COMPILED COMMENTS ON CLH CONSULTATION

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Last data extracted on 16.08.2023

Substance name: trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate)
CAS number: 70693-62-8
EC number: 274-778-7
Dossier submitter: Slovenia

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
11.08.2023	Germany	KMPS Registration Group	Company-Manufacturer	1

Comment received

CLH report, section 1.1, page 5, paragraph below table 1.1:
Comment:
It was established that the initially notified name for the active substance (pentapotassium bis(peroxymonosulphate) bis(sulphate)) was incorrect, primarily due to a violation considering a charge balance. In consequence the active substance has been renamed to trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate) where the positions of the protons are not specified. The applicant proposes to adapt the paragraph below the Table 1.1 by describing the reasons behind this change and for a better understanding of the structure of KMPS. The proposed adaptation is in line with the description given in the BPR Assessment Report on KMPS.

Proposed revision:
Initially, pentapotassium bis(peroxymonosulphate) bis(sulphate) was a notified name for the active substance. It was established that the name is incorrect, primarily due to a violation considering a charge balance. Consequently, the active substance has been renamed to trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate) where the positions of the protons are not specified. The active substance trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate) (hereafter: KMPS*) as manufactured comprises the hydrogen-bonded four-membered chain of the so-called triple salt (built by potassium peroxomonosulfate (KHSO5), potassium hydrogensulfate (KHSO4) and potassium sulphate (K2SO4)), which represents the active ingredient, some impurities and a small amount of residual humidity. A formula written as 2KHSO5.KHSO4. K2SO4 is not a true description of the actual chemical structure, since the structure does not consist of such three types of structural fragments (KHSO5, KHSO4 and K2SO4). Each potassium ion in the crystal structure is surrounded by oxygen atoms from all type of sulphate anions and hence the currently accepted correct formula is K5(HSO5)2(HSO4)(SO4). This compound K5(HSO5)2(HSO4)(SO4) is a conveniently stabilized crystalline form of Caro's acid, H2SO5, which itself is unstable. The biocidal effectiveness is due to the oxidative property of the peroxo- component in the substance, the peroxomonosulphate ion, $HSO5^{-}$.

CLH report, section A.1, page 13
Comment:
In the section A.1, p. 13 of the CLH report, the common name of the active substance: "Potassium peroxymonosulfate" has not been included in the Table A.1.

We propose to include this common name to align with the section A.3.5.1 of the CLH report, where this common name was reported.

ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment KMPS Registration Group confidential documents.zip

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2023	Germany		MemberState	2
Comment received				
The clear and comprehensive presentation of available data is very much appreciated.				

Date	Country	Organisation	Type of Organisation	Comment number
07.08.2023	France		MemberState	3
Comment received				
FRCA: We agree with the proposal for environmental classification.				

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2023	Germany		MemberState	4
Comment received				
No carcinogenicity studies are available for KMPS and available repeated dose toxicity studies as well as mutagenicity studies do not indicate a carcinogenic potential of the substance. Discussion of a possible non-genotoxic (cytotoxic) mode of action as provided by the DS is appreciated. Based on the available data base, classification of KMPS as carcinogenic is not warranted.				

MUTAGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2023	Germany		MemberState	5
Comment received				
No classification for Germ Cell Mutagenicity is supported based on negative in vivo data, in particular considering the negative Comet assay in tissues of first contact.				

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2023	Germany		MemberState	6
Comment received				
No classification for Reproductive Toxicity is supported since systemic effects on fertility are not expected and any potential developmental effects would be triggered by maternal toxicity due to the corrosive nature of KMPS.				

RESPIRATORY SENSITISATION

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2023	Germany		MemberState	7
Comment received				
As per CLP Regulation, KMPS requires classification as Resp. Sens. based on the classified impurity present at or above the SCL. It should be thoroughly discussed at RAC if absence of effects in workers (using PPE) and consumers (using highly diluted KMPS) is indeed enough to dismiss respiratory sensitisation as intrinsic property of the substance as is.				

