REGULATION (EC) NO 1272/2008 (CLP REGULATION),

ANNEX VI, PART 2

Proposal for Harmonised Classification and Labelling for a biocidal active substance

CLH REPORT

Trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate)

EC Number: 274-778-7

CAS Number: 70693-62-8

Index Number: Not applicable

Contact details of dossier submitter:

Chemicals Office of the Republic of Slovenia
Ajdovščina 4, 1000 Ljubljana
E mail: biocidi.uzk@gov.si

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STATEMENT OF SUBJECT MATTER AND PURPOSE OF THE CAR

Not applicable for the CLH report.

BPC OPINION

Not applicable for the CLH report.

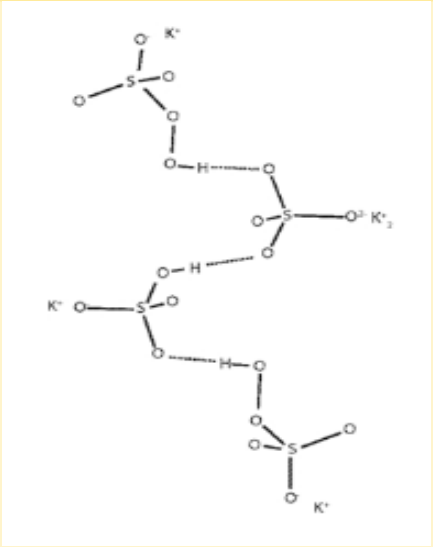
ASSESSMENT REPORT

SUMMARY

1. PRESENTATION OF THE ACTIVE SUBSTANCE

1.1 IDENTITY OF THE ACTIVE SUBSTANCE

Table 1.1 Main constituents

Main constituent	
Chemical Name	Trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate)
IUPAC name	Pentapotassium bis((hydroperoxysulfonyl)oxidanide) hydrogen sulfate sulfate
EC number	274-778-7
CAS number	70693-62-8
Index number in Annex VI of CLP	Not applicable
Minimum purity / content	≥ 89 %
Structural formula	

The active substance trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate) (hereafter: KMPS*) as manufactured comprises the so-called triple salt (a hydrogen-bonded four-membered chain that dissociates in aqueous solution to potassium peroxomonosulfate ($KHSO_5$), potassium hydrogensulfate ($KHSO_4$) and potassium sulphate (K_2SO_4)), which represents the active ingredient, some impurities, the anti-caking agent ($MgCO_3$) and a small amount of residual humidity. A formula written as $2KHSO_5.KHSO_4$. K_2SO_4 is not a true description of the actual chemical structure in which potassium ions are not associated with discrete anions, and hence the currently accepted correct formula is $K_5(HSO_5)_2(HSO_4)(SO_4)$. This compound $K_5(HSO_5)_2(HSO_4)(SO_4)$ is a conveniently stabilized crystalline form of Caro's acid, H_2SO_5, which itself is unstable. The biocidal effectiveness is due to the oxidative property of the peroxo- component in the substance, the peroxomonosulphate ion, HSO_5^-.

* The acronym KMPS stands for potassium monopersulfate, which is the common name for trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate). Pure potassium monopersulfate ($KHSO_5$) cannot be isolated in a stable, solid form. It exists as a component of the so-called triple salt. Therefore, KMPS is used to represent the active substance molecule trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate).

Table 1.2 Relevant impurities and additives

Relevant impurities and additives		
IUPAC name or chemical name or EC name	Maximum concentration in % (w/w)	Index number in Annex VI of CLP
-	-	-

Based on ECHA Guidance on Impurities and (degree of) purity in CLP and in the CLH process (August 2018) KMPS does not contain relevant impurities.

Intended Uses and Effectiveness

Table 1.3 Use of the active substance

Product type	PT 2: Disinfectants and algaecides not intended for direct application to humans or animal PT 3: Veterinary hygiene PT 4: Food and feed area PT 5: Drinking water
Intended use patterns	PT2: - Disinfection of swimming pools - Dipping of equipment - Surface disinfection of industrial areas by wiping with mop - Surface disinfection of industrial areas by manual spraying (low pressure) PT3: - Terminal disinfection of animal houses using a mechanical sprayer (low pressure) - Foot dips PT4: - Surface disinfection in food and feeding areas by wiping with mop - Surface disinfection in food and feeding areas by manual spraying PT5: - Disinfection of animal drinking water: Continuous water sanitation by dosing the header tank or application via a dosing system
Users	- Professional users - Non-professional users (general public) for swimming pool disinfection only

Table 1.4 Effectiveness of the active substance

PT2:

Function	Bactericide, fungicide, virucide
Organisms to be controlled	Bacteria Yeasts and fungi Viruses
Limitation of efficacy including resistance	The studies provided are sufficient to demonstrate innate efficacy for active substance approval. KMPS is an inorganic substance with an unspecific mode of action (multisite oxidation process), therefore the

	development of resistance to KMPS is highly unlikely event. Potential remedies should be available if true resistance is ever observed with KMPS.
Mode of action	KMPS releases reactive oxygen, which oxidises macromolecules of the cell wall, membranes and virus capsids leading to the cell wall disruption, loss of membrane integrity and disintegration of virus capsids. In addition, after penetration into cells or viruses, intracellular molecules such as amino acids, polypeptides, RNA and DNA are also oxidised leading to the disruption of protein synthesis and cell death.

PT3:

Function	Bactericide, fungicide, virucide
Organisms to be controlled	Bacteria Yeasts and fungi Viruses
Limitation of efficacy including resistance	The studies provided are sufficient to demonstrate innate efficacy for active substance approval. KMPS is an inorganic substance with an unspecific mode of action (multisite oxidation process), therefore the development of resistance to KMPS is highly unlikely event. Potential remedies should be available if true resistance is ever observed with KMPS.
Mode of action	KMPS releases reactive oxygen, which oxidises macromolecules of the cell wall, membranes and virus capsids leading to the cell wall disruption, loss of membrane integrity and disintegration of virus capsids. In addition, after penetration into cells or viruses, intracellular molecules such as amino acids, polypeptides, RNA and DNA are also oxidised leading to the disruption of protein synthesis and cell death.

PT4:

Function	Bactericide, fungicide, virucide
Organisms to be controlled	Bacteria Yeasts and fungi Viruses
Limitation of efficacy including resistance	The studies provided are sufficient to demonstrate innate efficacy for active substance approval. KMPS is an inorganic substance with an unspecific mode of action (multisite oxidation process), therefore the development of resistance to KMPS is highly unlikely event. Potential remedies should be available if true resistance is ever observed with KMPS.
Mode of action	KMPS releases reactive oxygen, which oxidises macromolecules of the cell wall, membranes and virus capsids leading to the cell wall disruption, loss of membrane integrity and disintegration of virus capsids. In addition, after penetration into cells or viruses, intracellular molecules such as amino acids, polypeptides, RNA and DNA are also oxidised leading to the disruption of protein synthesis and cell death.

PT5:

Function	Bactericide, fungicide, virucide
Organisms to be controlled	Bacteria Yeasts and fungi Viruses
Limitation of efficacy including resistance	The studies provided are sufficient to demonstrate innate efficacy for active substance approval. KMPS is an inorganic substance with an unspecific mode of action (multisite oxidation process), therefore the development of resistance to KMPS is highly unlikely event. Potential remedies should be available if true resistance is ever observed with KMPS.
Mode of action	KMPS releases reactive oxygen, which oxidises macromolecules of the cell wall, membranes and virus capsids leading to the cell wall disruption, loss of membrane integrity and disintegration of virus capsids. In addition, after penetration into cells or viruses, intracellular molecules such as amino acids, polypeptides, RNA and DNA are also oxidised leading to the disruption of protein synthesis and cell death.

2. PROPOSED HARMONISED CLASSIFICATION AND LABELLING OF THE ACTIVE SUBSTANCE ACCORDING TO THE CLP CRITERIA

2.1 PROPOSED HARMONISED CLASSIFICATION AND LABELLING FOR THE ACTIVE SUBSTANCE

Table 2.1 Proposed harmonised classification and labelling of the substance

	Index No	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATEs	Notes
				Hazard Class and Category Code(s)	**Hazard statement Code(s)**	**Pictogram, Signal Word Code(s)**	**Hazard statement Code(s)**	**Suppl. Hazard statement Code(s)**		
Current Annex VI entry										
Dossier submitter's proposal	TBD	274-778-7	70693-62-8	Acute Tox 4 Skin Corr. 1 Eye Dam. 1 Aquatic Acute 1 Aquatic Chronic 3	H302 H314 H318 H400 H412	GHS07 GHS05 GHS09 Dgr	H302 H314 H410	EUH 071	oral: ATE = 500 mg/kg bw M=1	
Resulting entry in Annex VI if adopted by RAC and agreed by Commission	TBD	274-778-7	70693-62-8	Acute Tox 4 Skin Corr. 1 Eye Dam. 1 Aquatic Acute 1 Aquatic Chronic 3	H302 H314 H318 H400 H412	GHS07 GHS05 GHS09 Dgr	H302 H314 H410	EUH 071	oral: ATE = 500 mg/kg bw M=1	

Table 2.2 Reason for not proposing harmonised classification and labelling and the status under CLH public consultation

Hazard class	Reason for not proposing classification and labelling	Within the scope of public consultation
Explosives	Data conclusive but not sufficient for classification	Yes
Flammable gases (including chemically unstable gases)	Not applicable (the substance is a solid)	No
Oxidising gases	Not applicable (the substance is a solid)	No
Gases under pressure	Not applicable (the substance is a solid)	No
Flammable liquids	Not applicable (the substance is a solid)	No
Flammable solids	Data conclusive but not sufficient for classification.	Yes
Self-reactive substances and mixtures	Not applicable (the substance is a solid)	No
Pyrophoric liquids	Not applicable (the substance is a solid)	No
Pyrophoric solids	Data conclusive but not sufficient for classification.	Yes
Self-heating substances and mixtures	Data conclusive but not sufficient for classification.	Yes
Substances which in contact with water emit flammable gases	Data conclusive but not sufficient for classification.	Yes
Oxidising liquids	Not applicable (the substance is a solid)	No
Oxidising solids	Data conclusive but not sufficient for classification.	Yes
Organic peroxides	Hazard class not applicable.	No
Corrosive to metals	Not applicable (substance is a solid with a melting point above 55 °C)	No
Desensitised explosives	Not applicable (the substance is not explosive)	No
Acute toxicity via oral route	Harmonised classification proposed: Acute Tox 4, H302	Yes
Acute toxicity via dermal route	Data conclusive but not sufficient for classification	Yes
Acute toxicity via inhalation route	Data conclusive but not sufficient for classification	Yes
Skin corrosion/irritation	Harmonised classification proposed: Skin Corr 1B, H314	Yes
Serious eye damage/eye irritation	Harmonised classification proposed: Eye Dam 1, H318	Yes

Respiratory sensitisation	Data conclusive but not sufficient for classification	Yes
Skin sensitisation	Data conclusive but not sufficient for classification	Yes
Germ cell mutagenicity	Data conclusive but not sufficient for classification	Yes
Carcinogenicity	Data conclusive but not sufficient for classification	Yes
Reproductive toxicity	Data conclusive but not sufficient for classification	Yes
Specific target organ toxicity-single exposure	Data conclusive but not sufficient for classification	Yes
Specific target organ toxicity-repeated exposure	Data conclusive but not sufficient for classification	Yes
Aspiration hazard	Hazard class not applicable	No
Hazardous to the aquatic environment	Harmonised classification proposed: Aquatic Acute 1, H400 (M=1) and Aquatic Chronic 3, H412	Yes
Hazardous to the ozone layer	Data conclusive, but not sufficient for classification	Yes

2.2.1 HISTORY OF THE PREVIOUS CLASSIFICATION AND LABELLING

Trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate) is biocidal active substance, not previously discussed and/or agreed by the TC C&L (Dir. 67/548/EEC) and/or RAC (CLP Regulation).

2.2 PROPOSED CLASSIFICATION AND LABELLING AND PACKAGING FOR THE REPRESENTATIVE PRODUCT(S)

Not applicable for the CLH report.

2.3 DATA SOURCES

The reference list is provided in Part D, Appendix V.
The main data source is CAR on KMPS. In addition, the data from the existing REACH registration dossier have been reviewed in ECHA-REACH-IUCLID:July 2022. Brief Profile - ECHA (europa.eu)

3. SUMMARY OF THE HUMAN HEALTH RISK ASSESSMENT

Not applicable for the CLH report.

3.1 SUMMARY OF THE ASSESSMENT OF EFFECTS ON HUMAN HEALTH

Not applicable for the CLH report.

3.2 REFERENCE VALUES

Not applicable for the CLH report.

3.3 RISK CHARACTERISATION

Not applicable for the CLH report.

4. SUMMARY OF THE ENVIRONMENTAL RISK ASSESSMENT

Not applicable for the CLH report.

4.1 FATE AND BEHAVIOUR IN THE ENVIRONMENT

Not applicable for the CLH report.

4.2 EXPOSURE ASSESSMENT

Not applicable for the CLH report.

5. ASSESSMENT OF EXCLUSION CRITERIA, SUBSTITUTION CRITERIA AND POP

Not applicable for CLH report.

A Assessment of intrinsic properties and effects of the active substance

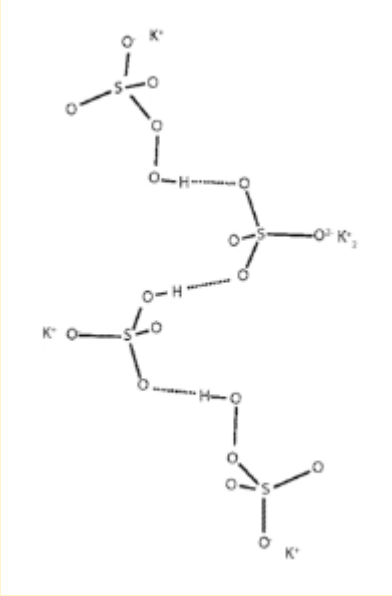
A.1. General substance information

A.1.1. Identity of the substance

Table A.1 Summary table on substance identity

Summary table on substance identity	
Common name	Trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate) Trade names: Caroat, Caroat(R), Kybreak, Oxone, Oxone (R), Oxone™
Chemical name (IUPAC name)	Pentapotassium bis ((hydroperoxysulfonyl)oxidanide) hydrogen sulfate sulfate
EC number	274-778-7
CAS number	70693-62-8
other CAS numbers (e.g. deleted, related, preferred, alternate)	70693-62-8
Molecular formula	$K_5H_3S_4O_{18}$
Molecular weight or molecular weight range	614.76 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable
Degree of purity (%)	≥ 89

Table A.2 Structural formula

Structural formula


A.1.2. Composition of the substance (reference specifications)

Table A.3 Main constituents

Main constituent					
Constituent (chemical name)	Typical concentration (%(w/w))	Concentration range (%(w/w))	Current CLH in Annex VI Table 3.1 (CLP)	Current self- classification and labelling (CLP)	Remarks / Discussion
Trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate)	≥ 89 %	-	-	Acute Tox. 4 H302 Skin Corr. 1 H314 Eye Dam. 1 H318 Aquatic Acute H400 Aquatic Chronic 3 H412	-

Table A.4 Impurities

See confidential Annex of this report.

Table A.5 Additives

Not relevant.

Table A.6 Concentration of constituents (main constituents, impurities, additives) in batches used for (eco)toxicity studies annd specification

Not relevant.

