonised Acute Toxicity Estimate (ATE) values may be included in Annex VI of CLP from 2016.

According to the classification, labelling and packaging (CLP) Regulation ((EC) No 1272/2008), "the acute toxicity estimate (ATE) for the classification of a substance or ingredient in a mixture is derived using:
- The LD50/LC50 where available
- The appropriate conversion value from Table 3.1.2 that relates to the result of a range test
- The appropriate conversion value from Table 3.1.2 that relates to a classification category"

Thus, the determination of a definitive ATE value is not mandatory and it is understood that it is only indicated when a LD50/LC50 value is available for the respective substance.

Most importantly, peracetic acid per se cannot exist as a stable isolated substance, but in an equilibrium mixture with hydrogen peroxide and acetic acid in aqueous solution. Pure peracetic acid is explosive and concentrations above 45% peracetic acid cannot be handled safely due to the explosive potential (CLH report for peracetic acid, version number 2.0, 24 June 2021, chapter 7, physicochemical properties). Accordingly, it is technically not possible to perform experimental studies with isolated PAA and acute toxicity data/definitive LD50/LC50 values are not available for pure/isolated peracetic acid.

Acute toxicity data have been generated with mixtures containing different concentrations of peracetic acid in combination with varying amounts of hydrogen peroxide and acetic acid and in some instances further ingredients (e.g., sulphuric acid, stabilizers). Thus, it is not considered appropriate to extrapolate an ATE value (LD50/LC50) for a pure substance based on mixture test results. It has to be taken into account that other components/factors could impact the outcome of the acute toxicity tests (e.g., hydrogen peroxide is classified for acute oral toxicity and acute inhalation toxicity; damage of the dermal barrier due to severe corrosivity can lead to systemic availability of other mixture components). Thus, the extrapolation approach taken is expected to overestimate the peracetic acid-induced effect. Accordingly, application of the proposed ATE values in the additivity formula will eventually lead to over-classification of peracetic acid containing mixtures.

However, as no actual LD50/LC50 values or results from range tests are available for isolated peracetic acid, results from the acute toxicity tests for peracetic acid containing mixtures can only be considered suitable to be used as surrogates for the determination of the appropriate classification category of peracetic acid and for similar peracetic equilibrium mixtures by expert judgement and application of the bridging principles, but not to derive definitive ATE values for a 100% pure substance which can technically not exist.

Furthermore, the extrapolation approach is considered not to correctly reflect the mode of action of peracetic acid for acute toxicity. The primary mode of action of peracetic acid is characterized by local irritation/corrosion. Thus, acute toxic effects of peracetic acid containing mixtures were secondary to primary local effects (irritation/corrosion) for all exposure routes, reflecting the irritant/corrosive properties of the test material. Severity of effects depended on the combination of both, peracetic acid concentration and volume of the test dose applied. For all routes, and most noteworthy, also in a 90-day oral toxicity study (Assessment Report Peracetic Acid, Product types 1-6, November 2015, Finland) no adverse systemic effects were detected at non-corrosive concentrations. Accordingly, data obtained for peracetic acid-containing mixtures show no clear dose-response relationship.

Although not considered scientifically justified (extrapolation from mixture to pure substance), use of ATE values derived for the oral and inhalation route in the additivity approach leads to classification of the respective peracetic acid containing mixtures in the same acute toxicity hazard class as the actual test results.

However, for the dermal route, data do not substantiate the proposed acute toxicity category 2 classification and application of the proposed ATE value of 56.1 mg/kg bw leads to over-classification of peracetic acid containing mixtures at a concentration of equal or greater than 5.61 % peracetic acid (category 3 instead of the category 4 determined for a concentration of 11.89% peracetic acid). More details are included in the comments to endpoint “Acute toxicity-dermal route”.

Specific comments regarding evaluated health hazards “Acute toxicity – oral route” and “Acute toxicity – dermal route”:

The comments below refer to the endpoint “Acute toxicity – oral route” (section 10.2 of the CLH report, page 15-27).

Eighteen animal studies on acute oral toxicity are reported and three of them are evaluated as key studies. In the reliable studies no consistent gender-specific effect was observed. Females were more sensitive than males in most cases, but not in all studies (Anonymous (1998c) A6.1.1/05 – males are more sensitive: Anonymous (1982), A6.1.1/03 – comparable sensitivity were observed between males and females). Furthermore, a different pattern in gender -specificity was also observed for the different doses applied within one experiment (Anonymous (1985), A6.1.1/02 – no gender-difference was shown at 1260 mg/kg bodyweight).

In the section “Conclusion on classification and labelling for acute oral toxicity” (section 10.1.3) of the CLH report an Acute Tox. Category 3 classification for 100 % peracetic acid (H301: Toxic if swallowed) with an oral ATE value of 70 mg/kg bw is proposed for the classification of mixtures containing peracetic acid. The proposed ATE value is the lowest LD50 value determined for females as the more sensitive gender according to the CLH report. However, the above-mentioned points do not fully support the conclusion drawn that females are more sensitive than males. Due to the non-consistent gender sensitivities, a combined LD50 value (males and females) (i.e. 1700 mg/kg bw corresponds to 85.0 mg/kg bw of a theoretical 100% peracetic acid) for classification purposes as derived in the assessment report (AR) on peracetic acid (PT1-6 and PT11/12) as well as on in situ generated peracetic acid (PT2-5) is considered more appropriate.

The comments below refer to the endpoint “Acute toxicity – dermal route” (section 10.2 of the CLH report, page 28-34).

Two acute dermal toxicity studies in rabbits are reported as key studies which were conducted by the same laboratory under similar conditions. Key study Anonymous 1996c was conducted with Proxitane AHC (4.89 % peracetic acid, 19.72 % hydrogen peroxide and 10 % acetic acid) and the study resulted in a combined acute dermal LD50 value of 1147 mg/kg bw corresponding to an extrapolated LD50 value of 56.1 mg/kg for a theoretical 100 % peracetic acid solution. However, key study Anonymous 1996d conducted with Proxitane WW12 (11.69 % peracetic acid, 18.05 % hydrogen peroxide and 20 % acetic acid) resulted in a combined acute dermal LD50 value of 1957 mg/kg bw corresponding to an extrapolated acute dermal LD50 value of 228.8 mg/kg bw for a theoretical 100 % peracetic acid solution. Thus, the study with the product with the higher peracetic acid concentration (Proxitane WW12) resulted in a lower acute dermal toxicity (9/10 animals dead at 2020 mg/kg bw and 2/10 animals dead at 500 mg/kg bw for 4.89% peracetic acid in contrast to 6/10 animals dead at 2020 mg/kg bw and 0/10 animals dead at 500 mg/kg bw). Acknowledging that peracetic acid is the only component classified with respect to acute dermal toxicity in the tested equilibrium mixtures, Proxitane WW12 (11.69 % peracetic acid) would be expected to reveal a higher acute dermal toxicity due to its higher peracetic acid content when compared to Proxitane AHC (4.89 % peracetic acid). The observed discrepancy could be explained by the corrosivity of both products. Toxic effects depend on the corrosive damage inflicted which can be expected to result in a certain randomness of effects, reducing overall reliability of acute dermal toxicity test results.