Date	Country	Organisation	Type of Organisation	Comment number
11.08.2023	Germany	KMPS Registration Group	Company-Manufacturer	8
Comment received				
CLH report, section A.3.5 – Skin sensitization and section A.3.6. – Respiratory sensitization In consideration of the data on respiratory and skin sensitization for KMPS the KMPS registration group agrees to the proposals for non-classification proposed by the dossier submitter. The KMPS registration group would like to share further information after thorough review of the existing data: • KMPS is a not skin sensitizer and was tested negative in an LLNA using material containing 2.86% of the dipotassium peroxodisulphate impurity (persulfate and peroxodisulphate are used as synonyms in this document). The highest concentration of KMPS used in this LLNA was 0.5% since higher concentrations caused unacceptable high skin irritation. • KMPS was not a skin sensitizer in a guinea pig maximization test (GMPT) using material containing 2% of the dipotassium peroxodisulphate impurity. • KMPS is a widely used chemical (also by consumers e.g. for pool disinfection as well as for denture cleansers), but there are no reports regarding respiratory sensitization in humans and no medical reports from manufacturing sites (at which KMPS is produced including the peroxodisulphate impurity) pointing towards respiratory sensitization (see confidential medical surveillance reports attached). • The KMPS impurity Dipotassium peroxodisulphate is a moderate skin sensitizer only. Usually skin sensitizers also being respiratory sensitizers are strong skin sensitizers. • The appropriateness of the long-lasting classification of persulfates as respiratory sensitizer is doubted in the light of a recent thorough evaluation of the literature and a recent literature review: In this literature review all available respiratory sensitization reports on persulfate salts were evaluated according to predefined inclusion/exclusion criteria and a predefined scoring system. Persulfate salts were assigned to the category "Questionable evidence" due to e.g., missing information about exposure characterization, specific antibody testing, respiratory re-challenge, confirmation of the exposed chemical, or a clear connection between exposure and occurrence of symptoms. To conclude in line with the dossier submitter, it is not considered appropriate to classify KMPS as skin and/or respiratory sensitizer, based on its impurity (Dipotassium peroxodisulphate) content being above the generic concentration limit. Further, in line with the dossier submitter, it is not considered appropriate to add the labelling EUH208 "contains dipotassium peroxodisulphate (CAS 7727-21-1) May produce an allergic reaction" since KMPS is a substance which includes the dipotassium peroxodisulphate impurity. KMPS including the impurity at appropriate high concentration was tested negative for skin sensitization and medical surveillance data on KMPS including the impurity do not support classification.				

ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment KMPS Registration Group confidential documents.zip

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2023	Germany		MemberState	9
Comment received				
Acute oral toxicity classification (Cat. 4 with an ATE of 500 mg(kg bw) is supported. No classification for acute dermal toxicity and for acute inhalation toxicity are also supported based on data with the active substance.				

Date	Country	Organisation	Type of Organisation	Comment number
11.08.2023	Germany	KMPS Registration Group	Company-Manufacturer	10
Comment received				
Comments of the KMPS Registration Group on the CLH report of Trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate) (KMPS) - [CAS No. 70693-62-8] related to respiratory tract corrosion CLH report, Table 2.1 Proposed harmonized classification and labelling of the substance We do not agree with labelling of KMPS as EUH071. Labelling with EUH071 (corrosive to the respiratory tract) shall be performed when a substance or a mixture is classified for acute inhalation toxicity and available data indicate that the mechanism of toxicity is corrosivity. KMPS is not proposed to be classified for acute inhalation toxicity as per CLH report which documents an acute inhalation toxicity study. The LC50 was above 5 mg/L (highest feasible concentration) in this 4h study and animals were exposed head-only study. The MMAD was equal or below 4 µm. For dusts and mists no classification is necessary when the LC50 is above 5 mg/L. EUH071 can be applied to inhaled corrosive substances NOT tested for acute inhalation toxicity. However, KMPS was tested for acute inhalation toxicity and the results of these studies do not warrant classification of KMPS for acute inhalation toxicity. Therefore, the labelling with EUH071 is not in line with the CLP criteria. ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment KMPS Registration Group confidential documents.zip				