A.1.3. Physical and chemical properties of the active substance

Table A.3 Physical and chemical properties of the active substance

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
Aggregate state at 20°C and 101.3 kPa	Powder	Visual	KMPS P-16, Batch No.: H-27841	Anonymous 2007a
Physical state (appearance) at 20°C and 101.3 kPa	Solid	Visual	KMPS P-16, Batch No.: H-27841	Anonymous 2007a
Colour at 20°C and 101.3 kPa	White	Visual	KMPS P-16, Batch No.: H-27841	Anonymous 2007a
Odour at 20°C and 101.3 kPa	Odourless	European Standard NF EN 12678	As given in section 4 of NF EN 12678.	Anonymous (2001)
Melting / freezing point	The substance decomposes before melting.	EC method A.1 (Melting temperature device with metal block)	Oxone® Monopersulfate compound, Batch No.: H-24607 The test substance decomposes before melting and therefore does not possess a melting point under the test conditions. An exothermic peak in the region 140-200 °C has been interpreted as decomposition process. Propose to close the point.	Anonymous 2002a
Boiling point	The test substance does not possess a boiling temperature at normal atmospheric pressure.	EC method A.2 (Differential scanning calorimetry) OECD Test	Oxone® Monopersulfate compound, Batch No.: H-24607 A single exotherm in the region 140-200 °C, which can be	Anonymous 2002a

		Guideline103	attributed to samples decomposition. An endotherm occurred in the range 235 – 250 °C, which corresponds with the melting of the decomposed sample that was observed in the melting point test.	
Relative density	2.35 at 20 °C	EC method A.3 (Pyknometer)	Oxone® Monopersulfate compound, Batch No.: H-24607	Anonymous 2002a
Vapour pressure	< 1.2 x 10^{-4} Pa at 20 ºC (extrapolated) < 1.7 x 10^{-4} Pa at 25 ºC (extrapolated)	EC method A4 (Effusion method – vapour pressure balance)	Oxone® Monopersulfate compound, Batch No.: H-24607 The test was performed between temperatures of 27 °C and 96 °C. As the readings for the first run were taken close to 25°C, the extrapolated results from this run are taken as the upper limit for the vapour pressure of the test substance. Additionally, the vapour pressure at 20 ºC is calculated by extrapolation.	Anonymous 2002a
Henry's law constant	2.04 x 10^{-7} Pa x m³ x mol^{-1}	Calculated	Calculated using the vapour pressure at 20 ºC (<1.21 x 10^{-4} Pa), the molecular mass (614.76 g/mol) and the solubility in water at 20 ºC (364 g/L).	Anonymous 2007e
Surface tension	σ = 72.9 mN/m temperature: 23 °C	EC method A.5 OECD Test Guideline 115	KMPS P-16, Batch No.: H-27841	Anonymous 2007a
Water solubility at 20 °C	364 g/L at 20 °C	EC method A6 (Flask method)	Oxone® Monopersulfate compound, Batch No.: H-24607	Anonymous 2002a
	pH 4: 25-30 % (w/v)	OECD Test Guideline	KMPS P-16, Batch No.: H-27841	Anonymous

	pH 7: 25-30 % (w/v) pH 9: 25-30 % (w/v) temperature: 22 °C 25-30 % (w/v) correspond to 250-300 g/L	105		2007a
Partition coefficient (n-octanol/water) and its pH dependency	log Pow < 0.30 temperature: 20 °C pH: pH dependence is not expected.	EC method A8 (Flask method)	Oxone® Monopersulfate compound, Batch No.: H-24607	Anonymous 2002a
Thermal stability and identity of breakdown products	An exotherm peak in the region 140-200 °C has been interpreted as decomposition process. An endotherm peak in the range 235-250 °C has been interpreted as the melting point (by comparison with the melting point measured by Capillary Melting Point. The thermal events in the DSC were unambiguously assigned. According to the results, the product is not thermally stable. The identity of breakdown products is not known.	DSC screening	KMPS P-16, Batch No.: H-27841	Anonymous 2007a
Reactivity towards container material	Packaging, multi-wall plastic lined paper bag, showed no signs of	OPPTS 830.6317	KMPS P-16, Batch No.: H-27841	Anonymous 2008a

	reactivity with the test substance after 12 months at room temperature.			
	Packaging, multi-wall plastic lined paper bag, showed no signs of reactivity with the test substance after 14 days at 54 °C.	OPPTS 830.6317 OPPTS 830.6313	KMPS P-16, Batch No.: H-27841	Anonymous 2007b
	Many years of practical commercial experience with KMPS show that the packaging materials used are compatible with the active substance. Furthermore reference is made to UN recommendation dangerous goods edition 15, packaging instructions P002, IBC 08.	-	-	-
Dissociation constant	pKa1 = 2.47 pKa2 = 7.06 temperature: 25 °C	OPPTS 830.6313	Oxone®, Batch No.: H-28462 The dissociation constants of the test substance were determined at a temperature of 25°C	Anonymous 2007c
Viscosity	-	-	Not applicable, KMPS is a solid and not a liquid.	-
Solubility in organic solvents, including effect of temperature on	-	-	Due to its oxidising properties, KMPS would react with organic solvents and therefore testing is	-

solubility			technically not feasible.	
Stability in organic solvents used in biocidal products and identity of relevant degradation products	-	-	Due to the reactivity of KMPS with organic solvents, it is not possible to formulate stable biocidal products of KMPS with organic solvents.	-

A.1.3.1. Physical hazards and respective characteristics

Table A.4 Physical hazards and respective characteristics

Hazard class / characteristics	Guideline and Method	Parameter(s)	Results / Waiver	Reference
Explosives	Regulation 440/2008 Method A.14: Test of Mechanical Sensitivity with Respect to Shock	Bursting into flame and/or a report	No positive results were obtained for the test substance in 21 successive drop impact tests conducted from a height of 140 cm.	Anonymous 2007d
	Regulation 440/2008 Method A.14: Test of Mechanical Sensitivity with respect to Friction	Crepitation and/or a report or bursting into flame	No positive results were obtained for the test substance in any of the 6 trials.	Anonymous 2007d
	Regulation 440/2008 Method A.14: Test of Thermal Sensitivity	Fragmentation of the tube into three or more pieces	No explosions were observed for the test substance with 2 mm diameter orifice plates.	Anonymous 2007d
Flammable gases	Not applicable	Not applicable	The study does not need to be conducted because the substance is a solid.	Not applicable
Flammable aerosols	Not applicable	Not applicable	The study does not need to be conducted because the substance	Not applicable

Hazard class / characteristics	Guideline and Method	Parameter(s)	Results / Waiver	Reference
			is a solid.	
Oxidising gases	Not applicable	Not applicable	The study does not need to be conducted because the substance is a solid.	Not applicable
Gases under pressure	Not applicable	Not applicable	The study does not need to be conducted because the substance is a solid.	Not applicable
Flammable liquids	Not applicable	Not applicable	The study does not need to be conducted because the substance is a solid.	Not applicable
Flammable solids	Regulation 440/2008. Method A.10: Flammability (solids)	Burning time and burning rate	Neither ignitability nor combustion propagation by the KMPS was detected.	Anonymous 2007c
Self-reactive substances and mixtures	Not applicable	Not applicable	KMPS does not possess self-reactive properties to be classified in any of the A-H types of the Class 4.	Not applicable
Pyrophoric liquids	Not applicable	Not applicable	The study does not need to be conducted because the substance is a solid.	Not applicable
Pyrophoric solids	Regulation 440/2008. Method A.13: Pyrophoric properties of solids and liquids	Ignition times ≤ 5 min	The pyrophoric properties of the test substance were determined at a temperature of 21 °C. KMPS is not ignitable.	Anonymous 2007c
Self-heating substances and mixtures	EC method A.16	Short-lived exothermic signal at T=127 °C	Oxone®, Batch No.: H-28462, purity of the test substance not	Anonymous 2008b

Hazard class / characteristics	Guideline and Method	Parameter(s)	Results / Waiver	Reference
			explicitly given In the A16 test for self-heating substances, the sample was found to decompose on heating. It was not a self-heating material. KMPS is not a self-heating material.	
Substances and mixtures which in contact with water emit flammable gases	Regulation 440/2008. Method A.12: Flammability (contact with water)	Spontaneous ignition or evolution of flammable gas at a rate greater than 1 L/kg of the substance per hour.	Maximum generation of 6 mL of non-flammable gases per 10 g of sample. KMPS in contact with water does not emit flammable gases.	Anonymous 2007c
Oxidising liquids	Not applicable	Not applicable	The study does not need to be conducted because the substance is a solid.	Not applicable
Oxidising solids	Regulation 440/2008. Method A.17: Oxidising properties (solids)	Maximum burning rate	Incomplete burning of cellulose mixtures.	Anonymous 2003
	UN Test O.1 (Manual of Tests and Criteria 2nd revised version)	Maximum burning rate	No oxidising solid	Anonymous 2002b
Organic peroxides	Not applicable	Not applicable	The study does not need to be conducted because the substance	Not applicable

Hazard class / characteristics	Guideline and Method	Parameter(s)	Results / Waiver	Reference
			does not fall under the definition of organic peroxides according to GHS and the relevant UN Manual of tests and criteria.	
Corrosive to metals	Not applicable	Not applicable	Study is technically not feasible.	Not applicable
Auto-ignition temperature (liquids and gases)	Not applicable	Not applicable	The study does not need to be conducted because the substance is a solid.	Not applicable
Relative self-ignition temperature for solids	Regulation 440/2008. Method A.16: Relative self-ignition temperature for solids	Sample temperature (auto-ignitable if T_{sample}≥400 °C).	Maximum sample temperature during the test (diagram Temperature-time in Appendix 2 of the study report) is T_{sample}=275°C.	Anonymous 2008b
Dust explosion hazard	Not applicable	Not applicable	The study does not need to be conducted because the substance is not a dust.	-
Desensitised explosives	Not applicable	Not applicable	The substance is not an explosive.	Not applicable

A.1.3.2. Assessment of physical hazards according to the CLP criteria

A.1.3.3. Explosives

Table A.9 Summary table of studies on explosive properties

Method	Results	Remarks	Reference
Regulation 440/2008. Method A.14: Test of Mechanical Sensitivity with Respect to Shock	No positive results were obtained for the test substance in 21 successive drop impact tests conducted from a height of 140 cm.	No explosive	Anonymous 2007d
Regulation 440/2008: Method A.14: Test of Mechanical Sensitivity with respect to Friction	No positive results were obtained for the test substance in any of the 6 trials.	No explosive	Anonymous 2007d
Regulation 440/2008: Method A.14: Test of Thermal Sensitivity	No explosions were observed for the test substance with 2 mm diameter orifice plates.	No explosive.	Anonymous 2007d

A.1.3.3.1. Short summary and overall relevance of the provided information on explosive properties

According to section 10.3.3.3 of Manual of Tests and Criteria Seventh Edition 2019, the test from series 2 and 3 are sufficient for the acceptance procedure for classification in Class I of substances not designed to have an explosion effect, but with potentially explosive properties.

By using the method A.14: Test of Mechanical Sensitivity with Respect to Shock no positive results were obtained for the test substance in 21 successive drop impact tests conducted from a height of 140 cm. According to section 13.4.2.4 Test criteria and method of assessing results, the test result for are negative "-" (no explosions occurred at impact energy = 48 J, far above the indicated threshold 2 J).

No positive results were also obtained for the test substance in any of the 6 trials by using method A.14: Test of Mechanical Sensitivity with respect to Friction. According to section 13.4.2.4 Test criteria and method of assessing results, the test results for KPMS must be labelled as »no reaction« which is equivalent to no explosivity.

In addition, no explosions were also observed for the test substance with 2 mm diameter orifice plates by using method A.14; Test of Thermal Sensitivity. According to section 12.5.1.3.4 test results for are labelled as "O" (tube unchanged). No signs of explosivity are detected.
To conclude no positive results were obtained for the test substance KMPS in any of used test methods (see also Table. A.12). As the results from the EU A.14 method are not conclusive, the screening procedure from section 2.1.4.3 of Annex I of CLP Regulation was undertaken, the structure of the KPMS shows that there are no chemical groups associated with explosive substances present.

A.1.3.3.2. Comparison with the CLP criteria

According to sections 2.1.4.2 and 2.1.4.3 of Annex I of CLP Regulation KMPS shall not be classified as explosive considering that are no chemical groups associated with explosive properties in the KMPS molecule as well as negative results of method EU A.14.

A.1.3.3.3. Conclusion on classification and labelling for explosive properties

No classification is proposed for KMPS regarding explosives hazards according to CLP criteria.

A.1.3.4. Flammable gases (including chemically unstable gases)

Not applicable for CLH report.

A.1.3.5. Flammable aerosols and aerosols

Not applicable for CLH report.

A.1.3.6. Oxidising gases

Not applicable for CLH report.

A.1.3.7. Gases under pressure

Not applicable for CLH report.

A.1.3.8. Flammable liquids

Not applicable for CLH report.

A.1.3.9. Flammable solids

Table A.5 Summary table of studies on flammable solids

Method	Results	Remarks	Reference
Regulation 440/2008. Method A.10: Flammability (solids)	Neither ignitability nor combustion propagation by the KMPS was detected.	No flammable solid	Anonymous 2007c

A.1.3.9.1. Short summary and overall relevance of the provided information on flammable solids

Powdery substances are to be considered as highly flammable when the time of burning in any tests carried out according to the test procedure described in Regulation 440/2008, Part A, A.10, 1.6.2 is less than 45 seconds.

Dimensions of powder train (250 mm long by 20 mm wide by 10 mm high) and time application of hot flame (max. 2 min) in accordance with section 33.2.4.3 of Manual of Tests and Criteria were used.

Neither ignitability nor combustion propagation by KMPS was detected.

A.1.3.9.2. Comparison with the CLP criteria

According to part 2, 2.7.2 of Annex I of the CLP Regulation, the substance shall not be classified as readily combustible solids since burning rate is extremely low to be measurable, KMPS did not ignite and propagate combustion along 200 mm of the powder train within 4 min.

A.1.3.9.3. Conclusion on classification and labelling for flammable solids

No classification is proposed for KMPS regarding flammable solids hazards according to CLP criteria.

A.1.3.10. Self-reactive substances

A.1.3.10.1. Short summary and overall relevance of the provided information on self-reactive substances

KMPS does not possess self-reactive properties to be classified in any of the A-H types of the Class 4, Division 4.1 of the UN RTDG Model Regulations based on:

1. Short-time exothermic event independent of temperature: an indistinguishable feature of substances undergoing self-decomposition reactions is the exponential acceleration of the kinetics with temperature. The results of the study shown in Doc. No. 141-0001 "KMPS: Laboratory study of relative self-ignition temperature" show a short exothermic event in the temperature-time plane with an onset <150°C and maximum energy release at <300 °C followed by abrupt relaxation to thermal equilibrium with oven temperature. No evolution of self-accelerating energy release was detected in the temperature ramping during the test. Instead of it, two endothermic signals were registered (probably fusion of part of the triple salt components, rearrangement of the crystalline structure).
2. Thermodynamic limitation of combustion reactions: is a strong oxidizing agent with a reduction potential much higher than oxygen or even hydrogen peroxide (redox potential >1.8 V). Combustion reactions (principal source of systems experiencing thermal runways) are not possible: oxygen does not have sufficient oxidative power compared to KMPS. The nature of the exothermic event in the self-ignitability study is likely to be associated with less energetic reactions such as homolytic cleavages of the O-O bond.

The presence of a single short-lived exothermic signal with no exponential increase with temperature in test A.16 and the thermodynamic limitation of exothermic reactions with oxidizing species such as Oxygen (>) exclude the possibility of self-reactive character in. Therefore, the tests designed for A-H types of Class 4, Division 4.1 of the UN RTDG Model Regulations are not necessary. Furthermore the screening procedure from section 2.8.4.2 of Annex I of CLP Regulation was undertaken and concluded that here are no chemical groups present in the KMPS with explosive or self-reactive properties, given in Tables A6.1 and A6.2 in Appendix 6 of the M4 UN RTDG, Manual of Tests and Criteria.

A.1.3.10.2. Comparison with the CLP criteria

According to section 2.8.4.2 of Annex I of CLP Regulation KMPS shall not be classified as self-reactive substances considering that there are no chemical groups present in the molecule associated with explosive or self-reactive properties.

A.1.3.10.3. Conclusion on classification and labelling for self-reactive substances

No classification is proposed for KMPS regarding self-reactive substances hazards according to CLP criteria.

A.1.3.11. Pyrophoric liquids

Not applicable for CLH report.

A.1.3.12. Pyrophoric solids

Table A.11 Summary table of studies on pyrophoric solids

Method	Results	Remarks	Reference
Regulation 440/2008. Method A.13: Pyrophoric properties of solids and liquids	Ignition times ≤ 5 min	The substance is not ignitable.	Anonymous 2007c

A.1.3.12.1. Short summary and overall relevance of the provided information on pyrophoric solids

A test was performed to determine if a solid ignites within five minutes of coming in contact with air. The recommended test method is given in the Regulation 440/2008 (equivalent to Test N.2 in Manual of Tests and Criteria). If the substance ignites within five minutes when added to an inert carrier and exposed to air, or a liquid substance chars or ignites a filter paper within 5 minutes when added and exposed to air, it is considered to be pyrophoric.

A.1.3.12.2. Comparison with the CLP criteria

According to part 2, 2.10.2. of Annex I of the CLP Regulation, the substance shall not be classified as pyrophoric solids as no ignition was detected within 5 minutes in contact with air.

A.1.3.12.3. Conclusion on classification and labelling for pyrophoric solids

No classification is proposed for KMPS regarding pyrophoric hazards according to CLP criteria.

A.1.3.13. Self-heating substances

Table A.6 Summary table of studies on substances which on self-heating substances

Method	Results	Remarks	Reference
EC method A.16	Short-lived exothermic signal at *T*=127 °C	No self-heating substance	Anonymous 2008b

A.1.3.13.1. Short summary and overall relevance of the provided information on self-heating substances

The absence of self-heating properties of KPMS is supported by the outcome in following test of Regulation 440/2008: Method A.10. Flammability (solids): negative (Anonymous 2007c))
Method A.16. Relative self-ignition temperature for solids: negative (Anonymous 2008b)
Method A.17. Oxidizing solids: negative (Anonymous 2003).

All tests cited above show negative results. As written in section 2.4.3 Division 4.2- Substances liable to spontaneous combustion of the Recommendations on the Transport of Dangerous Goods Model Regulations Vol I (2019), self-heating is a process where gradual reaction of a substance/mixture with oxygen (air) generates heat leading to auto-ignition if the heat production exceeds the rate of heat loss. The negative results of self-ignitability, flammability and oxidizing solids tests are indicative that self-heating phenomena in KMPS cannot lead neither to spontaneous (Method A.16) nor to external driven (e.g ignition sources in Method A.10 and A.17) oxidative reactions that trigger hazardous situations.

Section 2.11.4.2 Screening procedures and waiving of testing of the Guidance on CLP Criteria points out that careful interpretation of the A.16 test results must be taken towards the CLP classification for self-heating properties. Similarity of experimental conditions set up in the test A.16 to those specified in the Grewer Oven Test, mentioned as a screening method for this hazard in same section 2.11.4.2, allows the use of read-across approach for the prediction of self-heating behaviour in KMPS. In both methods, temperature of the oven is raised from ambient temperatures up to 300° - 400°C with slower heating rate in the method A.16 (0.5 °C/min) compared to the Grewer Oven Test (1-2 °C/min as indicated VDI 2263, part 1, 1990, Test methods for the Determination of the Safety Characteristics of Dusts).

The heating rate value set in method A.16 (0.5 °C/min) trigger more drastic scenarios for the manifestation of self-heating than the value set in the Grewer Oven Test (1-2 °C/min). The rate of transformation of a substance undergoing decomposition reactions follows the well-known differential equation:

$$\frac{d\alpha}{dt} = k(T)f(\alpha)$$

Where α represents the conversion factor, is *k(T)* the Arrhenius rate constant and $f(\alpha)$ is the conversion function. Applying the chain rule:

$$\frac{d\alpha}{dT} = \frac{1}{\beta}k(T)f(\alpha)$$

Where $\beta = dT/dt$ is the heating rate. Slower heating rate values increase the degree of decomposition of the substance at a given temperature and consequently the magnitude of exothermic signals in a temperature-time (T-t) diagram.