As studies were conducted under comparable conditions (same test laboratory, same test

method, same skin area treated, similar volumes of test material applied on a mL/kg bw basis), the results underline that acute toxicity effects of peracetic acid do not show a clear dose-response but depend on the extent of corrosive damage caused to skin and tissue of the individual test animals. Both products were tested undiluted and corrosive effects were observed as clinical signs. Air (Air bubbles), probably indicative of gas embolism (oxygen in blood vessels, generated by degradation of peracetic acid equilibrium solutions) and a possible cause of death, was observed in blood vessels, heart, and pericardium of test animals (section 10.2, table 15, Summary table of animal studies on acute dermal toxicity) which died during the studies. In contrast, no pathological findings were observed in test animals which survived the studies and were necropsied after 14 days.

After destruction of the skin barrier due to corrosivity, the tested mixture would be expected to become systemically available. Noteworthy, further substances contained in the tested mixture could act as confounding factors (influence the severity of effects observed) in addition to peracetic acid. Thus, differences in the severity of corrosive effects between animals of one tested dose group (e.g., due to higher volume of test substance concentrated in a test region, unnoticed damage of the skin due to clipping of the hair, different stability of peracetic acid in the tested solutions) could explain the observed differences.

The high reactivity and associated local mode of action of peracetic acid need to be taken into account as well in order to explain the effects observed after acute dermal dosing:

Peracetic acid is highly reactive, and therefore rapidly degraded upon contact with organic matter such as skin or mucous membranes of the gastrointestinal or respiratory tract. The toxicity of peracetic acid is mainly triggered by local irritation/corrosion at the site of first contact (portal-of-entry-effects). Hence, it is generally accepted that peracetic acid does not become systemically available upon contact with skin or mucous membranes of the gastrointestinal or respiratory tract. It is also evidenced by in vitro studies showing a rapid degradation of peracetic acid in rat blood. In rat blood diluted 1000 times, the half-life of peracetic acid was less than 5 minutes. For this reason, distribution of peracetic acid in the body is expected to be very limited, unless higher amounts of peracetic acid solutions can reach tissue and blood vessels through severely damaged skin.

Due to the underlying mechanism, which is characterized by direct chemical reactivity without primary systemic effects and metabolism, the observed acute dermal toxicity is considered dependent on the corrosive potential of the applied peracetic acid concentration (% in vehicle) and the applied volume rather than on the body dose (mg/kg body weight).

Accordingly, no systemic toxicity was observed for mixtures tested at non-irritant concentrations and only a temporary weight loss in some animals when tested at slightly irritant but non-corrosive concentrations as seen in key study number three, 0.89% peracetic acid (Anonymous (1994) A6.1.2/05). However, peracetic acid is rapidly absorbed through damaged skin when the skin barriers are destroyed due to the corrosivity of peracetic acid solutions (JACC Report 40 – Peracetic Acid and its Equilibrium Solutions (2001). This may explain why no systemic toxicity is observed at non-corrosive concentrations of peracetic acid containing mixtures.

In the section “Conclusion on classification and labelling for acute dermal toxicity” (section 10.2.3) of the CLH report the key study with Proxitane AHC (4.89 % peracetic acid) in rabbits is used to propose an acute dermal ATE value and classification for peracetic acid. An Acute Tox. Category 2 classification for 100 % peracetic acid (H310:

Fatal in contact with skin) with a dermal ATE value of 56.1 mg/kg bw for the classification of mixtures containing peracetic acid is proposed.

We propose that this approach (i.e. solely concentration-dependent extrapolation from the lowest LD50 value obtained) shall be reconsidered based on expert judgement considering the toxicological profile/local mode of action of peracetic acid and the missing dose/concentration-response relationship of the observed effects.

Moreover, it is noteworthy that peracetic acid is classified as skin corr. 1(A); H314 and based on its chemical characteristics and the fact that it has no potential for dermal absorption at non-corrosive conditions upon contact with skin, testing of corrosive peracetic acid containing mixtures would nowadays no longer be performed due to animal welfare reasons, and the acute dermal toxicity study would be waived instead. With a view to waiving of acute toxicity tests reference is made to the OECD “Guidance Document on Considerations for Waiving or Bridging of Mammalian Acute Toxicity Tests”, ENV/JM/MONO(2016)32, where under point 8 it is stated that “if an acute dermal toxicity waiver is granted on the basis of the test chemical being corrosive, the label would need to reflect the potential for corrosivity of the test chemical by the dermal route.” In point 14 it is further explained that “A dermal toxicity study may be waived if the test chemical is corrosive or severely irritating to skin (GHS Category 1). The determination of corrosion is based on in vivo, validated and/or accepted in vitro or other data, or in the absence of any other information, when the test chemical has a pH less than or equal to 2 or greater than or equal to 11.5”. When strictly following this guidance, only labelling of peracetic acid as skin corr. 1(A); H314 “Causes severe skin burns and eye damage“ would be warranted and a classification with respect to acute dermal toxicity would not be required when taking into account especially the requirements as set out in point 14 of the OECD guidance document which are completely fulfilled by the intrinsic properties of peracetic acid.

Accordingly, it is recognized that a number of strong acids (such as sulphuric, phosphoric, nitric or hydrochloric acid) or substances acting by a mode of action similar to that of peracetic acid (such as sodium hypochlorite or perchloric acid) are classified for their key toxic effect, i.e. as corrosive to skin but are not classified for acute dermal toxicity.

Taken together, all these facts do not warrant classifying peracetic acid into an even more stringent hazard category for acute dermal toxicity on the basis of a putative ATE value of 56.1 mg/kg bw (i.e. worst case LD50 value). Furthermore, it is also not reasonable that the extrapolated ATE value of 56.1 mg/kg bw (i.e. worst case LD50 value) shall be used for ATE calculations when classifying mixtures containing peracetic acid, due to the reasons listed below.

1. The second key study, conducted with Proxitane WW12 (11.69 % peracetic acid) revealed a much higher extrapolated ATE value of 228.8 mg/kg bw. This ATE value is a factor of 4 higher and this should be taken into account as Proxitane WW12 contains a higher concentration of peracetic acid which is the only component classified for acute dermal toxicity.

2. An acute dermal ATE value of 56.1 mg/kg bw does not correctly predict the acute dermal toxicity of certain mixtures containing peracetic acid. For example, the calculated ATE value of Proxitane WW12 (11.69 % peracetic acid) is 100/(11.69/56.1) = 479 mg/kg bw and this would be equivalent with a category 3 classification (H311 Toxic in contact with skin). However, the reliable study results obtained with Proxitane WW12 (Anonymous 1996d) revealed an LD50 of 1957 mg/kg bw (factor 4 higher) and this is equivalent with a category 4 classification (H312 Harmful in contact with skin). This

plausibility check clearly shows that the proposed acute dermal ATE value of 56.1 mg/kg bw needs revision as it does not correctly calculate the acute dermal toxicity category of Proxitane WW12 for which a valid acute dermal toxicity study is available. The results of the second key study overrules the outcome of the calculation method.

3. For acute oral toxicity the proposed ATE value is 70 mg/kg bw and the resulting classification is acute oral toxicity category 3 (H301: Toxic if swallowed). For acute dermal toxicity the proposed ATE value is 56.1 mg/kg bw and the resulting classification is acute dermal toxicity category 2 classification (H310: Fatal in contact with skin). This results in a more severe classification for acute dermal toxicity and this further supports the conclusion that the derived ATE value of 56.1 mg/kg bw for acute dermal toxicity does not reflect correctly the acute toxicity hazard potential by the dermal route.