OTHER HAZARDS AND ENDPOINTS – Skin Hazard

Date	Country	Organisation	Type of Organisation	Comment number
11.08.2023	Germany	KMPS Registration Group	Company-Manufacturer	11
Comment received				
This is the same comment as mentioned under acute toxicity since EUH071 is combination of acute inhalation toxicity and corrosion. Comments of the KMPS Registration Group on the CLH report of Trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate) (KMPS) - [CAS No. 70693-62-8] related to respiratory tract corrosion CLH report, Table 2.1 Proposed harmonized classification and labelling of the substance				

We do not agree with labelling of KMPS as EUH071.
Labelling with EUH071 (corrosive to the respiratory tract) shall be performed when a substance or a mixture is classified for acute inhalation toxicity and available data indicate that the mechanism of toxicity is corrosivity.
KMPS is not proposed to be classified for acute inhalation toxicity as per CLH report which documents an acute inhalation toxicity study. The LC50 was above 5 mg/L (highest feasible concentration) in this 4h study and animals were exposed head-only study. The MMAD was equal or below 4 µm. For dusts and mists no classification is necessary when the LC50 is above 5 mg/L.
EUH071 can be applied to inhaled corrosive substances NOT tested for acute inhalation toxicity. However, KMPS was tested for acute inhalation toxicity and the results of these studies do not warrant classification of KMPS for acute inhalation toxicity.
Therefore, the labelling with EUH071 is not in line with the CLP criteria.

ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment KMPS Registration Group confidential documents.zip

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2023	Germany		MemberState	12
Comment received				
Skin Corr. 1 classification is supported based on the discussion of available data provided by the DS.				

Date	Country	Organisation	Type of Organisation	Comment number
07.08.2023	Ireland	Lanxess	Company-Manufacturer	13
Comment received				
A.3.3.1.1. pages 55 to 56 For reasons of clarity, the sentence "Thus, these studies support the use of the generic concentration limit triggering classification of mixtures as skin irritant (according to Regulation 1272/2008) of 1 % as dermal NOAEC." should rather read "Thus, these studies support the use of the generic concentration limit triggering classification of mixtures containing skin corrosive substances as skin irritant (according to Regulation 1272/2008) of 1 % as dermal NOAEC." The suggestion is also provided in the attached document. ECHA note – An attachment was submitted with the comment above. Refer to public attachment TM-Arrow-KPMS CLH comments-3Aug23.pdf				

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2023	Germany		MemberState	14
Comment received				
Classification for Eye Dam. 1 is supported based on animal data and the fact that KMPS does warrant classification as corrosive to the skin.				