Results of test method A.16 and extrapolation to self-heating. According to the Frank-Kamenetzky theory, solid substances/mixtures with self-heating properties release energy with kinetics that grow exponentially with temperature (first-order reaction law). This fingerprint signal (represented by the Arrhenius term in the heat balance equation) is absent in the T-t diagram of KMPS tested in a 20 mm cubic container at temperatures up to 400 °C during the method A.16. Only a weak, short-lived exothermic signal at the onset temperature *T* = 127 °C with a maximum sample temperature of 275 °C was detected, probably associated with low energetic reactions such as homolytic cleavages of the O-O bond. On the basis of the molecular structure and thermodynamic principles, exothermic redox reactions leading to thermal runways (accelerated decomposition rate at higher T) have low probability of occurrence as KMPS lacks the electropositive character of oxidable substances (sp^3 hybridization *e.g* C-H in alkanes, atoms with low electron affinity *e.g* Fe in oxides) which correlates with a high standard reduction potential of KMPS relative to oxygen (E°_{KMPS}>1.8 V).

Two endotherm signals, additional to the exothermic event and indicative of melting, were recorded between approximately 175 °C and 250 °C in the T-t diagram of the test method A.16. Residues found below the empty screen sample cube after completion of the test confirmed that, at these high temperatures, sample underwent solid-liquid phase transition.

According to section 2.11.4.3 of the Guidance on CLP Criteria, self-heating substances or mixture must be classified into dangerous Category 1 (if a positive result is obtained in a test using a 25 mm sample cube at 140 °C) or warning Category 2 (if a positive result is obtained in a test using a 100 mm sample cube at 140, 120 or 100 °C). Based on read-across approach between the measured results in method A.16 (no self-ignitability interpreted in terms of thermodynamic suppression of redox reactions by high E°_{KMPS}) and the expected outcome in Grewer Oven Test, together with the absence of other hazards triggered by self-heating properties determine unequivocally that KMPS should not be assigned in any Category of the Division 4.2.

A.1.3.13.2. Comparison with the CLP criteria

According to part 2, 2.11.2 of Annex I of the CLP Regulation, the substance is not classified as self-heating substances since a positive result was not obtained in a test with more extreme conditions than those indicated in the test UN N.4 (25 mm sample cube at 140 °C or using a 100 mm sample cube at 140 °C).

A.1.3.13.3. Conclusion on classification and labelling for self-heating substances

No classification is proposed for KMPS regarding self-heating hazards according to CLP criteria.

A.1.3.14. Substances which in contact with water emit flammable gases

Table A.13 Summary table of studies on substances which in contact with water emit flammable gases

Method	Results	Remarks	Reference
Regulation 440/2008. Method A.12: Flammability (contact with water)	Maximum generation of 6 mL of non-flammable gases per 10 g of sample.	The substance in contact with water does not emit flammable gases	Anonymous 2007c

A.1.3.14.1. Short summary and overall relevance of the provided information on substances which in contact with water emit flammable gases

According to section 2.12.4.1 of CLP Regulation, the classification procedure for this class need not be applied as the chemical structure of the KMPS does not contain metals or metalloids. In addition, experience in handling and use shows that the KMPS does not react with water as well KMPS is known to be soluble in water to form a stable mixture.

Despite of the fact that all three conditions are fully met, the step 4 of the test method A.12 was performed as it is known that the substance does not react violently with water. The rate of evolution of gas was measured over a period of seven hours, at one-hour intervals. Based on the results of the test is possible to conclude that the substance KMPS is not a substance which in contact with water emit flammable gases.

A.1.3.14.2. Comparison with the CLP criteria

According to section 2.12.4.1 of Annex I of CLP Regulation, KMPS shall not be classified as self-heating substance as it does not contain metals or metalloids, does not react with water and it is soluble in water in stable mixture.

A.1.3.14.3. Conclusion on classification and labelling for substances which in contact with water emit flammable gases

No classification is proposed for KMPS according to the CLP criteria for substances which in contact with water emit flammable gases.

A.1.3.15. Oxidising liquids

Not applicable for CLH report.

A.1.3.16. Oxidising solids

Table A.14 Summary table of studies on oxidising solids

Method	Results	Remarks	Reference
Regulation 440/2008. Method A.17: Oxidising properties (solids)	Incomplete burning of cellulose mixtures.	No oxidising solid	Anonymous 2003
UN Test O.1 (Manual of Tests and Criteria 2nd revised version)	Does not ignite and burn. Mean burning time greater than that of a 3:7 mixture (by mass) of potassium bromate and cellulose.	No oxidising solid	Anonymous (2002b)

A.1.3.16.1. Short summary and overall relevance of the provided information on oxidising solids

Method A.17
Experimental conditions: In agreement with section 1.3 of the method A.17, barium nitrate (analytical grade) is used as reference substance for the test and the preliminary test. In agreement with section 1.6.2.1 of the method A.17, the ratio oxidizer/ cellulose was 2:1.

As the sample cone failed to burn to completion, cones consisting of KMPS (1part) and cellulose (1 and 2 parts) were prepared and tested. As neither mixture of 2:1, 1:1 or 1:2 test substance/cellulose burned to completion, KMPS is considered to be non-oxidising. By comparison, the reference mixture burned vigorously to completion in 30 seconds. No further testing was therefore necessary.

Un Test O.1
This test method is designed to measure the potential for a solid substance to increase the burning rate or burning intensity of a combustible substance when the two are thoroughly mixed. Tests are conducted on the substance to be evaluated mixed with dry cellulose in mixing ratios of 1:1 and 4:1, by mass, of sample to cellulose. However, the results are assessed on the basis of:

- The comparison of the mean burning time with those of the reference mixtures; and
- Whether the mixture of substance and cellulose ignites and burns.

Experimental conditions: In agreement with section 34.4.1.2 of Manual of Tests and Criteria (2019), potassium bromate as reference source was used and the ignition source (length, diameter, electrical resistance, electrical power) selected.

The approximate burning time was initially determined for one mixture from each of the ratios potassium bromate to cellulose (3:7, 2:3 and 3:2).)

The mean burning time for the five samples of the 3:7 w/w ratio of reference substance to cellulose was 100 seconds.

Since the test substance samples (in a mixture ratio 4:1 and 1:1 with cellulose) did not burn to completion and therefore exceeded the burning rate 3:7 ratio of the reference substance, the test substance should not be classified in Division 5.1.

A.1.3.16.2. Comparison with the CLP criteria

According to part 2, 2.14.2 of Annex I of the CLP Regulation, the substance is not classified as burning times of its mixture with cellulose in a ratio 3:7 are lower than the burning times of reference substances with cellulose. Incomplete burning of cellulose/active substance mixtures

was recorded.

A.1.3.16.3. Conclusion on classification and labelling for oxidising solids

No classification is proposed for KMPS regarding oxidising solids hazards according to CLP criteria.

A.1.3.17. Organic peroxides

A.1.3.17.1. Short summary and overall relevance of the provided information on organic peroxides

The study does not need to be conducted because the substance does not fall under the definition of organic peroxides according to CLP Regulation and the relevant UN Manual of tests and criteria. In accordance with Annex I section 2.15.1 of CLP Regulation only organic peroxides have to be tested according to the UN-MTC, Part II test series A-H. Based on the structure it can be concluded that the substance is not an organic peroxide. Thus, no tests were conducted.

A.1.3.17.2. Comparison with the CLP criteria

Not applicable as KPMS does not fall under the definition of organic peroxides according to part 2, 2.15.1 of Annex I of CLP Regulation

A.1.3.17.3. Conclusion on classification and labelling for organic peroxides

KMPS is not classified as organic peroxides.

A.1.3.18. Corrosive to metals

Not applicable for CLH report. According to section 2.16.4.1of CLP, "only substances and mixtures for which the application of the UN Test C.1 (described in part III, Section 37.4.1.1 of the UN-MTC)” is relevant and needs to be considered. Only solids having a melting point lower than 55 °C must be tested.

A screening of the temperature for solid-liquid phase transition of the three components in the triple salt was performed. All components have

melting point above 55 °C.

A.1.3.19. Desensitised explosives

Not applicable for CLH report as KMPS is not explosive.

A.1.4. Analytical methods for detection and identification

Not applicable for the CLH report.

A.2. Effects against target organisms

Function and field of use envisaged

The active substance KMPS shows a broad spectrum of antimicrobial activity and can function as a bactericide, fungicide and virucide. The uses assessed in the dossier are from the Main Group 1: Disinfectants, for the Product Types 2, 3, 4 and 5 (see table below).

KMPS is used by professional users to control pathogenic microorganisms causing infectious diseases of man and animals and to avoid contamination and consequently spoiling of food or feed. KMPS can be used by non-professional users (general public) for the disinfection of swimming pools only.

MG/PT	Field of use envisaged	Likely concentration at which KMPS (triple salt) will be used
MG01/PT2	Disinfection of swimming pools - professional and non-professional (general public) use	Shock-dosing: 500 mg/L pool water Maintaining dose: 130 mg/L pool water
	Dipping of equipment - professional use	5 g/L
	Surface disinfection of industrial areas by wiping with mop - professional use	5 g/L
	Surface disinfection of industrial areas by manual spraying (low pressure) - professional use	5 g/L
MG01/PT3	Terminal disinfection of animal houses using a mechanical sprayer (low pressure) - professional use	8 g/L
	Foot dips - professional use	8 g/L
MG01/PT4	Surface disinfection of food and feeding areas by wiping with mop - professional use	5 g/L
	Surface disinfection of food and feeding areas by manual spraying (low pressure) - professional use	5 g/L
MG01/PT5	Animal drinking water: continuous water sanitation by dosing the header tank or application via a dosing system - professional use	0.8 g/L

A.2.1. Intended uses

Not applicable for the CLH report.

A.2.2. Summary on efficacy

A.2.2.1. Efficacy

Not applicable for the CLH report.

A.2.2.2. Mode of action

KMPS releases reactive oxygen, which oxidises macromolecules of the cell wall, membranes and virus capsids in unspecific manner leading to the cell wall disruption, loss of membrane integrity and disintegration of virus capsids. In addition, after penetration into cells or viruses, intracellular molecules such as amino acids, polypeptides, RNA and DNA are also oxidised leading to the disruption of protein synthesis and cell death.

A.3. Assessment of effects on Human Health

General considerations to take into account in the assessment of effects on human health:

- KMPS was tested in toxicity studies with its impurities and anti-caking agent. KMPS trade names are reported in study summary tables in the same way that they were reported in study reports: Oxone® Monopersulphate Compound; Caroat® or CAROAT® Monopersulphate Compound; Impact®.
- The batches used in toxicity studies had a trihydrogen pentapotassium di(peroxomonosulfate) di(sulfate) ($K_5(HSO_5)_2(HSO_4)(SO_4)$) content of minimum of ≥ 89%. In some original study reports instead of purity of the active substance a concentration of the active component of the triple salt ($KHSO_5$ or active oxygen) or concentrations of all three components of the triple salt are reported. Purity is reported in study summary tables only when the data is available.

A.3.1. Toxicokinetics

No toxicokinetic and metabolism study of KMPS is available or has been performed. It should be noted that kinetic studies with the monopersulphate ion are technically not feasible due to the high instability of the compound.
A respective study is waived in accordance with Chapter 1.4.3 of the TNsG on Data Requirements, which states that a study can be waived if it is not scientifically necessary due to the intrinsic properties of the chemical or if other existing data can be used instead of the required data.

A.3.1.1. Short summary and overall relevance of the provided toxicokinetic information

Intrinsic properties of KMPS

The mode of action of KMPS is based on its oxidative reactivity. KMPS reacts rapidly with available organic material at the site of first contact leading to local corrosion/irritation. Only the breakdown products K^+ and SO_4^{2-} ions will remain to become systemically available and are thus the only relevant species for toxicokinetic and metabolic considerations. Moreover, since the oxidative reactivity of KMPS is solely chemically driven, the mode of action of KMPS is considered independent of the target species and target organs.

Existing data on breakdown products

The breakdown products of KMPS, i.e. K^+ and SO_4^{2-}, ions are chemically and biologically not further degradable because they constitute simple basic structures of inorganic nature. Furthermore, both ions are physiological essential elements of all living organisms. Detailed information on absorption, distribution and excretion of potassium ions (Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to the tolerable upper intake levels of Potassium; FAO/WHO expert consultation on Diet, Nutrition and Prevention of Chronic diseases (see Doc. No. 592-003) as well as sulphate ions (Anonymous, 1983a, J. Toxicol.-Clin.Toxicol. 1983, 20:107-114, see Doc. No. 592-002) are available, which are briefly summarized below.

Potassium is a normal constituent of the human body and of human food and it occurs widely in the environment, including all natural waters. A background document for development of WHO Guidelines for Drinking-water Quality states that currently, there is no evidence that potassium levels in municipally treated drinking-water, even water treated with potassium

permanganate or potassium chloride, are likely to pose any risk for health of consumers. WHO document Potassium in drinking water maintains that it is not considered necessary to establish a health-based guideline value for potassium in drinking-water, stating the following reason for not establishing a guideline value: "Occurs in drinking-water at concentrations well below those of health concern." (Table 8.7 Naturally occurring chemicals for which guideline values have not been established; WHO, 2011). Notably, WHO recommends limiting the consumption of drinking-water potassium-based water treatment (principally potassium chloride for regeneration of ion exchange water softeners), affecting only individuals in high-risk groups (WHO, 2011). The latest dietary recommendations for healthy adults (age 16 and above) by WHO (2012) is to increase potassium intake from food for reduction of blood pressure and risk of cardiovascular disease, stroke and coronary heart disease in adults to at least 90 mmol/day (3510 mg/day). WHO (2012) also suggests an increase in potassium intake from food to control blood pressure in children (age 2-16); the recommended 90 mmol/day should be adjusted downward, based on the energy requirements of children relative to those of adults. The later is set as conditional because only a few studies in children have considered the effects of increased potassium on possible adverse affect.The average daily intake of potassium is 2.7-4 g/day (EFSA Scientific Opinion on the use of potassium sulphate and sodium sulphate as sources of respectively potassium and sodium added for nutritional purposes to food supplements,, The EFSA Journal 2010; 8(12):1940). According to the Opinion on the tolerable upper intake levels of potassium, the available data are insufficient to establish a tolerable upper intake level (UL). Following a request from the European Commission, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) derived dietary reference values (DRVs) for potassium (Scientific opinion on dietary reference values for potassium, Anonymous, 2016). Available data cannot be used to determine the average requirement of potassium but can be used as a basis for deriving an adequate intake (AI). A potassium intake of 3,500 mg/day is considered adequate for the adult population and an AI of 3,500 mg/day for adult men and women is proposed. For infants and children, the AIs are extrapolated from the AI for adults by isometric scaling and including a growth factor. An AI of 750 mg (19 mmol)/day is set for infants aged 7–11 months. For children, AIs from 800 mg (20 mmol)/day (1–3 years old) to 3,500 mg/day (15–17 years old) are set. Considering that the daily accretion rate of potassium in fetal and maternal tissues can be met by the adaptive changes which maintain potassium homeostasis during pregnancy, the AI set for adults applies to pregnant women. For lactating women, the amount of potassium needed to compensate for the losses of potassium through breast milk is estimated and an AI of 4,000 mg (102 mmol)/day is proposed. Long-term intake of potassium as potassium chloride (~ 3 g/day) in addition to normal intake via food has been shown to have no adverse effects. Although case reports indicate that very large doses of potassium supplements can cause heart abnormalities and death, the National Academies of Sciences, Engineering, and Medicine (NASEM) committee also concluded that these reports do not provide sufficient evidence to set an UL (https://ods.od.nih.gov/factsheets/Potassium-HealthProfessional/#change, updated June 2, 2022).

Following oral intake, potassium ions are largely absorbed in the gastrointestinal tract (85-90%). High potassium ion intake can be tolerated by the human body, as excess potassium ions are rapidly excreted in the urine or taken up into cells. Extracellular potassium constitutes around 2 % of the potassium in the body, and is important especially for regulation of membrane potential. Potassium ion concentrations in plasma are tightly regulated within a range of 3.5 to 5 mmol/L (Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on the tolerable upper intake levels of Potassium, Doc. No. 592-003).

The kidneys represent the major excretory route for potassium ions. It has been shown that potassium ion balance in the body can be maintained for intakes up to 390 mg potassium/kg

bw/day as the kidney can efficiently adapt to high potassium intake (according to the Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on the tolerable upper intake levels of Potassium, Doc. No. 592-003).

In healthy people with normal kidney function, high dietary potassium intakes do not pose a health risk because the kidneys eliminate excess amounts in the urine. A delicate balance of potassium in the body involves a fine line of risk and benefit of potassium intake in different populations. Current guidelines recommend dietary potassium intake in the range of 90 to 120 mmol/day, well above the usual intake in worldwide populations. In some patients, however, excess dietary potassium intake results in hyperkalemia. Patients at risk include older patients and those with chronic kidney disease, congestive heart failure, or diabetes mellitus, especially with concomitant use of medications that inhibit the renin-angiotensin-aldosterone system inhibitors (RAAS) (Anonymous, 2018a). For patients with conservative renal failure, it is recommended that the serum potassium level should be regulated in the range of 4.0–5.4 mEq/L. However, since renal potassium excretion decreases as renal function declines, potassium restriction starts to become necessary after later stages of chronic renal disease CKD (Anonymous, 2021a). The 2004 Kidney Disease Outcomes Quality initiatives guidelines recommended limiting potassium to approximately 51-102 mEq/day (2-4 g/day), while the more recent KDIGO 2012 recommended that individuals with CKD should receive expert dietary advice on potassium intake (reviewed in Anonymous, 2023). Anonymous (2020d) concluded that further research is needed before dietary potassium restriction guidelines are made to prevent hyperkalemia in patients with advanced chronic kidney disease, as this generally varies according to the patient's age and comorbid conditions.