According to the Guidance Document on Considerations for Waiving or Bridging of Mammalian Acute Toxicity Tests, ENV/JM/MONO(2016)32, point 16/17, dermal toxicity is unlikely to result in a more severe classification than the corresponding oral hazard. In addition, in an older Sanco guidance document on dermal absorption it is stated that "Based on theoretical grounds and supported by a comparison of oral and dermal absorption data available for 12 pesticides, it is assumed that dermal absorption will not exceed oral absorption established by means of bile duct cannulation (unpublished data)." (Sanco/222/2000 rev. 7, 19 March 2004). Thus, it is not plausible, that the acute dermal toxicity especially for a non-systemically available substance is higher than its acute oral toxicity.

Accordingly, a moderate oral toxicity has been concluded for peracetic acid and dermal toxicity was considered lower in a previous hazard assessment for peracetic acid (JACC Report 40 – Peracetic Acid and its Equilibrium Solutions (2001). Furthermore, test results from acute oral toxicity studies (reliability 2, not key studies) presented in the CLH report support this conclusion.

Based on the proposed oral ATE value of 70 mg/kg bw mixtures are classified in category 3 for acute oral toxicity if the peracetic acid concentration is 23 % or higher (no other ingredient contributing to acute oral toxicity). However, based on a dermal ATE of 56.1 mg/kg bw mixtures are classified in category 3 for dermal toxicity if the peracetic acid concentration is 5.61 % or higher (no other ingredient classified for acute dermal toxicity). This shows a large and inappropriate difference in the cut off value for an acute toxicity category 3 classification between the oral and dermal route considering in parallel that the acute dermal toxicity of a substance is usually never more severe than its acute oral toxicity.

The discrepancy between the calculated ATE value of 56.1 mg/kg bw and the acute dermal hazard potential of peracetic acid containing solutions is also reflected in the CLH dossier, where it is stated that "based on the results obtained in rabbits, classification of the aforementioned formulations (PAA conc. 5-15 %) 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". However, application of the proposed ATE value in the additivity formula would result in a category 3 classification for product with a concentration equal to or higher than 5.61 % peracetic acid (assuming that no other ingredient is classified for acute dermal toxicity).

Based on the presented argumentation, the conclusion in section 10.2.3 of the CLH dossier that there is sufficient evidence to remove the asterisk from the classification for the dermal route and to apply a dermal ATE value of 56.1 mg/kg bw is not considered conclusive.

It is not considered justified to derive a definitive ATE for the dermal route based on the available data, and thus it is proposed to keep the current classification with Acute Tox. 4*; H312 for the dermal route to avoid over-classification of peracetic containing mixtures. Peracetic acid is classified with Skin corrosion 1A, and this hazard class is considered to be most appropriate hazard class to characterize the hazard potential of peracetic acid containing solutions upon contact with skin.

Attachment contains these comments in pdf format.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Peracetic acid - comments on CLH report - Oct 7_final.pdf

Dossier Submitter's Response

Thank you for your comments.

Regarding ATE values – COMMISSION REGULATION (EU) 2017/776 of 4 May 2017 states: (3) The Acute Toxicity Estimates (ATE) are mainly used to determine the classification for human health acute toxicity of mixtures containing substances classified for acute toxicity. The inclusion of harmonised ATE values in the entries listed in Annex VI to Regulation (EC) No 1272/2008 would facilitate the harmonisation of the classification of mixtures and provide support for enforcement authorities. The ATE values harmonised in accordance with Article 37 should be added in the penultimate column of Table 3.1 of Part 3 of Annex VI to that Regulation. **Pursuant to Article 38(1)(e) those values are to be mentioned in the opinions and decisions for harmonised classification.** The title of the column of Table 3.1 of Part 3 as well as section 1.1.2.3 of Part 1 of Annex VI to Regulation (EC) No 1272/2008 should be amended consequently.

Link: COMMISSION REGULATION (EU) 2017/ 776 - of 4 May 2017 - amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272 / 2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (europa.eu)

Also if we use the appropriate conversion values from Table 3.1.2, the converted acute toxicity point estimates are for oral toxicity 100 and for dermal toxicity 50, which means that for dermal toxicity it is actually lower value than proposed dermal ATE value of 56 mg/kg bw.

Regarding statement "*also in a 90-day oral toxicity study (Assessment Report Peracetic Acid, Product types 1-6, November 2015, Finland) no adverse systemic effects were detected at non-corrosive concentrations*" we have to take into account that the study was performed with a test substance of 5,5 % PPA. In the low-dose group (15/5 mg/kg bw/day) it corresponds to 0,83/0,28 mg/kg bw of 100% peracetic acid and mid-dose group (50/15 mg/kg bw/day) it corresponds to 2,75/0,83 mg/kg bw of 100% peracetic acid) so the concentrations were relatively low. In the high-dose group (150/100/50 mg/kg bw/day corresponds to 8,25/5,5/2,75 mg/kg bw of 100 % peracetic acid), a total of three males and nine females died or were killed prematurely between day 8 and day 71.

Regarding the acute dermal endpoint - It is known that PAA is a corrosive substance and mechanism or mode of action for acute dermal toxicity is behind the corrosivity. However, acute dermal toxicity is not the same hazard as corrosivity.

The skin of all animals was severely damaged due to the corrosive effects of the applied test substances and therefore the results can not be used to evaluate absorbtion of PAA

throught intact skin. The toxicity of PAA is due to its locally irritating properties, i.e. decomposition to hydrogen peroxide, oxygen and acetic acid. After contact with organs and tissues, hydrogen peroxide will undergo decomposition into water and oxygen. Oxygen bubbles liberated in the blood stream/capillaries may cause reduced blood flow and gas embolies as well as reversible blanching of the exposed tissue area. In acute dermal toxicity studies with 90% hydrogen peroxide in rabbits, cats, pigs and rats, Hrubetz et al. (1951) found that the rabbit appeared to be the most sensitive animal species. A high susceptibility of rabbits to embolism and interspecies differences in levels of tissue and blood catalases were noted. The authors also proposed that there may be more hydrogen peroxide available subcutaneously in rabbits to enter the blood stream and release oxygen which gives rise to lethal embolic effects.

We agree that there is a discrepancy between the acute dermal studies Anonymous 1996c and Anonymous 1996d, but we do not have an explanation to the reason why PAA concentration of 4,89 % gives lower LD50 value than PAA concentration of 11.69 %. Hydrogen peroxide concentrations were quite similar (19.72 % and 18.05 %) in both studies so we think that concentration of hydrogen peroxide can not explain the differences.

We would like to also highlight that we have dozen substances in Annex VI where acute dermal toxicity classification is stricter than acute oral toxicity classification so we have several examples where this is the case.

Regarding mixture classification - We agree that for peracetic acid a classification into hazard category 3 should be warranted for mixtures with a concentration equal to or higher than 5.61 % (if no other substance is classified for acute dermal toxicity).

RAC's response

RAC supports the DS's argumentations and conclusions.

Date	Country	Organisation	Type of Organisation	Comment number
26.08.2021	Denmark		MemberState	6

Comment received

DK CA BPR: Agree that the LD50 is highly variable and agree to the reasons presented by the dossier submitter. However, the chosen range of 70-93 mg/kg bw should justified further as there are LD50 values below those. This may be due to the studies with the lower LD50 values have reliability scores of 2, but looking through these studies, the deviations are of no significance for derivation of an LD50 value in several of these studies. Please consider, if Acute Tox 2, H300 is more appropriate.