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number

11.08.2023	Germany	KMPS Registration Group	Company-Manufacturer	15
Comment received				
This is the same comment as for respiratory sensitization since the topics are linked for this compound: CLH report, section A.3.5 – Skin sensitization and section A.3.6. – Respiratory sensitization In consideration of the data on respiratory and skin sensitization for KMPS the KMPS registration group agrees to the proposals for non-classification proposed by the dossier submitter. The KMPS registration group would like to share further information after thorough review of the existing data: • KMPS is a not skin sensitizer and was tested negative in an LLNA using material containing 2.86% of the dipotassium peroxodisulphate impurity (persulfate and peroxodisulphate are used as synonyms in this document). The highest concentration of KMPS used in this LLNA was 0.5% since higher concentrations caused unacceptable high skin irritation. • KMPS was not a skin sensitizer in a guinea pig maximization test (GMPT) using material containing 2% of the dipotassium peroxodisulphate impurity. • KMPS is a widely used chemical (also by consumers e.g. for pool disinfection as well as for denture cleansers), but there are no reports regarding respiratory sensitization in humans and no medical reports from manufacturing sites (at which KMPS is produced including the peroxodisulphate impurity) pointing towards respiratory sensitization (see confidential medical surveillance reports attached). • The KMPS impurity Dipotassium peroxodisulphate is a moderate skin sensitizer only. Usually skin sensitizers also being respiratory sensitizers are strong skin sensitizers. • The appropriateness of the long-lasting classification of persulfates as respiratory sensitizer is doubted in the light of a recent thorough evaluation of the literature and a recent literature review: In this literature review all available respiratory sensitization reports on persulfate salts were evaluated according to predefined inclusion/exclusion criteria and a predefined scoring system. Persulfate salts were assigned to the category "Questionable evidence" due to e.g., missing information about exposure characterization, specific antibody testing, respiratory re-challenge, confirmation of the exposed chemical, or a clear connection between exposure and occurrence of symptoms. To conclude in line with the dossier submitter, it is not considered appropriate to classify KMPS as skin and/or respiratory sensitizer, based on its impurity (Dipotassium peroxodisulphate) content being above the generic concentration limit. Further, in line with the dossier submitter, it is not considered appropriate to add the labelling EUH208 "contains dipotassium peroxodisulphate (CAS 7727-21-1) May produce an allergic reaction" since KMPS is a substance which includes the dipotassium peroxodisulphate impurity. KMPS including the impurity at appropriate high concentration was tested negative for skin sensitization and medical surveillance data on KMPS including the impurity do not support classification. ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment KMPS Registration Group confidential documents.zip				

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2023	Germany		MemberState	16
Comment received				
While no classification for KMPS as Skin Sens. is supported based on GPMT data and due to the limitations brought forward concerning human data, the LLNA should not be considered				

for classification purposes.
The study has several limitations and should be considered unreliable. First, the chosen positive control substance HCA in DMSO produced clearly irritative responses as per criteria set in the respective TG (i.e. ear thickness increase of significantly more than 25 % in all 5 control animals). Therefore, another positive control substance or vehicle should have been used to demonstrate sensitivity of the test system in the performing laboratory. Second, the choice of test concentrations is questionable. According to the full study report that has been made available to the DE-MSCA, concentration of and above 5 % of the test substance are clearly irritative. However, for concentrations 1 % and 2.5 % the irritation threshold is only ever met by one ear of one of the two animals (this was also true for the 0.05 % and 0.1 % groups). Furthermore, for the 1 % and 2.5 % groups, ear thicknesses on day 1 are smaller than in any other group. The irritative effect claimed is therefore attributable to the way study authors took group means. Ear measurements were taken on day 1 (before exposure), day 3, and day 6. Study authors took means of those single measurements to calculate mean percentages of increase, thus inflating the impact of single high values. However, when calculating increase percentages for single ears and taking the mean of these, the first concentration to exceed the 25 % threshold is 5 %. Hence, KMPS should have been tested up to 2.5 % and chosen concentrations were too low.

Date	Country	Organisation	Type of Organisation	Comment number
07.08.2023	France		MemberState	17
Comment received				
FR CA: A supplemental hazard statement EUH208 is proposed for KMPS due to the presence of impurity dipotassium peroxodisulphate (K2S208) at a concentration greater than that specified in Table 3.4.6 of Annex I of Regulation (EC) 1272/2008. From our understanding of the CLP regulation such hazard statement is applicable on mixtures but not active substance; therefore this statement should not be applied on KMPS. Furthermore, EUH208 is not reported in the table 2.1 p.9 of the document where EUH071 is presented. Is the EUH208 statement still supported by the dossier submitter? Please clarify.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Single Exposure