The sulphate ion is not considered to be toxic per se as it constitutes a physiologically essential mineral. Sulphate is produced by degradation and metabolism of sulphur organic and inorganic compounds present in food and drinking water. Gastrointestinal absorption of sulphate in humans can occur in the stomach, small intestine and colon. Absorption is a sodium-dependent active process. When soluble sulphate salts (e.g. sodium, potassium and ammonium sulphate) are consumed, more than 80% of oral sulphate doses are absorbed, as shown by isotopic tracer studies. After absorption, inorganic sulphate is freely distributed in blood and does not accumulate in tissues. The normal serum level of sulphate found in humans is 29 mg/L. Sulphates are usually eliminated by renal excretion in free unbound form or as conjugates of various chemicals (Anonymous, 2019b). In humans, 30.2 ± 17.2 % (mean ± SD) of the dose is excreted in the urine in the first 24 h after oral administration; for reference see Anonymous, 1983a. Sulphate that is not absorbed in the upper gastrointestinal tract passes to the large intestine and colon, where it is either excreted in the faeces, reabsorbed or reduced by anaerobic bacteria to metabolites, such as hydrogen sulphide (Anonymous, 2019b). No upper intake level for sulphate exists, but in 2008, the EFSA Panel on Food Additives and Nutrient Sources added to Food concluded, that a daily intake of sulphate ion up to 100 mg sulphate ion/kg bw/day (6 g sulphate ion) does not give rise to concern (Anonymous, The EFSA Journal, 2008, 814, 1-9).

Taken together, both breakdown products (i.e. potassium ions and sulphate ions) constitute physiologically essential metabolites in the human body which are efficiently excreted via the urine after oral uptake.

Conclusion

In view of the chemical behaviour of KMPS, i.e. oxidation at the site of first contact leading to local corrosion/irritation, and taking into account the knowledge on the absorption, distribution and excretion of potassium and sulphate ions, the performance of a toxicokinetic and metabolism study with KMPS is scientifically unjustified.

A.3.2. Acute toxicity / STOT SE

A.3.2.1. Acute oral toxicity

Table A.7 Summary table of animal studies on acute oral toxicity

Summary table of animal studies on acute oral toxicity						
Method, Guideline, GLP status, Reliability, Key/supportive study	Species, Strain, Sex, No/group	Test substance (including purity) Vehicle, Dose levels, Type of administration (gavage, in diet, other)	Signs of toxicity (nature, onset, duration, severity, reversibility, include concentrations)	Value LD50	Remarks (e.g. major deviations)	Reference
Acute oral toxicity- Acute toxic class method OECD 423 GLP: Yes Reliability: 1 Key study	Rat Sprague-Dawley (CD) M/F 3M + 3F/ 200 mg/kg bw 3 F/2000 mg/kg bw	Oxone® Monopersulphate Compound Vehicle: Distilled water 200 mg/kg bw/day (concentration of 20 mg/mL) 2000 mg/kg bw/day (concentration of 200 mg/mL) Gavage	Mortality: 3/3 F at 2000 mg/kg bw Clinical signs: - both doses: piloerection 1 h after treatment - 2000 mg/kg bw: hunched posture, lethargy, abnormal gait, reduced body temperature, body tremors, shallow respiration and pallor of skin with dull eyes in two females and partially closed eyelids and red staining around the uro/genital area in one female. Necropsy: - In deceased animals, congestion was noted in the subcutaneous tissue, brain, heart, lungs and spleen with pallor of the kidneys and pale patches on the liver and red fluid contents of the urinary bladder. Congestion and fluid contents were noted in the stomach and along the alimentary tract and in the urinary tract with enlarged, swollen or thickened tissues and dark and	LD_{50} = 500 mg/kg bw KMPS	None	Anonymous 2001a

			pale discolouration of the lining also in the stomach of all animals. Body weight: bw loss in 2/3 F treated with 2000 mg/kg bw			

No human data on acute oral toxicity of KMPS is available.

A.3.2.1.1. Short summary and overall relevance of the provided information on acute oral toxicity

Acute oral toxicity was studied in rats. Clinical signs observed in treated animals included hunched posture, lethargy, abnormal gait, reduced body temperature, tremors, shallow respiration, pale skin and dull eyes (in two rats), partially closed eyelids and redness around urogenital area (in one rat). The observed clinical signs are, along with piloerection (1 h after treatment at both doses), attributed to severe pain and inflammatory response at the point of contact (non-glandular stomach after dosing via gavage). Necropsies in deceased animals revealed congestion in subcutaneous tissue, brain, heart, lungs and spleen and pale liver and kidneys, red fluid in urinary bladder (in one or more animals). Congestion and fluid retention was found in gastrointestinal and urogenital tract. The wall of the two organ systems was thick, with dark or pale discolorations of the epithelia. The effects seen are resulting from primary local effects. No signs of toxicity (except piloerection) were observed in animals who received 200 mg of Oxone® Monopersulphate Compound (KMPS)/kg bw. Recovery of survived animals, judged by external appearance and behaviour, was completed by the day 3. No abnormalities were revealed for surviving animals.

Acute oral LD_{50} was estimated to be 500 mg/kg bw.

A.3.2.1.2. Comparison with the CLP criteria

Since no deaths occurred at 200 mg/kg bw and all animals died after the administration of 2000 mg/kg bw, the LD_{50} (oral) was determined to be 500 mg/kg bw according to OECD 423 Annex 2c. The reported oral rat LD_{50} of 500 mg/kg bw falls within the range for acute oral toxicity Category 4 of 300-2000 mg/kg bw. This warrants classification as Acute Tox. 4.

A.3.2.1.3. Conclusion on classification and labelling for acute oral toxicity

According to Annex I of CLP Regulation KMPS should be assigned the classification and labelling as Acute Tox. 4, H302 “Harmful if swallowed”.

It is proposed to assign an ATE of 500 mg/kg bw for acute oral toxicity.

A.3.2.2. Acute dermal toxicity

Table A.16 Summary table of animal studies on acute dermal toxicity

Summary table of animal studies on acute dermal toxicity						
Method, Guideline, GLP status, Reliability, Key/supportive study	Species, Strain, Sex, No/group	Test substance (including purity), Vehicle, Dose levels, Surface area,	Signs of toxicity (nature, onset, duration, severity, reversibility, include concentrations)	Value LD50	Remarks (e.g. major deviations)	Reference
Acute dermal toxicity OECD 402 GLP: Yes Reliability: 1 Key study	Rat Sprague-Dawley (CD) M/F 5/sex/dose	Oxone® Monopersulphate Compound Vehicle: distilled water 2000 mg/kg bw/day (concentration of 1667 mg/mL) covered area approx. 10% of the total body surface occlusive dressing 24 h exposure	Mortality: none Clinical signs: None. Dermal effects: Severe dermal irritation was seen in 3 animals following removal of the dressings persisting until study termination. Slight to well defined dermal irritation was observed in 6 animals following removal of dressings. These reactions had resolved completely by day 3 in 1 animal, day 5 in 1 animal and day 8 in 4 animals. In addition, localised necrosis, localised spots and/or scabbing, spots and/or scabbing over the majority of the treatment site, blanching over the majority of the treatment site, cracking of the skin at the edge of the blanched area and wet ulceration on the dose site were noted in a number of animals during the study. Necropsy: Macroscopic examination revealed necrotic area on the dose site of three animals and scabbing on the dose site of two animals. Body weight: Loss of body weight was recorded for 1 female and low body weight gains were recorded for 2 females on day 8.	LD_{50} > 2000 mg/kg bw	None	Anonymous 2001b

No human data on acute dermal toxicity of KMPS is available.

A.3.2.2.1. Short summary and overall relevance of the provided information on acute dermal toxicity

Acute dermal toxicity was studied in rats. There were no deaths and no systemic clinical signs observed. The treated animals showed significant dermal irritation, that persisted in three animals until study was terminated; slight to well defined dermal irritation was seen in 6 animals, but it resolved by day 3, 5, and 8, respectively. The skin damage included: localized necrosis, localized spots and/or scabbing, spots and/or scabbing over the majority of treatment site, blanching over the majority of treatment site, cracking of the skin of the blanched area and wet ulcerations. Loss of weight was observed in 1 female animal and low body weight gain in another two female rats.

Acute dermal LD50 was calculated to > 2000 mg/kg bw of Oxone® Monopersulphate Compound (KMPS). The study indicated that Oxone® Monopersulphate Compound causes local irritation of the skin.

A.3.2.2.2. Comparison with the CLP criteria

No mortalities were observed in rats dermally exposed to 2000 mg/kg bw KMPS. The reported dermal rat LD_{50} of > 2000 mg/kg bw is above the range for acute dermal toxicity Category 4 of 1000-2000 mg/kg bw, thus classification is not warranted.

A.3.2.2.3. Conclusion on classification and labelling for acute dermal toxicity

According to Annex I of CLP Regulation, KMPS does not warrant classification for acute toxicity regarding the dermal route of exposure. It is proposed to assign an ATE of > 2000 mg/kg bw for acute dermal toxicity.

A.3.2.3. Acute inhalation toxicity

Table A.17 Summary table of animal studies on acute inhalation toxicity

Summary table of animal studies on acute inhalation toxicity						
Method, Guideline, GLP status, Reliability, Key/supportive study	Species, Strain, Sex, No/group	Test substance (including purity), form (gas, vapour, dust, mist) and particle size (MMAD) Actual and nominal concentration, Type of administration (nose only / whole body/ head only)	Signs of toxicity (nature, onset, duration, severity, reversibility, include concentrations)	Value LC50	Remarks (e.g. major deviations)	Reference

Acute Inhalation Toxicity OECD 403 GLP was not compulsory at the time of study conduct Reliability: 1 Key study	Rat Crl:CD M 10/dose	Oxone® Monopersulphate Compound dust aerosol MMAD: 1.7 to 4.0 µm Actual concentration: 1.5, 3.9, 4.2 and 5.0 mg/L (higher atmospheric concentrations could not be generated under the conditions used in the study) Head-only exposure (4 h) 14 day post-observation period	Mortality: No animal died during the study duration. Clinical signs: During exposure: Reduced response to sound, ocular and nasal discharge increasing with concentration were observed. Rats exposed at 1.5 mg/L exhibited moderate lung noise immediately post exposure. Post-exposure: Rats exposed to 3.9, 4.2 and 5.0 mg/L exhibited alopecia around the eyes, cloudy eyes (some eventually turning black in colour), and severe discharge from eyes and nose. At 1.5 mg/L, only 1 cloudy eye (that turned black in colour) was noted. One rat exposed at 3.9 mg/L became hypersensitive to touch. Necropsy: No pathological findings reported. Body weight: Slight to severe weight loss was noted lasting 24-96 hours post-exposure. This was followed by a normal rate of weight gain.	LC_{50} > 5.0 mg/L	Only male rats were used in the investigation. In a comparable investigation performed with the KMPS containing product Virkon S in male and female rats of the same strain and source, male rats were demonstrated to be slightly more sensitive towards Virkon S dust than female rats (please refer to Document IIIA, Section A6.1.3/02 – read across study). Thus, the inhalation study reliably reflects and does not under-estimate the acute inhalation toxicity potential of Oxone® dust.	Anonymous 1980
Acute Inhalation Toxicity OECD 403 GLP: Yes Reliability: 1 Supportive study	Rat Crl:CD®BR M and F 5/sex/group	Virkon S (dust aerosol), containing 49.8 % Oxone monopersulfate compound MMAD: 3.1 - 3.8 µm Actual concentrations: 2.5, 3.1, 4.8 mg/L	Mortality: No deaths in the 2.5 mg/L group, 3/5 of male rats and 1/5 of female rats died in the 3.1 mg/L group, all male rats and 3/5 of the females of the 4.8 mg/L group died. Clinical signs: Clinical signs immediately following exposure: wet underbody, gasping, nasal and ocular discharges, hunched posture, lethargy, weakness, diarrhea,	LC_{50} = 3.7 mg/L	Supportive study	Anonymous 1995

		Nose-only exposure (4h) 14 day post-observation period	enophthalmus, and irregular respiration. Clinical signs during recovery period: nasal and ocular discharges, hunched posture, irregular respiration, lethargy, lung noise, weakness, enophthalmus, ruffled fur, gasping and diarrhea (corneal opacity of one female of the 4.8 mg/L group). Necropsy: No pathological findings reported. Body weight: All surviving rats experienced severe body weight losses up to five days following exposure. All males and most females had an overall weight gain by the end of the 14day recovery period.			

No human data on acute inhalation toxicity of KMPS is available.

A.3.2.3.1. Short summary and overall relevance of the provided information on acute inhalation toxicity

In an acute inhalation study performed with Oxone® Monopersulphate Compound (KMPS), male rats were exposed for 4 hours to a dust aerosol consisting of particles in the respirable range (MMADs < 4 µm). The results obtained showed that KMPS did not reveal an inhalation hazard up to and including the highest exposure level of 5 mg/L tested. LD_{50} was estimated to be > 5.0 mg/L. Thus, no classification and labelling with respect to acute inhalation toxicity is required for KMPS.

The LC50 value was calculated based on the study that used Oxone® Monopersulphate Compound (KMPS). Because only male rats were used in this study, the second study is presented as a supporting study to show that female rats are not more sensitive to KMPS. In the second study, animals were exposed to product Virkon S that contains 49.8% Oxone monopersulfate compound (KMPS) and other co-formulants (that are expected to cause more severe effects in animals than KMPS alone). In a comparable investigation performed with the KMPS containing product Virkon S in male and female rats of the same strain and source, male rats were demonstrated to be slightly more sensitive towards Virkon S dust than female rats. Thus, the inhalation study with Oxone® in male rats reliably reflects and does not underestimate the acute inhalation toxicity potential of Oxone® dust.

Both studies were performed according to valid guideline (OECD 403) and are considered reliable.

A.3.2.3.2. Comparison with the CLP criteria

No mortalities were reported in rats exposed head-only to 5.0 mg/L KMPS for 4 hours. The reported inhalation rat LD_{50} of > 5.0 mg/L is above the range for acute inhalation toxicity Category 4 of 1.0-5.0 mg/L, thus classification is not warranted.

Conclusion on classification and labelling for acute inhalation toxicity

According to Annex I of CLP Regulation, KMPS does not warrant classification for acute toxicity regarding the inhalation route of exposure.

A.3.2.4. Specific target organ toxicity – single exposure Category 1 and 2 (STOT SE 1 and 2)

From the acute toxicity studies following oral, inhalation or dermal exposure there was no clear evidence of non-lethal systemic effects on a specific target organ or tissues.

Symptoms that may be interpreted as neurotoxic effects were observed in several studies:

- A reduced response to sound was observed in acute inhalation toxicity study. This clinical sign is considered to be a behavioural sign attributed to severe pain and inflammatory response at the point of contact (the nasal airway and its contiguous - ears, sinuses, eyes).
- The clinical signs such as hunched posture, lethargy, abnormal gait, body tremors, staining of the urogenital area in the acute oral toxicity study; flat and hunched posture, underactivity, abnormal gait, partially closed eyes, piloerection/ungroomed in the *in vivo* micornucleus test; reduced spontaneous activity, prone position, ataxia in the *in vivo* Comet assay (please refer to Section A.3.8.2 for a summary of *in vivo* genotoxicity studies), are behavioural signs attributed to severe pain at the point of contact (nonglandular stomach, since the animals were dosed via gavage).

A.3.2.4.1. Short summary and overall relevance of the provided information on STOT SE 1 and 2

No effect relevant for classification of KMPS as STOT SE 1 or 2 were observed in any toxicological study.

A.3.2.4.2. Comparison with the CLP criteria

From the acute toxicity studies following oral, inhalation or dermal exposure and *in vivo* genotoxicity studies there was no clear

evidence of (non-lethal) effects on a specific target organ or tissues. Classifications regarding CLP Regulation for acute toxicity and corrosivity cover the toxicological effects of KMPS after single exposure. An additional classification as STOT SE 1 or 2 is therefore not appropriate.

A4.2.4.3 Conclusion on classification and labelling for STOT SE 1 and 2

No classification and labelling with respect to STOT SE 1 and 2 is required for KMPS according to CLP Regulation.

A.3.2.5. Specific target organ toxicity – single exposure Category 3 (STOT SE 3)

No animal study or human data investigating the irritation potential of KMPS to the respiratory tract or narcotic effects is available.

A.3.2.5.1. Short summary and overall relevance of the provided information on STOT SE 3

Based on the chemical mode of action of KMPS and on the results obtained in a skin corrosion/irritation study (please refer to chapter A.3.3), KMPS can be expected to have respiratory tract irritation or corrosion potential.

In an acute inhalation study performed with KMPS (please refer to chapter A.3.2.3.), signs of respiratory tract irritation were perceived in treated rats. During exposure, ocular and nasal discharge was observed in all animals, which increased with concentration of KMPS. During the 14-day post-observation period, discharge from eyes and nose was noted in rats exposed at the 3 highest concentrations. These findings are indicative of a respiratory tract irritation potential of KMPS. Corrosive effect of KMPS on the respiratory system cannot be excluded (please refer to chapter A.3.3).

Regarding narcotic effects, the effects such as lethargy and ataxia, observed in acute oral toxicity study and *in vivo* genotoxicity studies (please see Section A.3.2.4. Specific target organ toxicity – single exposure Category 1 and 2) are considered to be signs of general pain.

A.3.2.5.2. Comparison with the CLP criteria

KMPS is considered to be corrosive to the respiratory tract (please refer to Section A.3.3.2). As labelling EUH071 ‘Corrosive to the respiratory tract’ is applicable, a classification of STOT SE Cat 3 (H335) is not necessary.

The criteria for classifying KMPS as Category 3 for narcotic effects are not fulfilled.

A.3.2.5.3. Conclusion on classification and labelling for STOT SE 3

No classification and labelling with respect to STOT SE 3 is required for KMPS according to Annex I of CLP Regulation.

A.3.3. Skin corrosion and irritation

No *in vitro* study on skin corrosion and irritation was performed for KMPS.