Agree with Acute Tox 2, H310 (ATE 56 mg/kg bw) and Acute Tox 2, H330 (ATE 0.204 mg PAA/l)

Dossier Submitter's Response

Thank you for your comment. We have excluded studies where peracetic acid concentration is <5 % and Anonymous 1996b study (PAA concentration 11,69 %) as the results of the studies do not correlate with higher concentration studies.
Please also see the response to comment #4 (5).

RAC's response

RAC considers the DS's position reasonable.

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2021	France		MemberState	7

Comment received

Acute toxicity oral: In order to determine the oral acute toxicity classification of PAA, the DL 50 of the mixture containing PAA/H2O2/acetic acid is corrected by the concentration in PAA only. In this context, it is considered that the acute toxicity is linked only to PAA. However, acute oral toxicity is also reported for H2O2. Therefore, this correction may overestimate classification.
However, as no data on PAA only is available, we understand the proposal.

No comment on Acute toxicity – inhalation and Acute toxicity – dermal.

Dossier Submitter's Response

Thank you for your comment. We are aware of this problem and for this reason we have the following remark in the CLH dossier: "Note: this is a theoretical calculated value which does not take into account that both hydrogen peroxide and acetic acid contribute to the acute toxicity observed for the test substance via acute toxicity and/or corrosivity/irritative property".

RAC's response

RAC considers the DS's approach conservative, but overall adequate.

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
01.10.2021	Germany		MemberState	8

Comment received

DE-CA agrees with the classification as aquatic acute 1(H 400) but we do NOT agree with the proposed classification as aquatic chronic 2 (H411) based on the 72h NOEC value of 0.031 mg/L from the algae study. Instead, we propose a classification as aquatic chronic 1 (H410) based on the available long-term study with fish. In the CLH dossier this study got a reliability of 3, while in the PAR in the frame of assessment as biocidal active substance the same study was considered as valid with restrictions (reliability 2) and even the PNECwater is based on the NOEC from the long-term fish study.
The arguments for lowering of the reliability of the study to 3 in the CLH dossier is just, that the LOQ is very low and therefore analytical monitoring of the test substance concentrations could not be performed for all test substance concentrations. However, even the NOEC based on nominal concentrations (0.00225 mg/L = 2.23 µg/L) would already trigger a classification as H410.

Dossier Submitter's Response

Thank you for your comments.

Please also see the response to comments #10. The Dossies Submitter now considers that peracetic acid is not rapidly degradable. Since there are adequate chronic toxicity data available for only one trophic level, PAA should be classified according to the Figure 4.1.1 in the CLP and based on the most stringent outcome (surrogate method):

(a) according to the criteria given in Table 4.1.0(b)(i) or 4.1.0(b)(ii) (depending on information on rapid degradation), and
(b) (if for the other trophic level(s) adequate acute toxicity data are available) according to the criteria given in Table 4.1.0(b)(iii).

Both scenarios would result in the classification of Aquatic Chronic 1 with a M-factor of 1 for peracetic acid. The Dossier Submitter proposes this classification for peracetic acid based on the comments received from the public consultation.

The reliability of the chronic fish study (Anonymous 2007b) in the CLH dossier was evaluated for the classification purposes. The assessment as biocidal active substance follows different guidance than the guidance on the application of the CLP criteria (ECHA 2017). No sufficient evidence is available that the initial measured concentrations have been maintained throughout the test duration and can be used for the derivation of reliable NOEC value for the classification purposes. The CLP guidance is clear that when measured concentrations do not remain within 80-120 % of the nominal concentrations, the effect concentrations cannot be based on nominal or initial measured concentrations.

It seems that the fish are the most sensitive taxonomic group for the chronic toxicity of peracetic acid. Initially, the Dossier Submitter proposed the chronic classification to be derived based on the initial test concentrations extrapolated from the analytically verified highest test concentration. This approach followed the risk assessment under Biocidal Products Legislation. However, this approach was deemd appropriate for classification purposes after the ECHA accordance check, but the alternative approach is left for RAC to be evaluated and presented below.

Alternative approach by the DS if the study Anonymous 2007b is considered reliable for the classification purposes, which would trigger the classification of aquatic chronic 1 (H410) with M-factor of 100 (peracetic acid is now considered as non rapidly degradable).

11.6.1 Chronic toxicity to fish

Anonymous 2007b

An OECD TG 210 flow-through study under GLP for zebra fish (*Danio rerio*) (14.9 % w/w PAA) is available for peracetic acid (Anonymous 2007b). Initial nominal concentrations of 1.5, 5.0, 15, 50 and 150 µg TS/L corresponding to 0.2, 0.7, 2.2, 7.5, 22.4 µg PAA/L were used. At the start of the study 15 eggs per replicate with 4 replicates per test concentration were used. This study resulted in a 33d NOEC value of 0.00225 mg PAA/L based on nominal concentrations for post hatch survival and overall survival. 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. These effects occurred during the time window of post hatch day 6 to 15. No further significant reduction of the survival rate was observed in the last third of the study. Peracetic acid concentrations were analytically monitored via LC-MS/MS (by MTSO method) at the highest treatment level only. Due to the low sensitivity of the analytical method, actual concentrations were measured only in the stock solutions (all treatments) and the test solutions of the highest concentration level. Despite using a continuous flow-through test system, the measured concentrations in mixing chambers, and especially in test vessels, dropped below the limit of quantification of the method, 0.00754 mg PAA/L. Samples of the highest test concentration (150 µg TS/L) and control (mixing chamber and alternate replicates) were taken on days -1, 0 and at least weekly thereafter until end of exposure. In the mixing chambers where the stock solutions were mixed with the respective amount of tap water, no PAA could be measured during the first 15 study days (PAA < LOQ). During the first 21 days of the study the test concentration in the test solutions could not be verified (measured concentrations of PAA < LOQ). Even below LOQ for that period, the two highest test concentrations caused significant effect until day 18. On day 19 fish were transferred to bigger test

vessels. In order to maintain the test solution exchange rate in the larger aquaria (approx. 10-fold per day) the flow rates were increased by 5 times. At study days 20, 21, 27 and 29 (mixing chamber) and study day 27 and 29 PAA could be measured and accounted for 49 to 95 % of the nominal concentration in the mixing chambers and was 33 to 44 % of nominal in the test vessel (Table 1).

The number of hatched eggs was determined daily until day 8. On day 7 of the study, 98 % of all fertilized and living embryos in the control groups had hatched. At the end of exposure (after 33 days) the total length of all survivors was measured to the nearest 0.5 mm. No statistically significant adverse effect on the sublethal parameters hatching time, hatching success, swim-up of larvae and growth of surviving animals could be observed up to the highest tested concentration level. Post hatch success and survival of fish were statistically reduced at the end of the study at the two highest test concentrations (50 and 150 µg/L TS). Analytical measurement of the test concentration in the test vessels have been performed only for the highest test concentration, but otherwise the OECD TG 210 validity criteria were met. This study was given a reliability score of 2 by eCA and it is considered reliable and valid **key study** for classification purposes by eMSCA.