Date	Country	Organisation	Type of Organisation	Comment number
07.08.2023	Ireland	Lanxess	Company-Manufacturer	18
Comment received				
A.3.2.5. page 50 In the absence of a pathological manifestation of local irritation/corrosion in the respiratory tract, the effects reported are not considered to be sufficient for a classification of KMPS as STOT SE 3. In addition, the conclusion "As labelling EUH071 'Corrosive to the respiratory tract' is applicable, a classification of STOT SE Cat 3 (H335) is not necessary" is not agreed upon. Labelling with EUH071 can always be assigned alone considering Section 1.2.6. in Annex II of CLP and is not always linked to STOT SE 3, H335. RAC discussions on that endpoint are to be observed. A summary and justification against the proposed classification are provided in the attached document. ECHA note – An attachment was submitted with the comment above. Refer to public attachment TM-Arrow-KPMS CLH comments-3Aug23.pdf				

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2023	Germany		MemberState	19
Comment received				
Based on the highly irritative nature of the active substance and severe inflammatory responses observed at the site of initial contact, it is reasonable to assume that clinical signs observed in several studies were manifestations of pain and suffering rather than direct neurotoxic effects. Therefore, no classification for STOT SE (categories 1, 2, or 3 for narcotic effects) is supported. As regards STOT SE 3 (RTI) classification, since effects observed are rather of corrosive nature, labelling with EUH071 for these effects is more appropriate and therefore supported.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Repeated Exposure

Date	Country	Organisation	Type of Organisation	Comment number
07.08.2023	France		MemberState	20
Comment received				
FR CA: A classification STOT RE Category 1, H372 "Causes damage to organs (eyes) trough prolonged or repeated exposure" is proposed for KMPS based on the eye effects observed in a sub-acute inhalation study. This classification is not reported in the table 2.1 at the beginning of the document. Is this proposed classification still supported by the dossier submitter? Please clarify				

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2023	Germany		MemberState	21
Comment received				
The classification proposal for eye effects as STOT RE 1, H372, is supported.				

Date	Country	Organisation	Type of Organisation	Comment number
11.08.2023	Germany	KMPS Registration Group	Company-Manufacturer	22
Comment received				
Comments of the KMPS Registration Group on the CLH report of Trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate) (KMPS) - [CAS No. 70693-62-8] related to STOT RE CLH report, section A.3.7.4. Specific target organ toxicity – repeated exposure (STOT RE) The CLH report proposes classification of KPMS as STOT RE1 for eye effects for the following grounds: Section A.3.7.4.1: "In a subacute inhalation study the only significant adverse effect was on the eyes. There is no information available regarding the onset of eye effects. Effects were recorded twice: on the 12th day of the test (the 10th day of exposure) and the 25th day of the test (the 13th day of the postexposure period). The effects on the eyes in a subacute inhalation study appear to be dose- and time dependent. Similar effects on eyes were observed in the acute inhalation toxicity study where animals				

were exposed to 1.5, 3.9, 4.2 and 5.0 mg/L/4h: moderate to severe ocular discharge increasing with concentration during exposure, alopecia around the eyes, cloudy eyes (some eventually turning black in colour), and severe discharge from the eyes at the three highest exposure levels during a 14-day observation period. At 1.5 mg/L only 1 cloudy eye (that turned black in colour) was noted."

In Section A.3.7.4.3, the dossier submitter mentions:
"The effects in subacute inhalation study were seen at concentration that is 150 lower than the lowest concentration tested in the acute inhalation toxicity study and orders of magnitude lower than the basis for Eye Dam. 1 classification (0.1 g pure substance). Therefore, the classification is warranted also when considering additional considerations set out in CLP Guidance."

Reference is further made to Section 3.9.2.5.1, p 470 of the CLP guidance which clarifies that for corrosive substances it should be assessed whether the effect is a reflection of true repeated exposure or whether it is just acute toxicity.