Table A.18 Summary table of animal studies on skin corrosion/irritation

Summary table of animal studies on skin corrosion/irritation					
Method, Duration of study, Guideline, GLP status, Reliability, Key/supportive study	Species, Strain, Sex, No/group	Test substance (including purity), Vehicle, Dose levels Duration of exposure	Results Average score for erythema/eschar and oedema (24, 48, 72 h) per animal, observations and time point of onset, reversibility, other adverse local/systemic effects, histopathological findings	Remarks (e.g. major deviations)	Reference

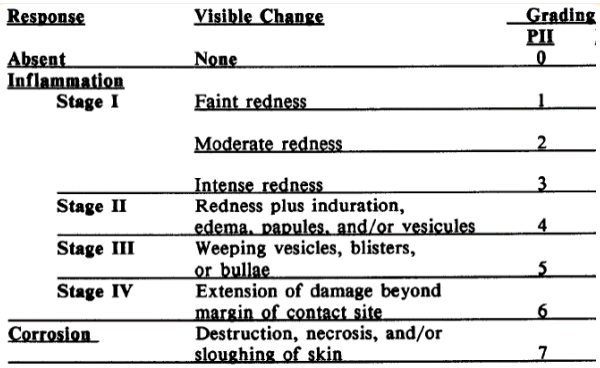
Acute dermal irritation/corrosion Comparable to OECD 404 GLP: No Reliability: 1 Key study	Albino rabbit White Russian F 3/group	Caroat® vehicle: not applicable, test material was applied undiluted 0.5 g test substance were moistened with 0.15 mL demineralised water occlusive dressing exposure duration: 4 h post-exposure period: 14 days examination time points 1 h, 24 h, 48 h, 72 h after removal of the test patches	Skin irritation index per animal (average of skin irritation scores at 24, 48, 72 h after exposure): -Erythema: 4.00, 4.00, 4.00 -Oedema: 0.67, 0.33, 0.67 Erythema was not reversible within 14 day of study duration. Oedema resolved completely by day 2. Coloration: The treated skin was white. Corrosion: Irreversible skin destruction of the treated skin was observed. Clinical signs: No systemic toxicity was stated and no mortalities occurred.	Deviations: - skin was not flushed with water after exposure; - no further information on the test substance (stability; purity) Study results indicate that KMPS should be classified as Skin Corrosive, due to skin discolouration and persisting erythema around the treated area for 14 days. However, because no washing of treated site was performed, duration of exposure could have been longer than 4 hrs and thereafter the proposed classification could be over conservative. According to criteria for classification in Regulation 1272/2008 the classification Skin Corr. 1 is proposed for KMPS regarding study results, while a subcategory cannot be proposed.	Anonymous 1983b

Table A.8 Summary table of human data on skin corrosion/irritation

Summary table of human data on skin corrosion/irritation				
Type of data/ report, Reliability**, Key/supportive study	Test substance (including purity), Vehicle	Relevant information about the study	Main effects, Observations	Reference
Direct	Impact®	A number of 109 adult human volunteers	In induction phase no adverse effects were	Anonymous

observations (Product investigations) no guideline available GLP: no Reliability: 2 (for skin irritating effects) Supportive study	Purity: 91 % Vehicle: distilled water	participated in an intensified version of the Shelanski and Shelanski Repeated insult patch test (one subject dropped out after first postapplication). Three different substances including KMPS were tested in parallel in the same individuals on different sites on the back. The study was designed to evaluate the skin sensitising potential of Impact®, but participants showed signs of skin irritation rather than skin sensitisation. Only effects related to skin irritation during the induction phase are reported here. During the induction phase, the patches were applied under occlusive conditions to the test persons for 24 h on 4 consecutive days/week for a total of 3 weeks. Test substance was applied as aqueous solution containing 7100 ppm (0.71 %) KMPS. No negative control group (occlusive patch without test substance) was included in the study. Scoring system:	detected on 17 out of 109 subjects on whom one or more post application examinations were conducted during this phase. Adverse skin changes were detected on 92 subjects: 5 faint (Grade 1) erythema, 15 moderate (Grade 2) erythema, 8 intense (Grade 3 erythema), 64 intense erythema with induration and/or vesicles (Grade 4). Only few visible skin changes of minor degree (grade 1-4) occurred during the first week of the study regimen (induction phase). 24 h exposure (scoring day 1): 1/109 subjects with skin changes grade 4 108/109 subjects scored with grade 0 48 h exposure (scoring day 2): 4/108 subjects with skin changes grade 1 1/108 subjects with skin changes grade 2 103/108 subjects scored with grade 0 72 h exposure (scoring day 3): 9/108 subjects with skin changes grade 1 2/108 subjects with skin changes grade 2 1/108 subjects with skin changes grade 3 1/108 subjects with skin changes grade 4 95/108 subjects scored with grade 0 96 h exposure (scoring day 4): 8/108 subjects with skin changes grade 1 5/108 subjects with skin changes grade 2 1/108 subjects with skin changes grade 3 2/108 subjects with skin changes grade 4 92/108 subjects scored with grade 0	1992a

Week	Volunteers with grade of skin reactions observed					Nr. affected
	0	1	2	3	4	
1	81	17	6	1	4	28
2	63	2	14	7	22	46

		 **Response** / **Visible Change** / **Grading PII** **Absent Inflammation** — None — 0 **Stage I** — Faint redness — 1 Moderate redness — 2 Intense redness — 3 **Stage II** — Redness plus induration, edema, papules, and/or vesicules — 4 **Stage III** — Weeping vesicles, blisters, or bullae — 5 **Stage IV** — Extension of damage beyond margin of contact site — 6 **Corrosion** — Destruction, necrosis, and/or sloughing of skin — 7	<table><tr><td>3</td><td>31</td><td>2</td><td>19</td><td>6</td><td>45</td><td>78</td></tr></table> During <u>week 2 and 3</u>, the number of visible skin changes increased over time. Thus, after repeated 24 h exposure under occlusive conditions, KMPS shows increasing skin irritating potential.	
Direct observations (Product investigations) no guideline available GLP: no Reliability: 2 (for skin irritating effects) Supportive study	Impact® Purity: 91 % Vehicle: distilled water	A number of 25 adult human volunteers participated in a patch test. All test subjects gave their prior informed consent for participation in this study. The study utilised a double-blind, non-placebo controlled, single-cell design to determine the adverse potentialities of the samples investigated on the skin of adult humans. Study subjects had already been participating for one week in a patch study regiment involving samples from other sponsors. The study was designed to evaluate the skin sensitising potential of Impact®, but participants showed signs of skin irritation rather than skin sensitisation. Only effects related to skin irritation during the induction phase are reported here. During the induction phase, the patches were applied under <u>occlusive conditions</u> to the test persons for 24 h on 4 consecutive days/week for a total of 3 weeks. Test substance was applied as aqueous solution containing 12 ppm, 150 ppm or	The following skin changes occurred during the <u>first</u> week of the study regimen (induction phase). <u>12 ppm group:</u> No adverse skin reactions were visible during the induction phase in the subjects. <u>150 ppm group:</u> No adverse skin reactions were visible during induction phase in the subjects. Faint erythema (score 1) were seen in one subject after 96 h of exposure. <u>7000 ppm group:</u> <u>24 h exposure (scoring day 2)</u>: 25/25 subjects with skin changes grade 0 <u>48 h exposure (scoring day 3):</u> 1/25 subjects with skin changes grade 4 24/25 subjects with skin changes grade 0 <u>72 h exposure (scoring day 4)</u>: 1/24 subjects with skin changes grade 1 1/24 subjects with skin changes grade 2 2/24 subjects with skin changes grade 4 20/24 subjects with skin changes grade 0 <u>96 h exposure (scoring day 5)</u>:	Anonymous 1992b

		7000 ppm KMPS. Subjects receiving 7000 ppm were split during week 3 with 13 subjects continued on 7000 ppm and 11 subjects receiving 150 ppm on naïve sites. No negative control group (occlusive patch without test substance) was included in the study. Scoring system: **Response** / **Visible Change** / **Grading PII** **Absent** / None / 0 **Inflammation** **Stage I** / Faint redness / 1 Moderate redness / 2 Intense redness / 3 **Stage II** / Redness plus induration, edema, papules, and/or vesicules / 4 **Stage III** / Weeping vesicles, blisters, or bullae / 5 **Stage IV** / Extension of damage beyond margin of contact site / 6 **Corrosion** / Destruction, necrosis, and/or sloughing of skin / 7	5/22 subjects with skin changes grade 1 2/22 subjects with skin changes grade 2 1/22 subjects with skin changes grade 4 14/22 subjects with skin changes grade 0 At the beginning of week 2, grade 4 skin reactions were seen in 10 individuals and grade 6 in one. During week 2 and 3, the number of visible skin changes increased over time. Notably, in 2 subjects, no skin changes at all were observed over the 3 weeks of repeated application of Impact® under occlusive conditions.	

A.3.3.1. Short summary and overall relevance of the provided information on skin corrosion/irritation

KMPS was tested for skin irritation in rabbits. After 4 h occlusive application of the substance, severe erythema of the treated skin was observed, which persisted for 72 h after exposure. For erythema, the mean score 24-72h after exposure in all three animals was 4.0. These erythemas were irreversible within the post-exposure period of 14 days. Oedema was less severe (very slight to slight). The mean scores 24-72 hrs were 0.67 in two animals and 0.33 in one animal. Oedema completely resolved within 2 days.

KMPS was found to be corrosive to the skin of rabbits. Irreversible destruction of the treated skin was observed.

However, the test substance was not washed from the skin after 4 hours of exposure. Therefore the skin irritating potential of KMPS could be overestimated in this study.

KMPS was used in two skin sensitisation/irritation human volunteer studies. In both studies aqueous solutions containing 7000 or

7100 ppm of KMPS have been demonstrated to be not irritating to human skin when applied for 24 h under occlusive conditions: Signs of skin irritation (grade 4) were seen in a single individual out of 109 volunteers treated with 7100 ppm and in none of the 25 volunteers exposed to 7000 ppm. However, with prolonged and repeated 24 h-exposure to KMPS at 0.71 or 0.70 % under occlusive conditions, incidence and severity of skin reactions was increasing. However, this exposure pattern represents a very worst-case scenario for the real-life dermal contact with KMPS. In addition, occlusion itself was reported to increase irritating potential of irritant chemicals.

In the second study, three concentrations of KMPS were tested (12, 150 and 7000 ppm). At 150 ppm only transient mild erythema was seen in three individuals, while at 12 ppm no signs of skin irritation were reported.

Based on mild signs of skin irritation observed after 24 hrs in only one volunteer exposed to 7000 or 7100 ppm, this concentration can be considered a short-term dermal NOAEC. As professionals as well as non-professionals are expected to wash their hands directly after contact with a corrosive substance, but at the latest after an 8 h day/shift, the study conditions are considered to represent a worst-case exposure pattern in comparison to the real-life situation.

As both studies by Anonymous, 1992a were designed as skin sensitisation studies, the study regimen is not considered optimal for derivation of a dermal NOAEC, and no such value was derived in the study reports. However, the studies by Bahr show that after 24 h of continuous exposure to KMPS (7000 / 7100 ppm, i.e. 0.7 % and 0.71 %, respectively) under occlusive conditions no significant skin irritation occurs. 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.

A.3.3.2. Comparison with the CLP criteria

According to CLP criteria a corrosive substance is one that produces destruction of the full thickness of the skin, in at least 1 tested animal after exposure under conditions of test in albino rabbits (OECD TG 404). The criteria for classification of KMPS as corrosive to skin are fulfilled based on the observations in test comparable to OECD 404 test. However, the test substance was not washed from the skin after 4 hours of exposure, therefore the data used for classification does not allow differentiation between the skin corrosion subcategories 1A/1B/1C. KMPS should be classified with skin corrosive Category 1.

According to Section 3.1.2.3.3 and Note 1 of Table 3.1.3 in Annex I to CLP, in addition to classification for inhalation toxicity, if data are available that indicate that the mechanism of toxicity was corrosivity, the substance or mixture shall also be labelled as ‘corrosive to the respiratory tract’ (see note 1 in 3.1.4.1). Corrosion of the respiratory tract is defined by destruction of the respiratory tract tissue after a single, limited period of exposure analogous to skin corrosion; this includes destruction of the mucosa. According to Section 1.2.6. in Annex II of CLP EUH071 ‘Corrosive to the respiratory tract’ is also warranted for substances and mixtures in addition to classification for skin corrosivity, if no acute inhalation test data are available and which may be inhaled.

KMPS is not acutely toxic via inhalation route, but it is corrosive to skin. KMPS can be inhaled (aerosols of dust or mist). Effects on respiratory tract considered relevant for classification purposes were observed in inhalation toxicity studies:

- Acute inhalation toxicity study (please refer to Section A.3.2.3.): Reduced response to sound, ocular and nasal discharge increasing with concentration were observed. Rats exposed at 1.5 mg/L exhibited moderate lung noise immediately post exposure. No pathological findings were reported at the necropsy.

- Sub-acute inhalation toxicity study (please refer to Section A.3.7.1.3.): The respiratory effects described were as follows: Slight lung noise at highest test-level 0.0431 mg/L. A preliminary experiment was conducted with doses of 100, 500, and 1000 mg/m^3, corresponding to 0.1, 0.5, and 1 mg/L/6h/day. These doses proved to be toxic after a few repeated exposures. After 3 exposures at 1 mg/L, 1 death had occurred, and most of the other high level dosage rats were in extremis condition. After 5 exposures at 0.5 mg/L, all rats were in extremis. Based on these observations, the high dosage levels were terminated and only 0.1 mg/L was continued through 10 exposures with definitive visible effects. The decision was made to continue this project using the lower dose levels of 0, 0.001, 0.01, and 0.05 mg/L, 6 hrs/day, 5 days/week, for two weeks.

eCA note: The applicant provided further data on the sub-acute inhalation toxicity study after the WG-I-2023 meeting that are available in Section A.3.7.1.3. These data were not reviewed by the WG and are not included in the CAR for active substance approval under BPR. The respiratory effects were described as follows:

- *high test level: lung noise (4/10 on day 3 of exposure, 2/4 on day 2 of postexposure) and gasping (1/10 on day 3 of exposure and day 1 of postexposure);*

- *intermediate test level: labour breathing (6/10 on day 4 of exposure, 10/10 on day 5 of exposure).*

Based on the available data, the corrosive effect of KMPS on the respiratory system cannot be excluded. Lack of pathological findings at the end of the post-exposure period in acute inhalation toxicity study could be due to reparative capacity of respiratory tract (Anonymous, 1994; Anonymous, 2020a). Injuries caused by corrosive effects could be repaired by the time of necropsy, which was done 14 days after exposure. Supplementary labelling with EUH071 "Corrosive to the respiratory tract" is therefore proposed.

A.3.3.3. Conclusion on classification and labelling for skin corrosion/irritation

KMPS is corrosive to animal skin (rabbit). Based on the results obtained for exposure duration of 4 h and taking into account the provisions of Annex I of CLP Regulation, KMPS is proposed to be classified and labelled as Skin Corr. 1 with the hazard statement H314: "Causes severe skin burns and eye damage".
Supplementary labelling with EUH071 "Corrosive to the respiratory tract" is proposed, based on the fact that the substance is corrosive and based on the possibility of the exposure to aerosols.

A.3.4. Serious eye damage and Eye irritation

No *in vitro* study on eye irritation of KMPS was performed.

Table A.9 Summary table of animal studies on serious eye damage and eye irritation

Summary table of animal studies on serious eye damage and eye irritation					
Method, Duration of study, Guideline, GLP status, Reliability, Key/supportive study	Species, Strain, Sex, No/group	Test substance (including purity), Vehicle, Dose levels Duration of exposure	Results Average score for corneal opacity, iritis, conjunctival redness and conjunctival oedema (24, 48, 72 h) per animal, observations and time point of onset, reversibility	Remarks (e.g. major deviations)	Reference
Acute eye irritation study OECD 405 GLP: No, but several quality assurance inspections were carried out Reliability: 2 Key study	Rabbit New Zealand White (outbred) Sex not stated 3 animals	RD/1/58 (KMPS) vehicle: 0.1 g in conjunctival sac of right eye left eye remained untreated and served as control	Instillation of the test material caused practically no initial pain responses in all animals. Instillation of test material into the conjunctival sac of three rabbits caused severe ocular lesions within 1 h. Animals were sacrificed 24 h after instillation of test substance due to ocular damage indicating necrosis. <u>Scores per animal at 24 h</u>: - Corneal opacity: 3, 3, 3 - Conjunctival redness: 3, 3, 3 - Chemosis: 3, 3, 2 - Iris: 0, 0, 0 Necrosis of conjunctival and nictitating membrane	KMPS is classified as skin corrosive. The study should not have been performed, because substances that are skin corrosive, are considered to be corrosive for the eye as well according to Regulation (EC) 528/2012 and Regulation (EC) 1272/2008. No further information on the test substance (stability, purity) is available.	Anonymous 1985

No human study on eye irritating potential of KMPS is available.

A.3.4.1. Short summary and overall relevance of the provided information on serious eye damage/eye irritation

Compound RD/1/85 containing KMPS was tested for eye irritation in rabbits. Instillation of 0.1 g into the conjunctival sac of three rabbits caused severe ocular lesions which were apparent in all animals within 1 h and justified the termination of the test on humane ground, 24 h after treatment.

Principal lesions include: opacity of cornea, beefy-red conjunctiva, chemosis and ocular discharge, necrosis of lower conjunctiva and nictitating membrane. These results indicate serious eye damage.

A.3.4.2. Comparison with the CLP criteria

According to CLP criteria a serious eye damaging substance is one that produces in at least one animal effects on the cornea, iris or conjunctiva that are not expected to reverse or have not fully reversed within an observation period of normally 21 days after exposure under conditions of OECD TG 405. The criteria for classification of KMPS as serious eye damaging Category 1 are fulfilled based on observations in OECD 405 test.

A.3.4.3. Conclusion on classification and labelling for serious eye damage/eye irritation

KMPS warrants classification as Eye Dam. 1, H318 "Causes serious eye damage" according to Regulation (EC) 1272/2008.

However, since KMPS has to be classified as Skin Corr. 1 and assigned H314 ("Causes severe skin burns and eye damage"), the risk of severe damage to eyes is considered implicit and H318 does not need to be indicated on the label due to redundancy in accordance with Article 27 of CLP Regulation.