Because the measured concentrations of the test item in the test solution did not maintain within ± 20 % of the nominal values, the eCA has presented a proposal for calculating the initial concentrations, which provide a more realistic exposure estimate than using nominal concentrations. The arithmetic mean exposure concentration in the study by Anonymous (2007b) cannot be determined, because the concentrations in test vessels have been analytically determined only at the highest treatment level (where the concentrations were <LOQ). Analytical verification of only the highest treatment level could be considered acceptable for PAA, because the sensitivity of the analytical method available was not adequate for the quantification of the lower treatment levels. The eCA calculated the $NOEC_{initial}$ to reduce the uncertainty related to the $NOEC_{nominal}$ (2.235 µg/L). The use of $NOEC_{nominal}$ would have been underestimating the aquatic chronic toxicity of PAA. The calculation of $NOEC_{initial}$ is based on the ratio of nominal to initial measured concentration at the highest treatment level (31 %) (Table 2: Peracetic acid concentrations in mixing chamber at the highest nominal treatment level of 22.35 µg PAA/L (measured as MTSO)). The applicably of the ratio of 31 % is based on the assumption that decomposition of PAA is independent of the concentration.

Table 1: The analytical measurements of PAA concentration at the highest nominal test concentration of 150 µg/L in the mixing chamber and in the test vessels in a flow-through system.

Sample	Mixing chamber 150 µg/L				Replicate 150 µg/L				Control
	(with fish)		(without fish)		with fish		without fish		
	Peracetic Acid								
Study day	Calc. conc. [µg/L]	RR [%]	Calc. conc. [µg/L]	RR [%]	Calc. conc. [µg/L]	RR [%]	Calc. conc. [µg/L]	RR [%]	Calc. conc. [µg/L]
-1	< LOQ	--	< LOQ	--	< LOQ	--	< LOQ	--	n.a.
0	< LOQ	--	< LOQ	--	< LOQ	--	< LOQ	--	n.a.
1	< LOQ	--	< LOQ	--	< LOQ	--	< LOQ	--	(7.94)[1)]
7	9.63	69	12.3	81	< LOQ	--	< LOQ	--	< LOQ
9	< LOQ	--	< LOQ	--	< LOQ	--	< LOQ	--	< LOQ
14	< LOQ	--	< LOQ	--	< LOQ	--	< LOQ	--	< LOQ
15	< LOQ	--	< LOQ	--	< LOQ	--	< LOQ	--	< LOQ
20	12.1	54	13.1	58	< LOQ	--	< LOQ	--	< LOQ
21	10.9	49	17.3	77	< LOQ	--	< LOQ	--	< LOQ
27	18.4	82	21.2	95	8.88	40	9.76	44	< LOQ
29	15.6	70	19.3	86	7.50	33	9.17	41	< LOQ

Nom. conc. = Nominal concentration
Calc. conc. = Calculated concentration of peracetic acid in dilution water (measured as MTSO)
RR = Recovery rate related to the nominal concentration
n.a. = not analysed
[1)] = derivatizing product was analysed; no reaction product of PAA

According to eCA, the initial concentrations of PAA in the study by Anonymous 2007b could be estimated with sufficient precision, if the following three assumptions are accepted:

1) Measured concentrations in the mixing chambers represents the actual initial exposure concentrations in the test vessels (this could be considered reasonable as the test vessels receive test solution from the mixing chambers).

2) The LOQ concentration divided by two (i.e. 3.77 µg/L) is used in cases where the actual measured concentration has been below the LOQ. This approach is recommended in the TNsG for Environmental effects assessments for biocidal active substances that rapidly degrade in environment compartments of concern, where it is stated that "...if analytical data indicate that the substance could not be quantified but was detectable, by the end of the study, the final concentration may be taken as half the limit of quantification (LOQ/2) for the method...". This, is considered reasonable even though no LOD has been given for the method. This approach can be considered as equivalent to CLP guidance 5.0 (2017).

3) The ratio of a nominal concentration to an initial concentration calculated for the highest treatment level can be applied to all lower treatment levels as well (this is applicable if the decomposition of PAA in the test system is independent of the concentration over the treatment levels of the study).

Table 2: Peracetic acid concentrations in mixing chamber at the highest nominal treatment level of 22.35 µg PAA/L (measured as MTSO).

Study day	With fish				
	Peracetic acid				
	Calc. Conc. [µg/L]	RR [%]			
0	3.77*	--			
1	3.77*	--			
7	9.63	43			
9	3.77*	--			
14	3.77*	--			
15	3.77*	--			
20	12.1	54			
21	10.9	49			
27	18.4	82			
29	15.6	70			

*LOQ/2

Calculated geometric PAA concentration in the mixing chamber was 6.99 µg/L (n=20) (Table 28). Geometric mean instead of arithmetic mean was preferred, because PAA could not be quantified throughout the test period. The concentration in the mixing chamber (= initial exposure concentration) is expected to be 6.99×100/22.35 = 31 % of nominal concentration. Consequently, the NOECnominal of 2.235 µg/L determined in the study by Anonymous (2007b) equals the NOECmeasured value of 2.235×0.31 = 0.69µg/L for peracetic acid. It should be noted that even the estimated NOECmeasured value does not represent the intrinsic toxicity of PAA, because the analytical data indicate that PAA concentrations in test vessels are lower than PAA concentrations in the mixing chambers, which have been used in determining the chronic toxicity value. **The NOEC value of 0.69 µg PAA/L** is the best conservative estimate for chronic toxicity of peracetic acid and the eMSCA considers it a reliable and valid **key endpoint** for the classification purposes for peracetic acid ...%.

RAC's response

RAC acknowledges that 72-hour E_rC_{50} of 0.05 mg PAA/L based on geometric measured concentrations for *Selenastrum capricornutum* is the lowest acute endpoint. However, regarding chronic toxicity, RAC recognises that chronic toxicity study to fish (*Danio rerio*) according to OECD TG 210 clearly indicates that fish are the most sensitive organisms in the case of chronic exposure. Although the aquatic chronic study with fish has an analytical issue (LOQ above quite all tested concentrations) and a device issue, since the fish were not correctly exposed to the substance during the first part of the test, RAC is of opinion that classification based on a reliable chronic test on fish would lead to a more stringent classification (in particular to higher M factor). Hence, RAC is of opinion that the available chronic toxicity study to fish (*Danio rerio*) according to OECD TG 210 cannot be fully disregarded.

The chronic toxicity study to fish (*Danio rerio*) according to OECD TG 210 meets OECD TG 210 validity criteria with exception that analytical measurement of the test concentration in the test vessels have been performed only for the highest test concentration because sensitivity of available analytical method was not adequate of the quantification at the lower levels. The NOEC value of 0.00225 mg PAA/L based on the nominal concentrations was below the analytical limit of quantification (0.00754 mg/L for PAA), and as measured concentrations do not remain within 80-120% of the nominal concentrations, the effect concentrations cannot be based on nominal or initial measured concentrations. As well the use of $NOEC_{nominal}$ would have been underestimating the aquatic chronic toxicity of PAA. Therefore, RAC is of the opinion that 33 d-$NOEC_{nominal}$ of 0.00225 mg/L cannot be considered as valid for classification purposes under CLP.

According, to the OECD TG 210, when the measured concentrations do not remain within 80-120% of the nominal concentration, the effect concentrations should be determined and expressed relative to the arithmetic mean concentration for flow-through tests. Still, 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. Nevertheless, analytical verification of only the highest treatment level could be considered acceptable for PAA, because the sensitivity of the analytical method available was not adequate for the quantification of the lower treatment levels.

The analytical measured concentration performed only at highest nominal concentration in the test vessels indicated that the concentrations in the test solutions of PAA were below LOQ during the first 21 days of the study. In the mixing chambers where the stock solutions were mixed with the respective amount of tap water, no PAA could be measured during the first 15 study days (PAA < LOQ). Therefore, RAC considers that, although analytical measurements have been performed, still there is no actual information on the analytical measured concentration in the test vessels at least at the start of the test. The CLP Guidance indicates that "...*in the absence of analytically measured concentrations at least at the start and end of test, no valid interpretation can be made and the test should be considered as invalid for classification purposes…*".