Thus, information on the onset of eye effects upon repeated inhalation exposure is important.
The data owner of the 14-day study (Anonymous 1981) would like to clarify some points in this respect: The 14-day subacute study was performed in two phases.

1) Phase I was an initial study where the animals were exposed to nominal 100, 500, 1000 mg/m3 (actual 110, 320, 790 mg/m3, respectively). Those concentrations are equivalent to 0.11, 0.32, and 0.79 mg/L. The animals of the highest concentration were sacrificed after 3 exposures, the animals of the mid concentration were terminated after 5 exposures, whereas the animals of the low concentration survived. The animals were observed daily for clinical signs and the raw data can be found from page 52 onwards of the report (see confidential document submitted). On exposure 2, the high and mid concentrations animals showed moderate to severe ocular discharge up to corneal opacity. Animals of the low concentration also showed those effects from exposure day 4 (see pp. 100-103). Thus, eye effects were early after exposure and are acute effects.

2) Phase II was the following phase done at lower concentrations. These are the concentrations reported in Table A.24 of the CLH report i.e. nominal 0, 0.001, 0.01, 0.05 mg/L, measured 0, 0.0014, 0.0101, and 0.0431 mg/L, respectively. Close inspection of the raw data of this part reveal that clinical signs were recorded daily but are difficult to read due to bad handwriting. However, the spacing from the lowest concentration in Phase I (0.11 mg/L) to the high concentration in Phase II (0.05 mg/L) was rather small. A very detailed examination of the eyes was, however, performed on two occasions as mentioned in the CLH report (10th exposure day and 13th post-exposure day). Since the effects (Blood clots, slight to severe opacity, eye sensitive to light) after post-exposure period at 0.11 mg/L (Phase I) and 0.05 mg/L (Phase II) are comparable, one can assume that damage to the eyes was an immediate effect also in Phase II. In Phase II, slight to severe ocular discharge was noted already on the first day of exposure for the intermediate concentration (0.01 mg/L) which was due to an overdosing / technical error on that day. In fact, at the beginning of the exposure for about 5 min heavy dust atmosphere in the chamber that coated the walls with compounds was observed. The severity of effects on eye for the intermediate concentration didn´t further increase. Overall, the effects on eyes seen in the intermediate concentration are very difficult to understand since it is unknown whether or not the overdosing caused the effects on eyes.

3) Information on particle size: During Phase I of the subacute inhalation toxicity study, the particle sizes were determined (see pp 67, 75, 81) to be 2, 2.4, and 3.5 µm for the low,

mid, and high concentration, respectively. Although the particle sizes were not determined in Phase II of the study, Phase II was done directly after Phase I (i.e. the last exposure in Phase I was on the 10-October-1980, the first exposure of Phase II was on the 13-October-1980). One can therefore infer the particle size to which animals were exposure during Phase II from the measured particle sizes in Phase I. Since the particle sizes determined in Phase I were below 4 µm, this is also expected for Phase II. We would suggest to clarify this point in the CLH report Table A.24.
In addition to all the above, medical surveillance data from production do not mention adverse effects of the material on eyes (see confidential medical surveillance report submitted, Anonymous 2023).

To conclude, the onset of effects on eye upon exposure to dust is an immediate / acute effect upon inhalation exposure. The lowest acutely irritation concentration from the 3 studies (acute inhalation study and Phase I and Phase II of the subacute inhalation study) is most likely between 0.11 and 0.32 mg/L. Likewise, the lowest irritating concentration from repeated inhalation exposure is difficult to determine due to the overdosing in Phase II intermediate concentration, however, it is likely 0.05 mg/L. Overall, the difference between effects from acute and repeated inhalation on eyes is much less than 150 but rather around 6.
The effects on eye were seen quickly after exposure also in the repeated subacute inhalation studies and represent the result of acute toxicity / corrosivity. Therefore, KMPS does not warrant classification as STOT RE1 H372 (eyes, inhalation route) despite the NOAEC 0.0014 mg/L from the respective study is lower than 0.06 mg/L (the cut-off value as per CLP used for classification).