A.3.5. Skin sensitisation

Table A.10 Summary table of animal studies on skin sensitisation

Summary table of animal studies on skin sensitisation					
Method, Duration of study, Route of exposure (e.g. topical/intradermal, induction/challenge if relevant), Guideline, GLP status, Reliability, Key/supportive study	Species, Strain, Sex, No/group	Test substance (including purity), Vehicle, Dose levels, Duration of exposure	Results (e.g. EC3-value or amount of sensitised animals at induction dose)	Remarks (e.g. major deviations)	Reference
Skin sensitisation study, Local Lymph Node Assay in mice (LLNA-BrdU ELISA); OECD 442b GLP: Yes Reliability: 2 Key study	CBA/J mice, Female 5/control 5/test dose group	CAROAT® Monopersulphate Compound, with impurity dipotassium peroxodisulphate ($K_2S_2O_8$), 2.86 %; Dose levels: 0.1%, 0.25%, and 0.5% KMPS (w/v) in DMSO (w/v) in DMSO; Exposure: the test article, vehicle control (DMSO), and positive control (hexyl cinnamic aldehyde, HCA) solutions were administered by topical application to the dorsum of	All animals survived the in-life phase of the study. There were no difficulties noted in administration of the test article or with its adherence to the dosed ears. Body weight changes were normal. None of the test article treated groups had ear swelling or resulted in more-than-moderate local dermal irritation. The Stimulation Index (SI) of the positive control group, 25% HCA, was 3.1. The group SI values for the test article were as follows: 1.0 for 0.1% (w/v), 1.3 for 0.25% (w/v) and 1.0 for 0.5% (w/v) KMPS in DMSO.	Positive control, 25% HCA, had 40% increase in ear thickness on Day 6.	Anonymous, 2020

		each ear, once daily for three consecutive days.	Topical application of test article KMPS at 0.1%, 0.25%, and 0.5% (w/v) in DMSO resulted in SI values less than 1.6 (SI < 1.6), and therefore the test article is not a dermal sensitizer in the Local Lymph Node Assay in Mice.		
Skin sensitisation study, Magnusson-Klingmann method OECD 406 GLP: Yes Reliability: 1 Key study	Albino Guinea pig Dunkin-Hartley Males 5/control 10/test dose group	Oxone® Monopersulphate Compound in sterile water; impurity dipotassium peroxodisulphate ($K_2S_20_8$), 2.0% Intradermal induction (day 1): 0.1 mL of 0.25 % (w/v) Oxone® Monopersulphate Compound dilution in water, 1:1 mixture of FCA/water and 0.25% (w/v) test item in a 1:1 mixture of FCA/water Topical induction (day 8): 20% (w/v) Oxone® Monopersulphate Compound in water Topical challenge	<u>Intradermal injections:</u> Necrosis was recorded at sites receiving FCA in test and control animals. No irritation was seen in the test animals at sites receiving Oxone® Monopersulphate Compound, 0.25 % (w/v) in water for irrigation and no irritation was observed in control animals. <u>Topical application:</u> Well defined to moderate erythema, accompanied by blanching of the dose site, was observed in all test animals following topical application with Oxone® Monopersulphate Compound, 20 % (w/v) in water for irrigation. No erythema was seen in the control group. <u>Challenge:</u> There were no dermal reactions seen in any of the test or control animals.	None	Anonymous 2001c

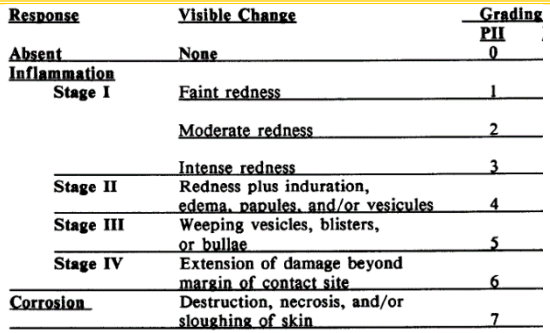
		(day 22): 5 % (w/v) and 2.5 % (w/v) of Oxone® Monopersulphate Compound in water Positive control: Hexyl cinnamic aldehyde (HCA)	None of the animals of the control or test group showed clinical signs of toxicity and no mortalities were observed. There were no effects on body weight of animals in the main study. None of the animals demonstrated any evidence for an allergic reaction. Oxone® Monopersulphate Compound is therefore not considered to be a potential skin sensitiser.		

Table A.22 Summary table of human data on skin sensitisation

Summary table of human data on skin sensitisation				
Type of data/report, Reliability, Key/supportive study	Test substance (including purity), Vehicle	Relevant information about the study (e.g. description of the test subjects (general population/selected/unselected dermatitis patients/workers), exposure data (induction dose, daily and overall exposure)	Main effects, Observations	Reference
Direct observations (Product investigations) no guideline available GLP: no Reliability: 3 (for skin sensitising effects) Supportive study	Impact®, impurity dipotassium peroxodisulphate ($K_2S_2O_8$), content of impurity not stated Purity:	A number of 109 adult human volunteers participated in an intensified version of the Shelanski and Shelanski Repeated insult patch test. Three different substances including KMPS were tested in parallel in the same individuals on different sites on the back. The study was designed to evaluate the skin sensitising potential of Impact®, but participants showed signs of skin irritation rather than skin sensitisation. Only effects related to skin sensitisation are reported here.	Distinct skin reactions were observed after induction and challenge phase in some individuals. The challenge applications at naïve sites induced skin reactions in 42 % of the participants following application of Impact, respectively. However, from a scientific point of view the study has several limitations which distinctly influence the reliability and significance of the results: - Sensitisation is an immune	Anonymous 1992a

	91% Vehicle: distilled water	During the induction phase, the patches were applied under occlusive conditions to the test persons for 24 h on 4 consecutive days/week for a total of 3 weeks. Test substance was applied as aqueous solution containing 7100 ppm KMPS. During the challenge phase, the patches were applied under occlusive conditions to the test persons for 24 h on 4 consecutive days/week for one week. Test substance was applied as aqueous solution containing 7100 ppm KMPS. No negative control group (occlusive patch without test substance) was included in the study. Scoring system: **Response** / **Visible Change** / **Grading PII** **Absent** — None — 0 **Inflammation** **Stage I** — Faint redness — 1 Moderate redness — 2 Intense redness — 3 **Stage II** — Redness plus induration, edema, papules, and/or vesicules — 4 **Stage III** — Weeping vesicles, blisters, or bullae — 5 **Stage IV** — Extension of damage beyond margin of contact site — 6 **Corrosion** — Destruction, necrosis, and/or sloughing of skin — 7	response to the application of a test substance and sensitisation can generally only be observed at low, non-irritating concentrations. - As the concentrations used for the induction and challenge phase were identical and have been shown to be irritating in some individuals after repeated 24 h-exposures under occlusive conditions, it is not possible to distinguish between an irritant and a sensitisation skin response in the study. - All three test substances were concurrently tested in the same individuals; therefore, no conclusion can be drawn for the sensitising properties of the individual substances, especially when considering that one tested substance is classified as respiratory and skin sensitizer. The results obtained in this study are not scientifically robust enough to derive any conclusions on the sensitising properties of either substance tested.	
Direct observations (Product investigations) no guideline available GLP: no	Impact®, impurity dipotassium peroxodisulphate ($K_2S_2O_8$),	A number of 25 adult human volunteers participated in a patch test. All test subjects gave their prior informed consent for participation in this study. The study utilised a double-blind, non-placebo controlled, single-cell design to determine the adverse potentialities of the	Minor degrees of erythema were seen in one to two subjects during both the primary/activation and challenge phase with 12 ppm. Faint erythema were seen in one subject during the primary/activation phase (150 ppm) and transient erythema in	Anonymous 1992b

Reliability: 3 (for skin sensitising effects) Supportive study	content of impurity not stated Purity: 91% Vehicle: distilled water	samples investigated on the skin of adult humans. Study subjects participated in a patch study regiment involving samples from other sponsors during the course of the study. The study was designed to evaluate the skin sensitising potential of Impact®, but participants showed signs of skin irritation rather than skin sensitisation. Only effects related to skin irritation during the induction phase are reported here. During the induction phase, the patches were applied under occlusive conditions to the test persons for 24 h on 4 consecutive days/week for a total of 3 weeks. Test substance was applied as aqueous solution containing 12 ppm, 150 ppm or 7000 ppm KMPS. Subjects receiving 7000 ppm were split during week 3 with 13 subjects continued on 7000 ppm and 11 subjects receiving 150 ppm on naïve sites. During the challenge phase, the patches were applied under occlusive conditions to the test persons for 24 h on 4 consecutive days/week for one week. For challenge, the same concentrations as used for the induction phase were used for subjects receiving 12 ppm and 150 ppm; subjects induced with 7000 ppm received 150 ppm during challenge. No negative control group (occlusive patch without test substance) was included in the study. Scoring system:	another subject during the challenge phase (150 ppm) disappearing within 24 hours. Signs of skin irritation were observed in individuals exposed to 7000 ppm during induction phase. During challenge with 150 ppm, no adverse effects were detected in any of the 24 subjects of the 7000 ppm group. During the additional challenge procedure with 22 subjects receiving 3500 and 7000 ppm Impact® for 24 or 48 h respectively, 9 subjects were scored for skin changes, with 3 subjects showing skin changes only on sites where Impact® was applied for 48 h. Grade 4 skin changes were visible only in 4 of these subjects. The skin reactions noted at 7000 ppm or 150 ppm cannot unequivocally be attributed to a skin sensitising response since, from a scientific point of view, the study has several limitations which distinctly influence the reliability and significance of the results: - Sensitisation is an immune response to the application of a test substance and sensitisation can generally only be observed at low, non-irritating concentrations. - The concentrations used for the induction and challenge phase was identical for the 12 ppm, and 150 ppm group. For the 7000 ppm group, the concentration has	

			been shown to be irritating in some individuals after repeated 24 h-exposures under occlusive conditions. Thus, it is not possible to distinguish between an irritant and a sensitisation skin response in the study. - Other test substances which were not specified in the study report were concurrently tested in the same individuals during the course of the study. Therefore, no firm conclusion can be drawn on the sensitising potential of KMPS. Based on the results obtained in this study and taking into account the limitations of this test as well as the study design, a skin sensitising effect of KMPS could not be proven and the skin reactions noted suggest a concentration-dependent irritating effect to the skin rather than a skin sensitising potential of the test substance.	

A.3.5.1. Short summary and overall relevance of the provided information on skin sensitisation

The sensitizing potential of topically applied CAROAT® Monopersulphate Compound (KMPS) was investigated using the Local Lymph Node Assay in Mice, utilizing the BrdU ELISA method. The test article concentrations of 0.1%, 0.25% and 0.5% (w/v) KMPS in DMSO were chosen such that the maximum concentration tested avoided both overt systemic toxicity and more-than-moderate local dermal irritation. The moderate sensitizer (and irritant) 25% HCA was tested as a positive control and DMSO as vehicle control. Five groups of female CBA/J mice (five animals per group) were treated by topical application. There were no difficulties noted in administration of the test article or with its adherence to the dosed ears. Body weight changes were normal. None of the test article treated groups

had ear swelling or resulted in more-than-moderate local dermal irritation. The positive control, 25% HCA, had a greater than 25% increase in ear thickness on Day 6 and enlargement of the lymph nodes. Based on experience at the testing facility, this occurs in the majority of studies when using 25% HCA in the vehicle DMSO. The Stimulation Index (SI) of the positive control group, 25% HCA, was 3.1. The group SI values for the test article were as follows: 1.0 for 0.1% (w/v), 1.3 for 0.25% (w/v) and 1.0 for 0.5% (w/v) KMPS in DMSO.

Consequently, topical application of test article KMPS at 0.1%, 0.25%, and 0.5% (w/v) in DMSO resulted in SI values less than 1.6 (SI < 1.6), and therefore the test article is not a dermal sensitizer in the Local Lymph Node Assay in Mice.

The skin sensitisation potential of Oxone® Monopersulphate Compound (KMPS) was investigated in a guinea pig maximization test. In the range finding study, after topical application of KMPS, the following effects were observed: 25% (w/v) to 100% (w/v): necrosis; 20% (w/v): slight to moderate erythema with slight oedema; 10% (w/v): slight to well-defined erythema with slight oedema; 5% (w/v), 1% (w/v), 0.1% (w/v), 0.05% (w/v), 0.01% (w/v): no erythema, no oedema. OECD TG 406 recommends: "The concentration of test chemical used for each induction exposure should be well tolerated systemically and should be the highest to cause mild-to-moderate skin irritation. The concentration used for the challenge exposure should be the highest non-irritant dose." 20% (w/v) was used for induction topical application as this was the highest concentration that produced some irritation but did not adversely affect the animals. 5% (w/v) and 2.5% (w/v) were used for topical challenge as 5% (w/v) was the highest concentration not giving rise to irritating effects.
Following intradermal injection necrosis was recorded at sites receiving FCA in test and control animals. No irritation was seen in the test animals at sites receiving Oxone® Monopersulphate Compound 0.25 % (w/v) in water for irrigation and no irritation was observed in control animals receiving water for irrigation.

Well defined to moderate erythema, accompanied by blanching of the dose site, was observed in all test animals receiving Oxone® Monopersulphate Compound 20 % (w/v) in water for irrigation. No erythema was seen in the control group.

Following challenge application, no dermal reactions were seen in any of the test or control animals. Consequently, all ten test animals gave negative responses leading to the conclusion that KMPS is not considered to be a potential skin sensitiser.

In two human volunteer studies, distinct skin reactions were observed after induction at 7100 ppm and challenge at 7100 ppm or induction at 7000 ppm and challenge at 150 ppm in some individuals. However, no firm conclusions on skin sensitisation potential of KMPS can be drawn due to limitations in the study design (same concentration used for induction and challenge, irritating effects after repeated 24-h exposures under occlusive conditions, concurrent application of other (sensitising) test substances). However, at 150 ppm and 12 ppm only mild skin reactions were seen after exposure to KMPS in a small number of individuals. The skin reactions noted at 7000 or 7100 ppm suggest a concentration-dependent irritating effect to the skin after repeated exposure rather than a skin sensitising potential of KMPS.

KMPS contains impurity dipotassium peroxodisulphate ($K_2S_20_8$), which has a harmonised classification as Skin sensitiser Cat. 1: H317 and Respiratory sensitiser Cat. 1: H334. The content of potassium persulphate is higher than the trigger value for classification for Skin sens. 1 and Respir. sens. 1. However, a LLNA test and a guinea pig skin sensitisation study (Magnusson-Klingman method) were performed with KMPS and thereafter no classification is required regarding skin sensitising potential according to criteria of Regulation 1272/2008. An impurity potassium persulfate (K2S208, CAS 70693-62-8) is proposed to contribute to labelling EUH208 "Contains dipotassium peroxodisulphate (CAS 7727-21-1). May produce allergic reaction". As it does not contribute to classification, it is not considered relevant impurity according to ECHA Guidance on Impurities and (degree of) purity in CLP and the CLH process (August 2018). As it is not relevant for other sections, the content of impurity is addressed only in this section.

The applicant has submitted an overview of the sensitisation data on KMPS in which it is explained that KMPS does not need to be classified as a skin or respiratory sensitiser (Anonymous 2016a). The overview includes a brief summary of the risk assessment for Oxone which is actually based on the risk assessment for Virkon S. The exposure scenario includes application of Virkon S by fogging. Virkon S contains 50 % Oxone. It is reported that exposure levels are below DNEL and AEL demonstrating low risk to operators, but reference values are not stated in the brief summary. This risk assessment demonstrates that a high exposure to Oxone is not expected to present a sensitising risk because of the presence of $K_2S_20_8$ as an impurity.
Skin sensitisation studies were performed with KMPS containing potassium persulphate as impurity. A Guinea pig Maximisation test by Anonymous, 2001c was conducted with Oxone and it did not induce skin sensitisation in exposed animals.

In the KMPS REACH dossier another skin sensitisation study is presented with Caroat. No skin sensitising properties were observed on epidermal challenge with 3 % concentration following intradermal injection of 0.05 % and epidermal application of 10 % test substance. This study has a reliability score 2 in the REACH registration dossier since identity and purity of the test substance was not fully specified. Additionally, the concentration of potassium persulphate in Caroat tested in the skin sensitisation study is not reported.

Three more skin sensitisation studies with KMPS are summarised in the REACH dossier. All studies were interpreted by applicant as negative but have low reliability scores (3) due to insufficient reporting of the identity of test substance and, not being performed according to principles of the GLP, which was not required at the time and two of them were performed according to Buehler method of the Guinea pig maximisation test with 3 inductions what is considered not to be sensitive enough. The applicant also reports three skin sensitisation studies performed with Virkon S that contains 50 % Oxone. In two Guinea pig Maximisation tests it did not elicit skin sensitising reactions in exposed animals. Additional test was performed according to the Buehler method which also gave negative result. But also for these studies there is no information on the content of potassium persulphate impurity.

Medical surveillance data on workers in manufacturing and packaging of Oxone was submitted. It did not indicate any cases of skin or respiratory senisitivity of workers being in contact with KMPS. Incidence reports from a previous and current manufacturing periods were searched for reports that could be related to skin or respiratory sensitisation. In the period of 2002-2016 six entries only were referring to sensitisation or allergy. The claims were unsubstantiated or unclear, with various products cited or misuse was involved, and any reported effects do not appear to be characteristic of dermal sensitisation rather than other effects such as irritation. It is

also not clear whether effects observed were due to Oxone or other components of Virkon S.