However, CLP Guidance as well indicates that "*…where concentrations at the end of test are below the analytical detection limit, such concentrations shall be considered to be half that detection limit…*". In addition, BPR Guidance states that "*…if analytical data indicates that the substance could not be quantified by the end of the study, the final concentration may be taken as half the limit of quantification (LOQ/2)…*". RAC recognises that both Guidance's referring to the concentrations at the end of the test, however as analytical measurements have been performed, RAC could accept assumption that LOQ concentration divided by two could be used in cases where the actual measured concentration is below the LOQ.

PAA concentrations analytically determined in test solution via LC-MS/MS (by MTSO method) at the highest nominal concentration level (0.02235 mg PAA/L).

Study day	PAA concentrations in mixing chamber at the highest nominal treatment level of 22.35 µg PAA/L (measured as MTSO).		
	Calc. conc. [µg/L]	Calc. conc. by using LOQ/2 [µg/L]	RR [%]
0	<LOQ	3.77*	--
1	<LOQ	3.77*	--
7	9.63	9.63	43
9	<LOQ	3.77*	--
14	<LOQ	3.77*	--
15	<LOQ	3.77*	--
20	12.1	12.1	54
21	10.9	10.9	49
27	18.4	18.4	82
29	15.6	15.6	70
$Geomean_{calculated}$	-	**6.99**	-
Calc. conc. – Calculated concentration of PAA in test solution (measured as MTSO) LOQ – Limit of Quantification (7.54 µg PAA/L) *LOQ/2			

Although RAC recognises that analytical data indicate that PAA concentrations in test vessels were lower than PAA concentrations in the mixing chambers, still RAC could assume that analytical measured concentration at the highest nominal concentration in the mixing chambers represents the actual initial exposure concentration in the test vessels. This assumption seems reasonable as the test vessels receive test solution from the mixing chamber.

Still, RAC cannot confirm that ratio of a nominal concentration to an initial concentration calculated for the highest treatment level can be applied to all lower treatment levels as there are no information on independency of decomposition of PAA in the test system and the concentration over the treatment levels of the study. However, this assumption could be accepted by RAC because the sensitivity of the available analytical method was not adequate for the quantification of the lower treatment levels.

Therefore, assuming the above rationale, RAC agrees that calculated geometric mean of 6.99 µg PAA/L in the mixing chamber instead of arithmetic mean as indicated in OECD TG 210, is preferred because PAA could not be quantified through the test period. Consequently, RAC agree that the concentration in the mixing chamber (equal to initial exposure concentration) is expected to be 31 % (6.99×100/22.35) of nominal concentration. Thus, the $NOEC_{nominal}$ of 2.235 µg PAA/L determined in the study equals to the $NOEC_{measured}$ of 0.69 µg PAA/L (2.235×0.31).

Although RAC does not opposite to the concentration estimation which was provided by the DS, RAC would like to stress that NOEC value of 0.69 µg PAA/L seems to be a reliable and conservative estimation approach for chronic toxicity of PAA. Furthermore, it seems that estimated $NOEC_{measured}$ value of 0.69 µg PAA/L will not properly represent the intrinsic toxicity of PAA, because the analytical data indicate that PAA concentrations in test vessels are lower than PAA concentrations in the mixing chambers, which have been used in determining the chronic toxicity value.

However, taking into account all overall information, RAC assumes that provided $NOEC_{measured}$ value of 0.69 µg PAA/L is a reliable and valid endpoint for the classification purposes under CLP.
Overall, RAC considers that the lowest acute endpoint for aquatic acute classification is the 72-hour E_rC_{50} value for *Selenastrum capricornutum* of 0.05 mg PAA/L based on geometric measured concentration. The lowest chronic endpoint for aquatic chronic classification is the 33-days NOEC value for *Danio rerio* of 0.00069 mg PAA/L based on estimated concentration.

Date	Country	Organisation	Type of Organisation	Comment number
07.10.2021	United States of America	Peracetic Acid Registration Group (PAR)	Industry or trade association	9

Comment received

None

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Peracetic acid - comments on CLH report - Oct 7_final.pdf

Dossier Submitter's Response

Thank you for providing your comments

RAC's response

Noted.

Date	Country	Organisation	Type of Organisation	Comment number
07.10.2021	United Kingdom	Heath and Safety Executive	National Authority	10

Comment received

Degradation:
The DS proposes that the substance is rapidly degradable based on a weight of evidence. However, we are unclear whether the classification criteria for rapid degradability have been met due to the following reasons:
• The sampling times and degradation measurements during the OECD TG 301E study (Anonymous, 1986; 2002) mean it is unclear if the 10-day window was met. Please could the DS consider the degradation curve for the study to help identify the start of the 10-day window and further understand whether the 10-day window was met?
• DT50 values from the hydrolysis study by Anonymous (2007c;e) determined at 25 °C have been used to demonstrate rapid primary degradation because these are below the CLP trigger of 16 days. For comparison with the hazard classification criteria, these DT50 values should be corrected to 12 °C as the environmentally relevant temperature in European surface waters (ECHA, 2017).
• The studies by Yuan et al (1997a;b) identified actetic acid (CAS 64-19-7) and hydrogen peroxide (CAS 7722-84-1) as hydrolysis products. Based on the hydrolysis DT50 values

above (Anonymous, 2007c;e), the CLH DS considered that PAA met the criteria for rapid degradation given that acetic acid and hydrogen peroxide do not have harmonised classifications as hazardous to the aquatic environment. However, we note that the lead REACH Registrant for hydrogen peroxide includes a self-classification as Aquatic Chronic 3 (ECHA, 2021). This self-classification is supported by the Daphnia magna and Skeletonema costatum NOEC values of 0.63 mg/L in the REACH registration dossier when hydrogen peroxide is considered rapidly degradable (ECHA, 2021). On this basis, we do not consider that the hydrolysis studies can be used alone to conclude that PAA is rapidly degradable for the purpose of hazard classification.
• The half-lives from the OECD TG 209 study (Anonymous, 2001) and the non-guideline degradation study in effluent by Anonymous (2007d) relate to primary degradation and dissipation, while the levels of mineralisation are unknown and ultimate degradation cannot be clearly demonstrated. Degradation products were not analysed and it cannot be demonstrated that any degradation products do not meet the classification criteria as hazardous to the aquatic environment.

Ecotoxicity:
We feel the disregarded GLP chronic toxicity to Danio rerio (OECD TG 210, Anonymous 2007b) and GLP chronic toxicity to Daphnia magna (OECD TG 211 Anonymous, 2000b) studies 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 (72-h NOErC 0.031 mg PAA/L).

Looking at the registration information, test guideline validity criteria for controls were met for both studies although we recognise there are limitations with the analytical verification. From the available information it appears stock solutions used in the flow through systems were broadly in line with nominal concentrations indicating the test systems was dosed with near nominal concentrations. While nominal or initial measured concentrations may not be ideal, we note that study endpoints based on nominal, initial measured or mean measured if possible to calculate, are likely to be more sensitive than the algal NOErC. Finally, we note endpoints from these studies were considered relevant for the biocides risk assessment.