The table mentioned can be found in the respective attached statement.

ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment KMPS Registration Group confidential documents.zip

Date	Country	Organisation	Type of Organisation	Comment number
09.08.2023	United Kingdom	Health and Safety Executive	National Authority	23
Comment received				
STOT RE We note the proposal for classification with STOT RE 1 (eyes). However, given the substance is also corrosive to the skin, it is possible the eye damage described in the sub-acute inhalation toxicity study (Anonymous, 1981) could reflect the corrosive nature of the substance. It would be useful to provide information on when these effects were first observed to help discriminate between a true repeated dose effect and local site of contact.				

Date	Country	Organisation	Type of Organisation	Comment number
08.08.2023	Germany	Lanxess	Company-Manufacturer	24
Comment received				
The CLH report for trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate) (KMPS) contains inconsistencies between the classification proposal (Tables 2.1 and 2.2) and the classification proposal made for the STOT RE category. Whereas no classification for STOT RE is proposed in Table 2.1, the conclusion stated in Section A.3.7.4.3 is that KMPS, in addition to the classification as Eye Dam.1, should be classified as STOT RE1 for the eye damage observed in the subacute inhalation study				

(Anonymous, 1981).
In support of this classification proposal, the DS cites the CLP guidance stating that "effects occurring at a concentration one order of magnitude lower than the concentration causing acute effects, may warrant a classification as STOT RE, even if the substance is already classified as corrosive".
The subacute LOAEC for eye irritation was 0.0101 mg/L. In contrast, an eye irritation/corrosivity study features instillation of 100 mg of test substance. The eye irritation/corrosivity study is not aimed at the identification of a NOAEC for eye irritation. The daily observations recorded during the subacute inhalation show that an instilled amount much smaller than 100 mg cause eye irritation/damage. In the subacute inhalation study, rats were exposed head-only, i.e., the KPMS dust is also targeted towards the eyes. KMPS is highly soluble in water and KMPS dust will thus readily adhere to the watery surfaces of nasal and ocular mucosa exposed in the inhalation study. This can lead to the build-up of irritant or corrosive local concentrations of KMPS during each exposure session. The daily observations from the subacute inhalation study show that "slight ocular discharge (red)" was already observed 30 min into the first exposure session at the lowest test concentration of 0.001 mg/L (notebook page 52). Section 3.8.1.6.(c) of Regulation 1272/2008 expressively states that serious eye damage/eye irritation is not included under the STOT SE hazard category. Being clearly an acute effect, the observed severe eye irritation does not qualify for the STOT RE hazard category either.
The eye irritation observed in the subacute inhalation study thus qualifies as an acute effect covered by the Eye Dam.1 classification. Classification as STOT RE1 is not justified.

Date	Country	Organisation	Type of Organisation	Comment number
07.08.2023	Ireland	Lanxess	Company-Manufacturer	25
Comment received				
A.3.7.4. Pages 80 - 82. Classification is recommended in the text but not in the proposed CLH (Table 2.1, page 9). The ocular effects observed in the 14-day inhalation toxicity study in male rats result from the acute local irritation/corrosive properties as well as mechanical effects of KMPS dust in animal eyes. Thus, the observed effects are not a result of a repeated exposure regime. This characteristic mode of action of KMPS has been accordingly accounted for by a classification with Skin. Corr. 1, H314, and Eye Dam. 1, H318. An additional classification of KMPS with STOT RE 1, H372 (eyes) is not considered to be warranted. A detailed summary of the evidence and justification against classification are provided in the attached document. ECHA note – An attachment was submitted with the comment above. Refer to public attachment TM-Arrow-KPMS CLH comments-3Aug23.pdf				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
09.08.2023	United Kingdom	Health and Safety Executive	National Authority	26
Comment received				
Rapid degradability/transformation The hydrolysis study results showed that the degradation of trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate) (KMPS) was slower in the buffer solution at pH 4 with a DT50 >800 hours (>33 days) at 20°C which is above the hazard classification criterion of 16 days. Studies on the transformation in water containing oxidisable substances at similar				

low pH levels are not available. Therefore, we are uncertain if the substance rapidly transforms to non-hazardous forms under all environmentally relevant conditions.