A case of a 55-year old man using a hot tub (containing potassium peroxymonosulfate, KMPS) is reported (Anonymous, 2004a). The man experienced skin eruption and wheezing related to the recent use of a hot tub treated with potassium peroxymonosulfate, an active ingredient of Oxone™, for disinfection. These symptoms cleared after avoidance of the disinfectant product. The authors conclude that KMPS was the case of the rush and pulmonary symptoms. The patient had positive patch test result for potassium peroxymonosulfate KMPS at 5% *in pet* (*in petrolatum*; Vaseline), and also a questionable reaction to potassium dichromate from the patch test. Potassium dichromate may cause allergic respiratory reaction (Anonymous 2016b). In addition, KMPS at 5% is clearly corrosive to skin, reason why KMPS is classified as Skin Corr. 1 according to the CLP. Consequently, the effects of 5% KMPS as observed in the human patch test are rather considered as irritant (irritant contact dermatitis) and not as allergen (allergic contact dermatitis) reactions. Quantification of exposure concentrations for potassium peroxymonosulfate was absent, and exposure to other potential sensitizing agents were not documented in this case report (Anonymous, 2016c).
Oxone is also widely used as a denture cleaner and as oxidant in swimming and spa pools. The denture cleaner is usually a tablet, containing 10 % Oxone, which should be dissolved in a glass of tap water. People using such tablets are in skin contact with the tablet first and later with the solution. According to manufacturers and suppliers of dissolving tablets for denture cleaning 10 millions of users are annually exposed to Oxone on a daily bases. Regarding such a widespread use of Oxone numerous reports of sensitising reactions would be expected if KMPS induced sensitising reactions in exposed individuals.

Considering all the available information we conclude that KMPS is not a skin sensitiser.

A.3.5.2. Comparison with the CLP criteria

According to the Guidance on the Application of the CLP Criteria substances shall be classified as skin sensitizers in accordance with two criteria (Table 3.4.2): i) if there is evidence in humans that the substance can lead to sensitisation by skin contact in a substantial number of persons, or ii) if there are positive results from an appropriate animal test.

In a LLNA test, the SI value was less than 1.6 (SI < 1.6), and therefore the KMPS is not a dermal sensitizer. In a guinea pig maximisation test none of test animals responded with signs of skin sensitisation. Human data support the results of animal test. The classification of KMPS as skin sensitizer is not warranted.

As KMPS contains impurity dipotassium peroxodisulphate ($K_2S_20_8$) which has a harmonised classification as Skin Sensitiser 1, H317 and Respiratory Sensitiser 1, H334 and is present in a concentration greater than that specified in Table 3.4.6 of Annex I of Regulation (EC) 1272/2008 the active substance KMPS shall be labelled with EUH208 "Contains dipotassium peroxodisulphate (CAS 7727-21-1). May produce an allergic reaction."

A.3.5.3. Conclusion on classification and labelling for skin sensitisation

According to the criteria of CLP Regulation, KMPS does not warrant classification as skin sensitiser. The active substance KMPS warrants labelling EUH208 "Contains dipotassium peroxodisulphate (CAS 7727-21-1). May produce allergic reaction.", according to CLP Regulation.

A.3.6. Respiratory sensitisation

No animal or human data is available on respiratory sensitisation potential of KMPS.

A.3.6.1. Short summary and overall relevance of the provided information on respiratory sensitisation

KMPS contains impurity dipotassium peroxodisulphate ($K_2S_20_8$) which has a harmonised classification as Skin Sensitiser 1, H317 and Respiratory Sensitiser 1, H334. The concentration of the impurity in KMPS is above the generic concentration limit of 1 % triggering classification as Skin Sens. 1 or Resp. Sens. 1.

Currently no testing method is available for respiratory sensitisation and therefore this classification is based only on human data. As summarised by the applicant, medical surveillance data on workers involved in KMPS manufacture and packaging did not indicate any cases of respiratory sensitivity after exposure to KMPS.

Applicant also reports further detailed review of health records for personnel (33) involved in Oxone manufacture. Results obtained from occupational health surveillance questionnaires and pulmonary function tests indicate that there are no pulmonary symptoms reported and no chronic obstructive pulmonary disease observed amongst these employees during 2013 and 2016. Workers in the production of KMPS are considered to have the highest potential exposure to KMPS, even though RMM are used. These data further indicate that KMPS, including its impurities, is not a respiratory sensitiser.

Additionally, KMPS is widely used in swimming and spa pools and as denture cleaners. Due to use of denture cleaning tablets alone 10 millions of people in Europe are estimated to be in contact with KMPS on daily bases. Regarding daily exposure of so many people numerous reports of sensitising reactions would be expected if KMPS would exert respiratory sensitising potential. However in open literature we did not find any publication regarding respiratory sensitisation related to KMPS exposure.

A.3.6.2. Comparison with the CLP criteria

According to the Guidance on the Application of the CLP Criteria substances shall be classified as respiratory sensitizers in accordance with two criteria (Table 3.4.1): i) if there is evidence in humans that the substance can lead to specific respiratory hypersensitivity, or ii) if there are positive results from an appropriate animal test. There are currently no standard tests and no OECD test guidelines

available for respiratory sensitisation.

KMPS is not a skin sensitiser, and thus is not considered to have respiratory sensitisation potential. This conclusion is supported by data from medical surveillance of workers at their KMPS manufacturing sites where no evidence for respiratory hypersensitivity was seen (see chapter A.3.6.1). Additionally, case reports would be expected in the open literature due to widespread use of KMPS also among general public (e.g. in disinfection of swimming and spa pools and denture cleaners).

A.3.6.3. Conclusion on classification and labelling for respiratory sensitisation

According to the criteria of CLP Regulation, KMPS does not warrant classification as respiratory sensitiser.

A.3.7. Repeated dose toxicity/STOT RE

A.3.7.1. Short term repeated dose toxicity

A.3.7.1.1. Short-term oral toxicity

Table A.23 Summary table of oral short-term animal studies (usually 28-day studies)

Summary table of oral short-term animal studies (usually 28-day studies)						
Method, Duration of study, Route of exposure (gavage, in diet, other) Guideline, GLP status, Reliability, Key/supportive study	Species, Strain, Sex, No/group	Test substance (including purity), Vehicle, Dose levels, Duration of exposure	NOAEL, LOAEL	Results (all dose levels including severity and magnitude of all effects, including also target organs)	Remarks (e.g. major deviations)	Reference
14-days oral toxicity study Route of	Rat CD (Crl: CD (SD) IGS BR)	Oxone® Monopersulphate Compound	NOAEL > 1000 mg/kg bw/day (corresponding toNOAEC > 100	Clinical signs: There were no clinical signs indicative of systemic toxicity noted. No deaths occurred.	Only 3 instead of 5 animals/dose were used in the study (dose-	Anonymous 2001d

exposure: gavage Study similar and in accordance with OECD 407 GLP: Yes Reliability: 2 Supportive study	Males and females 3/dose/sex	Vehicle: deionised water 0, 50, 400 and 1000 mg/kg bw (corresponding to 0, 5, 40, 100 mg/mL) Gavage 14 days	mg/mL) LOAEL was not determined in the study.	At 40 mg/mL (400 mg/kg bw), salivation was noted for 2/3 males and for all animals at 100 mg/L (1000 mg/kg bw). This effect is assumed to result from the taste of test substance. Food consumption: Transient higher food consumption in both sexes considered not toxicologically relevant. Body weight: There was no toxicologically relevant effect; test group animals actually gained more weight and had a higher terminal body weight than control animals. Macroscopic examination: Cysts in the kidneys were noted in 1/3 females at 100 mg/mL (1000 mg/kg bw/day) and 2/3 males and 2/3 females at 40 mg/mL (400 mg/kg bw/day) compared with none in the controls. These cysts were spontaneous lesions and were not considered to be related to treatment.	range finding study), no histopathological, haematological or clinical chemistry examination was performed and no urinalysis. Study is considered supportive.	

Oral gavage with Oxone® Monopersulphate Compound (KMPS) at doses of up to 1000 mg/kg bw/day for 14 days were well tolerated by rats of both sexes.

Oxone® Monopersulphate Compound was administered to rats by gavage for 14 consecutive days at doses of 0, 50, 400 and 1000 mg/kg bw/day (corresponding to 0, 5, 40, 100 mg/mL) according to the OECD Guidance 407 and GLP. Animals were observed once daily and clinically checked on weekly basis until sacrificed on day 15.

No deaths occurred. There were no clinical signs of systemic toxicity in this study. Transiently higher food consumption and increased body weight gain compared to controls was seen in all groups of treated animals, but was not dose dependent and therefore considered to be not test substance related. Salivation was observed in 2/3 males receiving KMPS at doses of400 mg/kg bw/day and all animals receiving KMPS at 1000 mg/kg bw/day, but this might be due to the unpleasant taste of the compound. Kidney cysts were found in 1/3 females receiving KMPS at 1000 mg/kg bw /day and 2/3 males and 2/3 females receiving 400 mg/kg/bw/day. Since increased incidence of kidney cysts was not dose related and also not reported in 90-days rat study the cysts were considered to be spontaneous lesions and not induced by Oxone® Monopersulphate Compound.

The NOAEL for Oxone® Monopersulphate Compound in this study is >1000 mg/kg/bw/day.

The study is considered reliable with restrictions due to following reasons: only 3 instead of 5 animals/dose were used in the study (dose-range finding study), no histopathological, haematological or clinical chemistry examination was performed and no urinalysis.

No human data on short-term oral toxicity is available for KMPS.

A.3.7.1.2. Short-term dermal toxicity

No animal or human data on short-term dermal toxicity is available for KMPS.

A.3.7.1.3. Short-term inhalation toxicity

Table A.24 Summary table of inhalatory short-term animal studies (usually 28-day studies)

Summary table of inhalatory short-term animal studies (usually 28-day studies)						
Method, Duration of study, Guideline, GLP status, Reliability, Key/supportive study	Species, Strain, Sex, No/ group	Test substance (including purity), form (gas, vapour, dust, mist) and particle size (MMAD), Actual and nominal concentration, Type of administration (nose only / whole body/ head only), Duration of exposure	NOAEL, LOAEL	Results (all dose levels including severity and magnitude of all effects, including target organs)	Remarks (e.g. major deviations)	Reference
Sub-acute	Rat	Oxone® Monopersulphate	Local effects:	Clinical signs: Eye irritation	Only male	

Inhalation Toxicity (14 days) Study performed comparably with OECD 412 GLP: No, was not compulsory at the time of study conduct Reliability: 2 Key study	Crl:CD Males 10/dose	Compound Dust aerosol MMDA not stated Target concentration: 0, 0.001, 0.01, 0.05 mg/L Analytical concentration: 0, 0.0014, 0.0101, 0.0431 mg/L Head-only exposure 6 h/day 5 days/week 14-days exposure 13 days post-exposure period	LOAEC: 0.0101 mg/L (10.1 mg/m³) NOAEC: 0.0014 mg/L (1.4 mg/m³)	(alopecia around the eye, conjunctival swelling, severe opacity, corneal ulceration and haemorrhage, corneal vascularisation, discharge and crusty scab around the eyes) at mid and high test-level; slight lung noise (at high test-level). The 13-day observation period allowed only partial recovery from ocular effects. Body weight: Decreased body weight gain was noted at the high test-level on days 10-16 and at mid test-level on day 12. Gross findings: Ocular discharge, swollen eyelids with hair loss, cloudy appearance of the cornea were noted at mid and high test-level. Microscopic lesions: Eye lesions (blepharitis, keratitis, corneal vascularisation, iritis, degeneration of the lens) were noted at mid and high test-level. The 13-day observation period allowed only partial recovery from ocular effects. Organ weights: No effects. Clinical chemistry: No toxicologically relevant effects.	rats were used (not considered to have compromised the study results as male rats were shown to be the more sensitive sex in the acute inhalation toxicity study). Particle size not analysed. Food/water consumption not investigated.	Anonymous 1981

In a sub-acute inhalation toxicity study, rats received Oxone® Monopersulphate Compound (KMPS) as dust aerosol at actual (measured) concentrations of 0, 0.0014, 0.0101 and 0.0431 mg/L. No deaths occurred. Transient decrease in body weight was observed at 0.0431 mg/L on days 10-16 and at 0.0101 mg/L on day 12.

Mid and high test-levels of KMPS caused alopecia around the eye, conjunctival swelling, severe opacity, corneal ulceration and

haemorrhage, corneal vascularisation, and clear discharge. In general, a dry, crusty scab was formed around the eyes, keeping them closed unless forced open. One control rat had a cloudy, glazed right eye. A slight lung noise in high test-level rats was observed during exposure.

Individual pathology data from gross and histopathological examinations were recorded after the 10th exposure when 5 rats from each level were selected at random and sacrificed for gross and histopathological examination. Remaining rats were sacrificed on the 13th observation day for an identical examination. The organs and tissues examined included: ear pinna, skin, thymus, mediastinal tissue, spleen, bone marrow (sternum), heart, trachea, lungs, esophagus, stomach, small intestines (duodenum, jejunum, and ileum), large intestines (cecum and colon), liver, kidneys, testes, epididymides, thyroids, adrenals, brain, eyes, and any other tissues observed to be abnormal at necropsy.

Based on this, one can assume that the tissues and organs not examined at necropsy were normal, but there is no clear indication of this and it could only be concluded that there is no histopathological data available for the nasal cavity and possible deposition of KMPS particles therein.
At necropsy, no gross findings were observed in control or low level rats. Intermediate and high level rats generally had ocular discharge, swollen eyelids with hair loss, and a cloudy appearance of the cornea. Microscopic lesions attributable to the test compound were limited to the eyes and eyelids of rats exposed at the 2 highest exposure levels. These changes included:
blepharitis, keratitis, corneal vascularisation, iritis, inflammatory exudate in the anterior and posterior chambers of the eye, haemorrhage mainly in the vitreous body of the eye and degeneration of the lens (cataract). These findings were equal in severity in the mid and high test groups but higher in incidence in the high test group. The 13day observation period allowed only slight recovery of these lesions (irreversible damage). No eye damage occurred at the low test-level.

In rats receiving the highest concentration, 3/10 leukocytosis was reported, that could be due to inflammation of damaged eyes.

At the high test-level, increased serum glutamic-oxalacetic acid, glutamic-pyruvic transaminase and urea nitrogen activities and depressed levels in alkaline phosphatase, and serum creatinine were measured. After 13 days of recovery, glutamic-pyruvic transaminase, glutamic-oxalacetic acid, creatinine levels and total protein levels were statistically lower than controls. This effect is not considered to be treatment related. The decrease in the creatinine level was not dose-dependent and was not considered to be toxicologically relevant. Changes seen on the alkaline phosphatase level were shown to be completely reversible during the recovery period.

Rats receiving the highest concentration had an elevated blood urea nitrogen, which was no longer observed after recovery period. Urinary pH was depressed in rats at treated with the high dose. Following the recovery period slight decrease in urinary pH was still seen, but not was not considered to be adverse.

The critical effect observed in the sub-acute inhalation study was severe eye damage of exposed animals. No true systemic toxicity observations were reported in this study. The NOAEC of 0.0014 mg/L (1.4 mg/m^3) is based on clinical signs of the eyes and histological

eye findings observed at the next higher test concentration (LOAEC of 0.0101 mg/L (10.1 mg/m^3)).

eCA note: The applicant provided further data on the sub-acute inhalation toxicity study after the WG-I-2023 meeting (copies of the notebook containing the raw data for the preliminary experiment and part of the data for the main study presented above). These data were not reviewed by the WG and are not included in the CAR for active substance approval under BPR:

- *Test concentrations in the preliminary experiment:*
  a) target concentrations: 100, 500, and 1000 mg/m^3, corresponding to 0.1, 0.5, and 1 mg/L/6h/day;
  b) analytical concentrations: 110, 320, and 790 mg/m^3, corresponding to 0.11, 0.32 and 0.79 mg/L/6h/day.
- *Exposure time in preliminary experiment: 3 days high dose, 5 days intermediate dose, 10 days low dose.*
- *Information on particle size is not available for the main study. However, there is data available for the preliminary experiment. Particle size information is available in terms of raw data. From these data, graphs were drawn to determine the 50% cumulative mass percent. The following particle sizes for a 50% cumulative mass percent can be indicated: low level 2 µm and 3.3 µm (two data sets available), intermediate level 2.4 µm, and high level 3.5 µm.*
- *The reason stated in the notebook for conducting the main study at lower doses was the severe weight loss and ocular damage in rats in the preliminary experiment.*
- *Clinical signs in rats in the preliminary experiment: eye irritation (alopecia around the eye, conjunctival swelling, severe opacity, corneal ulceration and haemorrhage, corneal vascularisation, discharge at all test levels, necrotic eyes at low test level, conjuctival haemorrhage, necrotic eyelid at intermediate test level); lung noise and gasping (at high test level); labored breathing (intermediate test level). The postexposure period (21 days at the high test level, 19 days at the intermediate test level, 13 days at the low test level) allowed only partial recovery from ocular effects. The onset of severe effects on exposure day 2 for high and intermediate test levels and day 4 for low test level.*
- *For the main study, observations (raw data) are available for the first seven exposure days. For all exposure concentrations, including control, slight to severe ocular and nasal discharge, usually red, and in some animals, dry red, has been reported. In high test level animals, discharge was caked aroud the eyes and nose on the 6th and 7th exposure days.*

No human data on short-term inhalation toxicity of KMPS is available.