If the above chronic toxicity to fish and invertebrates studies are not considered reliable for hazard classification and the substance is considered not rapidly degradable (see comments above), we note that the surrogate approach with the acute Daphnia magna endpoint becomes relevant for the Aquatic Chronic classification.

References:
ECHA (2017) Guidance on information requirements and chemical safety assessment. Chapter R.7b: Endpoint Specific Guidance. Versions 4.0. European Chemicals Agency, Helsinki, Finland.
ECHA (2021) Registration dossier for hydrogen peroxide [ONLINE] European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/registration-dossier/-/registered-dossier/15701 (Accessed September 2021).

Dossier Submitter's Response

Thank you for your comprehensive comments. Regarding the degradation tests, the data available on the OECD TG 301E (Anonymous, 1986; 2002) is, unfortunately, not sufficient for obtaining degradation curve to clarify whether the 10-day window was met or not. Furthermore, taking into account the deviations of the test guideline and the deficiencies of the study (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), the study cannot be used to conclude that PAA is readily biodegradable. However, the it is considered as

supporting information on rapid degradation. The same applies to the OECD TG 209 (Anonymous, 2001) and the non-guideline degradation study (Anonymous, 2007d).

Regarding the the hydrolysis study by Anonymous (2007c;e), the DT50 values corrected to 12°C were not originally presented due to uncertainties possibly involved with extrapolations. However, rough hydrolysis temperature correction estimates (following the equation t ½ (X°C) = t ½ e (0.08 (T - X)) according to ECHA, 2017) are available (values in brackets were recalculated with FOCUS Degradation Kinetics Report, 2006):

<u>For 760 mg PAA/L (corrected from 25°C to 12°C):</u>

pH 4 = 62 h (45.7 h) → 175.4 h (129.3 h)
pH 7 = 63 h (60.3 h) → 178.2 h (170.6 h)
pH 9 = 64 h (6.3 h) → 181.1 h (17.8 h)

<u>For 76 mg PAA/L (corrected from 25°C to 12°C):</u>

pH 4 = 48 h (46.7 h) → 135,8h (132.1 h)
pH 7 = 48 h (31.7 h) → 135,8 h (89.7 h)
pH 9 = 3.6 h (- h) → 10,2 h (-)

After the temperature correction, the longest half-life (i.e. 64 h at pH 9 for 760 mg PAA/L according the original study results) is 181.1 hours (corresponding approximately 7.5 days).

With regard to your comments on the degradation products of PAA, the Dossier Submitter is very pleased that you noticed hydrogen peroxide being classified as Aquatic Chronic 3. For some reason, perhaps because checking twice the classification of acetic acid or something, the Dossier Submitter did not notice this but it indeed needs to be taken into consideration when assessing the degradability of PAA. According to point 4.1.2.9.4 of Annex I, hydrolysis can not be considered to reflect environmental degradation of PAA as the hydrolysis product fulfils the criteria for classification as hazardous to the aquatic environment. Therefore, PAA should be considered as **not** rapidly degradable for the purpose of hazard classification. The Dossier Submitter apologises for the inconvenience caused by not double checking classifications of degradation products.

Regarding the disregarded studies on ecotoxicity, please see our response to comment #8. Peracetic acid is now considered as not rapidly degradable and would results in a classification of Aquatic Chronic 1 with a M-factor of 1.

RAC's response

Two available ready biodegradability studies according to OECD TG 301E indicated degradation between 66 to 98% by DOC removal method and 44 to 75% by TOC removal method within 14 to 28 days. However, it was not demonstrated that a degradation sufficient to pass the ready biodegradability criteria was attained within a 10-d window after the 10% degradation was reached.
Two closed bottle tests according to OECD TG 301D are available but considered not suitable for the assessment of the biodegradation of PAA, because the test is based on measurement of the biological oxygen consumption and, therefore, it is not suitable for the reliable biodegradation assessment of the substance since the PAA itself liberates oxygen upon decomposition and, moreover, production of oxygen also due to the decomposition of hydrogen peroxide.
Therefore, RAC consider 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) has not been achieved within 10 days from the onset of biodegradation.
Active sludge respiration inhibition test according OECD TG 209 and non-guideline studies describing the degradation and decomposition of PAA in different water types and water sources indicate primary degradation and dissipation of PAA, however, cannot demonstrated that ultimate biodegradation of the substance (i.e. full mineralisation) is achieved. As well, in these studies degradation products were not analysed, therefore it cannot be demonstrated that the formed degradation products do not fulfil the criteria for classification as hazardous to the aquatic environment.
Two hydrolysis studies according OECD TG 111 indicate that PAA is hydrolytically instable with DT_{50} values of 46.7h (pH 4) and 31.7h (pH 7) at 25 °C. Recalculated DT_{50} values at the environmentally relevant temperature in European surface waters of 12 °C was of 181.1 hours (approximately 7.5 days). However, as one of the hydrolysis products (hydrogen peroxide) fulfils the criteria for classification as hazardous to the aquatic environment, hydrolysis studies cannot be considered for rapid degradation.
Provided information on indirect photochemical degradation is difficult to use for classification purposes as actual degree of photochemical degradation in the aquatic environment depends on local conditions and the hazard of the degradation products is not known. Therefore, photochemical degradation is not considered for rapid degradation.
Overall, due to the results summarised above, RAC considers that, despite hydrolysis and indicated primary degradation and dissipation, PAA is not ultimately degraded to > 70 % within 28 days (equivalent to a half-life < 16 days), or rapidly transformed to non-classifiable products. Consequently, RAC considers that PAA does not fulfil the criteria for rapidly degradability.
Regarding exotoxicity please see RAC answer to comment No. 8.

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2021	France		MemberState	11

Comment received

We agree with the new proposal of classification:
Aquatic Acute 1, M-factor=10,
Aquatic Chronic 2.
Please see further comments below for more considerations on this classification.

For sake of clarity, the author name of every study (except studies carried out on vertebrates) could have been mentioned instead of “Anonymous”.

Whole e-fate section: For sake of clarity, reliability score for each e-fate study could have been added, as it was done for ecotoxicological studies.

Page 3, Table 6: In the table, please note that the M-factor is an acute one.

Page 38, Table 19: Please note that according to the Biocides report, the first test about ready biodegradability is a modified OECD 301 E.

Page 39, Table 19: In the Hydrolysis section, 3) Transition metal catalysed decomposition equation should be 2CH3CO3H + Mn+ ☐ 2CH3CO2H + O2 + Mn+ to be balanced in terms of oxygen atoms.

Page 40: Table 19: In the column Remarks of the study “Anonymous, (2000a)”, the sentences “Increased salinity of the water resulted in enhanced decomposition. This may be explained by the high pH of seawater” were corrected by the CA in the Biocidal IIIA document with: “Increased salinity of the water at higher initial peracetic acid

concentration resulted in enhanced decomposition" to indicate that the effect of salinity on degradation rate is only seen at the higher initial concentration.

Page 40, Table 19: Please note that the study “Anonymous, (2007d)” is GLP.

Page 40, Table 19: In the Hydrolysis section, please note that EU Method C.7 of Anonymous (1995a), the DT50 for abiotic degradation at pH 4 = 31.2h was obtained at 25°C and not 50°C.

Page 44, 11.1.4.2: In the study “Anonymous, 2007d”, the mixture indeed contains 15.2% of PAA but 23.5% of H2O2 and not 25.3%.

Page 44, 11.1.4.2: In the paragraph of the study “Anonymous, 2003a”, it seems that the pH and conductivity of the treated soil was monitored for 9 days and not several hours.