In addition, the CLH DS noted that the formation of hydrogen peroxide via hydrolysis occurs after a long time and in negligible amounts. The lead EU REACH Registrant for hydrogen peroxide includes a self-classification as Aquatic Chronic 3 which is supported by the available data (ECHA, 2022a). On this basis, is there any further/more definitive information on the rate of formation of hydrogen peroxide from KPMS to understand if degradants are considered non-classifiable for hazard classification?

Bioaccumulation potential
The CLH DS concluded that the substance has no potential for bioaccumulation due to the log KOW <4 combined with the view that KMPS dissipates rapidly in the environment. We note that log KOW is not applicable to assess the bioaccumulation potential of such inorganic substances. Given our uncertainty about the rapid degradability/transformation conclusion and the lack of other bioaccumulation data, we are unclear if it is possible to conclude on the bioaccumulation potential.

Ecotoxicity
Endpoints for the Skeletonema costatum study are provided for the 96-hour study duration only in the CLH report and the EU REACH registration (ECHA, 2022b). However, 72-hour endpoints would be preferable as the CLH DS noted that the validity criteria in the current version of OECD TG 201 were met during the first 72-hours of the Skeletonema costatum study, whereas "control behaviour becomes too variable after 96 hours, because exponential growth is not maintained". Please can 72-hour endpoints be presented?

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

ECHA (2022b) EU REACH registration dossier for pentapotassium bis(peroxymonosulphate) bis(sulphate) [ONLINE] European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/en/registration-dossier/-/registered-dossier/15990/1/1 (Accessed August 2023).

Date	Country	Organisation	Type of Organisation	Comment number
07.08.2023	France		MemberState	27
Comment received				
FR CA: Regarding the chronic toxicity in seawater, toxicity data from Anonymous 2007f are included in the Table A.36. No summary of this study on the chronic data is available below the Table A.36. These chronic values differ from the latest version of the CAR of KMPS we received, that mentioned a NOErC (96h) = 0.295 mg/L instead of 0.444 mg/L as presented in the CLH report. Note that this value of NOErC (96h) = 0.295 mg/L is also mentioned p.117 of the CLH report. This editorial mistake does not have impact on the environmental classification. In addition this study is presented in the Table A.38 in the section invertebrates instead of Algae				

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2023	Germany		MemberState	28
Comment received				
Section A4.2.3.1 (P.111 & 113): Regarding the acute/short-term toxicity to algae, please include “72h-NOEC” as heading in the table for the value 0.43 mg/L of the P.subcapitata test. Please also include in the description of the algae test the following information: “In BPC-ENV WG I-2023, it was agreed that the endpoints need to be recalculated based on the geomean approach following the guidance in Vol. IV Part B+C (2017) for rapidly degrading substances taking ½ LOQ as concentration at the end of the test. For the highest test concentration the geometric mean calculated with the nominal concentration and ½ LOQ equals 0.866 mg KMPS/L, corresponding to 86.6% of nominal. This may be extrapolated to all test concentrations resulting in nominal endpoints to be corrected by a factor 0.866.”.				

PUBLIC ATTACHMENTS
1. TM-Arrow-KPMS CLH comments-3Aug23.pdf [Please refer to comment No. 13, 18, 25]

CONFIDENTIAL ATTACHMENTS
1. KMPS Registration Group confidential documents.zip [Please refer to comment No. 1, 8, 10, 11, 15, 22]