Page 45, 11.3.1: Please note that in the AR of 2019, the calculated Koc is 1.46 l/kg and not 1.02 l/kg. It seems that it has been calculated with a Log Kow of -0.26.

Page 46, 11.4.2: No BCF seems to have been calculated in the AR of 2019 or the final IIA of 2015. Therefore, no reference to the CAR should be mentioned for this input.

Page 51, Table 27: In the CAR of PAA (IIA, 2015) and AR of 2019, the study on Zebra fish permits to derive a NOEC value (initial measured) of 0.00069 mg PAA/L, the first NOEC based on nominal concentration of 0.00225 mg PAA/L was not considered in the Biocides Dossier. Indeed, a factor of 31% is considered to take into account the large differences between nominal and actual exposure concentration.

Page 52-54, 11.6.1/2: We agree with the new calculations of the hazard values (ErC50/NOEC) for the algae study based on the geometric mean concentrations. We also agree that the chronic fish and daphnia studies present analytical deficiencies. However, they revealed that fish or daphnids could be the most sensitive species in chronic studies and it should someway be taken into account in the classification. Indeed, in the CLP guidance (Annex I, Table 4.1.0), no classification option is available for rapidly degradable substance for which adequate chronic toxicity data are not available (iii). The chronic test on fish suffer of both analytical issue (LOQ above quite all tested concentrations) and a device issue, since the fish were not correctly exposed to the substance during the first part of the test. However, the test clearly shows that fish are the most sensitive species in the case of chronic exposure and an available reliable chronic test on fish would have led to a more stringent classification. From one side, the CLP guidance does not allow to take toxicities which are below the available limit of quantification into account, which would have however led to a strongest classification. From another side, we can understand that applying a worst case chronic classification for a substance which is so fast degradable could be questionable.

Dossier Submitter’s Response

Thank you for your support and comprehensive comments.

In accordance with the new ECHA policy related to General Data Protection Regulation the Author names from non published studies are deleted from the CLP classification dossier and replaced with “Anonymous xxxx”. The Dossier Submitter notes that the Table 6 is in accordance with the ECHA accordance check.

Regarding the environmental fate section, the Dossier Submitter agrees that reliability scores of each studies could have been added in order to unify the presentation of

evaluation of environmental hazards section. Furthermore, the Dossier Submitter welcomes the other clarifications and corrections you suggested and apologize the errors made. Regarding your comments on the ecotoxicity section, the Dossier Submitter thanks you for your support to this complex case. Please also see the response of the Dossier Submitter to the comment #8. Peracetic acid is now considered as not rapidly degradable and would results in a classification of Aquatic Chronic 1 with a M-factor of 1.
RAC's response
Please see RAC answers to the comment No. 8 and 10.

OTHER HAZARDS AND ENDPOINTS – Physical Hazards

Date	Country	Organisation	Type of Organisation	Comment number
08.10.2021	Germany		MemberState	12
Comment received				
Flammable liquids: The decision on removing the harmonised classification as Flam. Liq. 3, H226 by dossier submitter is based on one single PAA-formulation which is not representative. The justification (see CLH report 8.5.3) that the flash point is not relevant because the SADT is below 60 °C only applies to the SADT in a 50 kg package. However, in Table 10, the SADT has been determined for a 24 m3 tank transport, therefore the justification is scientifically incorrect. In conclusion the flash point as criteria for classification as flammable liquid has to be experimentally determined and specific concentration limits cannot be established due to the variability of the composition. Organic peroxides ./. Oxidising liquids The criteria for classification as an Organic Peroxide depends on the given criteria in Section 2.15.2.1 of Annex I, Part 2 to CLP: Any organic peroxide shall be considered for classification in this class, unless it contains: a) not more than 1,0 % available oxygen from the organic peroxides when containing not more than 1,0 % hydrogen peroxide; or b) not more than 0,5% available oxygen from the organic peroxides when containing more than 1,0 % but not more than 7,0 % hydrogen peroxide. With regard to the available oxygen and hydrogen peroxide contents of the PAA mixture, point a) corresponds to: 4.75 % PAA with maximum 1 % H2O2 and point b) corresponds to: 2.375 % PAA with maximum 7 % H2O2. These PAA-mixture shall not be considered for classification as an Organic peroxide and may be assigned to another class e.g. Oxidizing liquid. An exceptional case is a peroxyacetic acid formulation classified under UN 3149 of the United Nations Recommendations on the Transport of Dangerous Goods, Model Regulation. UN 3149, HYDROGEN PEROXIDE AND PEROXYACETIC ACID with acid(s), water and not more than 5 % peroxyacetic acid, STABILIZED Peroxyacetic acid formulation meeting the criteria for UN 3149 shall be classified as Ox. Liq. 2, H272. Criteria for UN 3149 are laid down in SP 196: Formulations which in laboratory testing neither detonate in the cavitated state nor deflagrate, which show no effect when heated under confinement and which exhibit no explosive power may be carried under this entry.				

The formulation must also be thermally stable (i.e. the SADT is 60 °C or higher for a 50 kg package). Since the chemical identification is "peracetic acid …%" with no further SID parameters like concentration limits for peracetic acid, hydrogen peroxide, acetic acid and additives, and that only equilibrium products in aqueous solutions should be taken into account a harmonised classification cannot be proposed. The different classifications of PAA formulations are also listed in the UN RTDG, which are cited in the CLH report Section 8.14.2: A list of currently classified organic peroxides is included in the UN RTDG Model regulations, Section 2.5.3.2.4. Peroxyacetic acid with concentration ≤ 43% is classified as organic peroxide type D, E or F. In contrast to the Dossier submitter, we see no reason to maintain the classification as Org. Perox. D ****, as Peroxyacetic acid with concentration ≤ 43% given in UN RTDG does not correlate with the undefined concentration limits of "peracetic acid …%" in Annex VI to CLP Regulation. In addition, it has been found several times in the past that the meaning of **** was not correctly interpreted by manufacturers, importers, downstream users or suppliers. Therefore, a classification for the hazard class Organic peroxides should be the responsibility and obligation of the person placing the product on the market.
Dossier Submitter's Response
Thank you for your comprehensive comments. We agree that the entry should be simplified by omitting the classifications for the physical hazards. We agree with the justification regarding the flash point and classification as flammable liquid as well as for organic peroxide. We came into a conclusion in our assessment that the 4 asterisks (****) in the classification as Org. Perox. D cannot be removed because the entry might be assigned to a different category or another hazard class and the correct classification shall be confirmed by testing. By removing the classification Org. Perox. D**** classification requirements are clear for companies.
RAC's response
The RAC supports retaining the current classification as Org. Perox. D with the addition of note T.

Date	Country	Organisation	Type of Organisation	Comment number
07.10.2021	United States of America	Peracetic Acid Registration Group (PAR)	Industry or trade association	13
Comment received				
None ECHA note – An attachment was submitted with the comment above. Refer to public attachment Peracetic acid - comments on CLH report - Oct 7_final.pdf				
Dossier Submitter's Response				
Noted				
RAC's response				
Noted.				

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON PERACETIC ACID ... %

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2021	France		MemberState	14
Comment received				
No comment.				
Dossier Submitter's Response				
Noted				
RAC's response				
Noted.				

PUBLIC ATTACHMENTS
1. Peracetic acid - comments on CLH report - Oct 7_final.pdf [Please refer to comment No. 3, 5, 9, 13]