A.3.7.2. Sub-chronic repeated dose toxicity

A.3.7.2.1. Sub-chronic oral toxicity

Table A.25 Summary table of oral sub-chronic animal studies (usually 90-day studies)

Summary table of oral sub-chronic animal studies (usually 90-day studies)						
Method, Duration of study, Route of exposure (gavage, in diet, other), Guideline, GLP status, Reliability, Key/supportive study	Species, Strain, Sex, No/ group	Test substance (including purity), Vehicle, Dose levels, Duration of exposure	NOAEL, LOAEL	Results (all dose levels including severity and magnitude of all effects, including also target organs)	Remarks (e.g. major deviations)	Reference
Sub-chronic oral toxicity study Route of exposure: gavage OECD 408 GLP: Yes Reliability: 1 Key study	Rat Crl:CD®(SD) IGS BR M/F 10/sex/ group	Oxone® Monopersulphate Compound Vehicle: deionised water 0, 25, 200, and 600/1000 mg/kg bw (0, 2.5, 20, 60/100 mg/mL) Gavage 7d/week 13 weeks Functional and observational battery and	NOAEL 200 mg/kg bw/day (20 mg/mL) LOAEL: 600 mg/kg bw/day (60 mg/mL)	Clinical signs: Salivation, piloerection, abnormal gait, gasping, hunched posture, noisy respiration, wet coat, and paddling of forepaws were mostly noted at the highest concentration. Mortality: At 1000 mg/kg bw/day, 3 males and 1 female were humanely sacrificed in weeks 3 and 4. Body weight: Decreased body weight was noted in males for all test concentrations. Food consumption: Reduced food consumption was noted in males at the highest test concentration. Food conversion efficiency: Lower food conversion efficiency was noted for animals at the highest	Due to 4 unscheduled deaths, the highest test dose of 1000 mg/kg bw was reduced to 600 mg/kg bw after 4 weeks of treatment	Anonymous 2002a

		motor activity assessments were performed during the study before initiation of treatment and during the 12th week of treatment. A shortened battery was performed during weeks 11 and week 13.		test concentration. Water consumption: No changes were observed. Haematology and clinical chemistry: No adverse treatment related changes were noted. Organ weights (bw adjusted): Higher group mean liver (males and female) and adrenal weights (males) were noted but either not considered adverse or related to treatment. Macroscopic/microscopic examination: Decedents: Congested GIT and necrotic and inflammatory lesion of the stomach and the small intestine were considered factors contributing to death. Survivors: Thickening of the forestomach and inflammation, oedema, haemorrhage in the mucosal and submucosal areas, epithelial necrosis, ulceration and hyperplasia were noted at the highest test concentration. The effects observed can be attributed to local oxidative reaction at the site of first contact. No signs of true systemic toxicity were observed in the study. No behavioural changes were noted which are considered to be indicative for neurotoxicity.		

In a sub-chronic oral toxicity study, rats received 0, 25, 200 and 1000 mg/kg bw/day Oxone® Monopersulphate Compound/mL (concentrations 0, 2.5, 20 and 200 mg/mL) 7 days per week for 13 weeks. Due to 4 unscheduled deaths in weeks 3 and 4, the highest

dose was reduced to 600 mg/kg bw/day at the end of week 4.

In all 4 decedent animals, necrotic and inflammatory lesions of the stomach and the small intestine were considered factors contributing to death.

Histopathological changes were evident in surviving animals receiving Oxone® Monopersulphate Compound (KMPS) at concentrations of 1000/600 mg/kg bw/day for 13 weeks. The target organ was identified as the stomach with inflammatory, degenerative and hyperplastic changes mainly in the forestomach (findings including inflammation, oedema, haemorrhage in the mucosal and submucosal areas, epithelial necrosis and ulceration, and epithelial hyperplasia). Related macropathological changes such as thickening of the forestomach were also apparent. No histopathological changes were noted at 25 or 200 mg/kg bw/day.

The pathological findings seen in the stomach are considered to be a direct local effect following bolus administration and the oxidative reaction mechanisms of KMPS at the site of first contact, and are as such not considered to be associated with systemic toxicity.

Post-dosing salivation was noted for all animals at 1000 mg/kg bw/day and also noted among animals receiving 200 mg/kg bw/day. During the 4th week of treatment with 1000 mg/kg bw/day in some rats a transient piloerection, abnormal gait, gasping and hunched posture were noticed 1-2 h after intake. During the first 4 weeks of treatment, some animals showed pronounced lung sounds. Incidences of wet coat, paddling of forepaws and piloerection were noted among animals receiving 600 mg/kg bw/day during week 12 and 13. The signs (except pronounced lung sounds) are behavioural signs attributed to severe pain and inflammatory response at the point of contact (nonglandular stomach when dosed via gavage).

Higher body weight adjusted group mean liver (males and female) and adrenal (males) weights were noted but either not considered adverse or related to treatment.

There were no adverse treatment related changes in clinical chemistry parameters or haematology.

Rats receiving Oxone® Monopersulphate Compound up to and including the highest concentration of 1000/600 mg/kg bw/day showed no signs of systemic toxicity. The effects observed at doses of 1000/600 mg/kg bw/day (LOAEL) were lesions of the stomach, which are a consequence of the direct local effect following bolus administration of Oxone® Monopersulphate Compound. Thus, the NOAEL is considered to be 200 mg/kg bw/day.

Systemic effects noted at 600 mg/kg bw/day including decreased body weights, food consumption, and food conversion efficiency are considered to be secondary to corrosive/irritative effects at the site of entry into organism and not related to primary toxicity. This is plausible based on the mode of action of KMPS.

Functional and observational battery and motor activity assessments were performed during the study before initiation of treatment

and during the 12th week of treatment.

A shortened battery was performed during weeks 11 and week 13. No behavioural changes were noted which are considered to be indicative for neurotoxicity.

No data on human sub-chronic oral toxicity of KMPS is available.

A.3.7.2.2. Sub-chronic dermal toxicity

No animal or human data on sub-chronic dermal toxicity is available for KMPS.

A.3.7.2.3. Sub-chronic inhalation toxicity

No animal or human data on sub-chronic inhalation toxicity is available for KMPS.

A.3.7.3. Long-term repeated dose toxicity

A.3.7.3.1. Long-term oral toxicity

No animal or human data on long-term oral toxicity is available for KMPS.

A.3.7.3.2. Long-term dermal toxicity

No animal or human data on long-term dermal toxicity is available for KMPS.

A.3.7.3.3. Long-term inhalation toxicity

No animal or human data on long-term inhalation toxicity is available for KMPS.

A.3.7.4. Specific target organ toxicity – repeated exposure (STOT RE)

A.3.7.4.1. Short summary and overall relevance of the provided information on STOT RE

For KMPS, one 14-day and one 90-day oral toxicity study in rats, one 14-day inhalation toxicity study in rats and developmental toxicity study in rats are available. No chronic studies have been performed with KMPS.

No effect relevant for classification of KMPS as STOT RE 1 or 2 were observed in 14-day and 90-day oral toxicity studies in rats and developmental toxicity study in rats. Due to its oxidative and corrosive/irritating properties, KMPS will cause destruction of mucous membranes at the point of contact in nonglandular stomach when applied via gavage. These effects are considered to be of local nature due to the reaction of the substance with the surrounding tissue. Systemic toxicity would therefore occur only secondary to locally irritating effects at the site of first contact. In the available studies there are no indications for any other mechanism of toxicity than the local corrosion/irritation. Since this mode of action is chemically driven, it is not species specific.

Moreover, breakdown products of KMPS are potassium and sulphate ions, which are both hydrophilic essential metabolites. Bioaccumulation of the degradation products in the body is thus not expected. Application of KMPS in concentrations which do not cause irritation/corrosion, results in physiological concentrations of potassium and sulphate ions. Thus, no adverse effects besides the local corrosion/irritation are expected.

The clinical signs of piloerection, abnormal gait, gasping, hunched posture, were noted 1-2h after dosing. Thus, the onset of the clinical signs is directly related to dosing rather than a systemic effect. The signs are behavioural signs attributed to severe pain and inflammatory response at the point of contact (nonglandular stomach when dosed via gavage).

Kidneys were examined in the 14-days oral toxicity study, the 90-days oral toxicity study and the developmental toxicity study. Cysts in kidneys were reported in the 14-days oral toxicity study and showed a non-dose dependent incidence: in the highest group (1000 mg/kg bw/day) 1/3 females had cysts and in the medium group (400 mg/kg bw/day) 2/3 females and 2/3 males. Cysts in kidneys were reported in the 90-days oral toxicity study only in the control group (3/10 females). Kidneys were also examined in the 14-days inhalation study. However, no cysts in kidneys were reported. Based on the overall data set, the incidence of cysts in kidneys are not considered test-substance related but a random finding.

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.

A.3.7.4.2. Comparison with the CLP criteria

From the oral repeated dose toxicity studies there was no clear evidence of (non-lethal) effects on a specific target organ or tissues.

From inhalation toxicity studies, the effects on eyes are considered relevant for classification.

According to Regulation (EC) 1272/2008 (Annex 3.9.1), substances can be classified for STOT RE in Category 1 based on observations from appropriate studies in experimental animals in which significant and/or severe toxic effects, of relevance to human health, were produced at generally low exposure concentrations. Guidance dose/concentration for inhalation exposure considered applicable for

subacute inhalation study is C ≤ 0.06 mg/litre/6h/day. The eye effects in this study can be considered severe and relevant to human health. Exposure concentrations where effects occurred were 0.0101 and 0.0431 mg/L/6h/day which are below the guidance concentration of 0.06 mg/litre/6h/day.

Additional considerations are set out in CLP Guidance (Section 3.9.2.5.1, p. 470):

"Substances (or mixtures) classified as corrosive may cause severe toxicological effects following repeated exposure, especially in the lungs following inhalation exposure. In such cases, it has to be evaluated whether the severe effect is a reflection of true repeated exposure toxicity or whether it is in fact just acute toxicity (i.e. corrosivity). One way to distinguish between these possibilities is to consider the dose level which causes the toxicity. If the dose is more than half an order of magnitude lower than that mediating the evident acute toxicity (corrosivity) then it could be considered to be a repeated-dose effect distinct from the acute toxicity. In this case, classification as specific target organ toxicant (repeated exposure) would be warranted even if the substance (or mixture) is also classified as acutely toxic and/or corrosive.

In assessing non systemic effects caused by irritating/corrosive substances it should be kept in mind, that the guidance values /criteria for STOT-RE of the CLP were derived from acute toxicity criteria (lethality based) assuming that systemic effects show a time dependent increase of severity due to accumulation of toxicity and taking also adaptive and detoxification processes into account. The effect considered in this context was lethality. This indicates that classification was intended for the presence of severe health damage, only. (see ECBI/67/00, (2000) in EU Commission Summary Record of Meeting of the Commission Working Group on C&L of Dangerous Substances ECBI/44/01)."

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.

Classification STOT RE 1, H372 for local ocular effects is therefore proposed.

A.3.7.4.3. Conclusion on classification and labelling for STOT RE

KMPS warrants classification STOT RE Category 1, H372 "Causes damage to organs (eyes) trough prolonged or repeated exposure" according to CLP Regulation.

A.3.8. Genotoxicity / Germ cell mutagenicity

A.3.8.1. *In vitro*

Table A.26 Summary table of *in vitro* genotoxicity studies

Summary table of in vitro genotoxicity studies					
Method, Guideline, GLP status, Reliability, Key/supportive study	Test substance (including purity), Vehicle, Doses	Relevant information about the study (e.g. organism (e.g. bacteria), cell type, strains)	Results (including cytotoxicity and +/-S9 mix)	Remarks (e.g. major deviations)	Reference

Bacterial reverse mutation test (Ames Test) OECD 471 GLP: Yes Reliability: 1 Key study	Oxone® Monopersulphate Compound Vehicle: deionised water 5 to 5000 µg/plate First test (range finding): +S9 mix/-S9 mix: 5000, 1500, 500, 150, 50, 15 and 5 µg/plate Main test: +S9 mix: 5000, 1500, 500, 150 and 50 µg/plate, -S9 mix: 500, 150, 50, 15 and 5 µg/plate	*Salmonella typhimurium,* TA1535, TA1537, TA98, TA100 and *Escherichia coli* WP2 Positive controls: +S9 mix: 2-Aminoanthracene, Benzo[a]pyrene -S9 mix: Sodium azide, 9-Aminoacridine, 2-Nitrofluorene, 2-(2-Furyl)-3-(5-nitro -2-furyl)acrylamide 2 independent tests (plate incorporation and pre-incubation test) were performed	Not mutagenic No increase in number of revertant colonies was observed under study conditions in the presence or absence of metabolic activation (S9 mix). Cytotoxicity: - in all strains at 5000 µg/pl. (+S9 mix) - in E. coli at 1500 µg/pl. (-S9 mix) in *S. typhimurium* at 500 µg/pl. (-S9 mix)	/	Anonymous 2001e
Mammalian chromosome aberration test OECD 473 GLP: Yes Reliability: 1 Key study	Oxone® Monopersulphate Compound Vehicle: water First test: +S9 mix/-S9 mix: 312.5, 625 and 1250 µg/mL Second test:	Human peripheral blood lymphocytes Positive controls: +S9 mix: cyclophosphamide -S9 mix: Mitomycin C	KMPS increased the frequency of chromosomal aberrations under the test conditions. Positive in the presence and absence of S9. No increase in polyploid cells was noted. Clastogenic effects: at 1250 µg/mL (+S9 mix/-S9 mix)	Deviations: continuous treatment with test substance not performed (1.5 cell cycle), only 200 metaphases scored	Anonymous 2001f

	+S9 mix/-S9 mix: 0, 500, 1000 and 1250 µg/mL Treatment time: 3 h Recovery time: 17 h		Reduction in the mitotic index to 52% (-S9 mix) and 45% (+S9 mix) of the solvent control at 1250 µg of KMPS/mL		
In vitro mammalian cell gene mutation assay OECD 476 GLP: Yes Reliability: 1 Key study	Oxone® Monopersulphate Compound Vehicle: water <u>Preliminary test</u>: +S9 mix/-S9 mix: 39-5000 µg/mL <u>Test 1</u>: +S9 mix: 200-1200 µg/mL, -S9 mix: 100-800 µg/mL <u>Test 2</u>: +S9 mix: 200-1000 µg/mL, -S9 mix: 200-700 µg/mL	Mouse lymphoma L5178Y cells (TK±) <u>Positive controls</u>: +S9 mix: 3Methylcholanthrene -S9 mix: Methylmethanesulphonate	KMPS induced gene mutations under conditions of this test in the presence and absence of metabolic activation (S9 mix). Positive results were noted at the following test concentrations: <u>Test 1</u>: +S9 mix: 600 or 800 µg/mL, -S9 mix: 400 or 500 µg/mL <u>Test 2</u>: +S9 mix: 700 or 800 µg/mL -S9 mix: 400 – 600 µg/mL	Deviations: RS (relative survival) used to measure cytotoxicity, mutant frequency of negative control above the recommended acceptable spontaneous mutant frequency, colony sizing not performed; mutant frequency in control groups was within the HCD range.	Anonymous 2002b
In vitro mammalian cell gene mutation assay OECD 490	Oxone™ Monopersulfate Compound Purity: > 90% (93.07%)	Mouse lymphoma L5178Y cells ($TK^{+/-}$) Positive controls: +S9 mix: B[a]P	KMPS did not increase mutant formation under conditions of this test in the presence and absence of metabolic activation (S9 mix). The test item was neither	Large and small colonies were differentiated allowing the assessment for both mutagenic	Anonymous 2019a

GLP: Yes Reliability: 1 Key study	Pre-experiment: + / - S9-mix: 25, 50, 150, 500, 1000, 2000 µg/mL Main test: + / - S9-mix: 50, 100, 125, 250, 500, 1000 and 2000 µg/mL	-S9 mix: Methylmethane-sulphonate and Ethylmethane-sulphonate	mutagenic nor clastogenic under the conditions of the study.	and clastogenic activity.	

A.3.8.2. *In vivo*

Table A.27 Summary table of *in vivo* genotoxicity studies

Summary table of in vivo genotoxicity studies					
Method, duration of study, Guideline, GLP status, Reliability, Key/supportive study	Test substance (including purity), Vehicle, Doses	Relevant information about the study (e.g. species and strain, sex, no per group, route, frequency of application, sampling times, duration of exposure)	Main effects, Observations (specify regarding dose and sampling time)	Remarks (e.g. major deviations)	Reference

Mammalian Erythrocyte Mouse Micronucleus Test OECD 474 GLP: Yes Reliability: 1 Key study	Oxone® Monopersulphate Compound Preliminary study: 1500, 1750, 2000 mg/kg bw (corresponding to 75, 87.5, 100 mg/mL) Main study: Males: 0, 437.5, 875, 1750 mg/kg bw (corresponding to 0, 21.88, 43.75, 87.5 mg/mL) Females: 0, 500, 1000, 2000 mg/kg bw (corresponding to 0, 25, 50, 100 mg/mL) Positive control: Mitomycin C: 12 mg/kg bw	Mouse CD-1 Preliminary study: 2/sex/group Main study: 5/sex/group 12/sex/ group for 1750 mg/kg bw (males) and 2000 mg/kg bw (females) Single exposure by gavage Post-exposure period: 24, 48 h	Clinical signs: At 1750 mg/kg bw (males) and 2000 mg/kg bw (females), fast and irregular respiration, flat and hunched posture, underactivity, abnormal gait, partially closed eyes, piloerection/ungroomed and incidence of weight loss was recorded. No significant increase in number of micronucleated immature (polychromatic) or mature (normochromatic) erythrocytes at either sampling time in male and female animals (P>0.01). No significant decrease in the proportion of immature erythrocytes at either sampling time in male animals (P>0.01). Statistically significant decrease in the proportion of immature erythrocytes at the 24 h sampling time was observed in female animals, but not at 48 h sampling interval.	Reduction in the PCE/(PCE+NCE) ratio in female mice at the 24 h sampling time is considered to be a direct consequence of the local toxicity of KMPS rather than related to systemic toxicity. These signs were noted during the first 24 hours of treatment which is consistent with the observations made in the acute oral study in rats. Deviations: 2000 PCE scored for the presence of micronuclei Concentration and stability of the dosing solutions was not assessed during the study.	Anonymous 2001g
***In vivo* Mammalian Alkaline Comet Assay** OECD 489 GLP: Yes	Oxone™ Monopersulfate Compound Purity: 89.55%	Rat Crl: WI (Han) Preliminary study:	Result: The test item tested negative for the induction of DNA breaks in any of the tissues evaluated, under the conditions of this study.	Devation: Limited HCD for forestomach (6 studies negative control, 9 studies positive control)	Anonymous 2021

Reliability: 1	Preliminary study: 75, 125, 250, 500, 750, 1000 and 2000 mg/kg bw, 1 animal/sex/dose, except 3 animals/sex/dose at 750 mg/kg bwMain study: 0, 150, 300, 600, 750 mg/kg bw Positive control: Ethyl methanesulfonate: 250 mg/kg bw	Both sexes Main study: 5 males per group	Preliminary study: Dose-range finding study determined no sex differences in toxicity and identified 750 mg/kg bw as maximum tolerated dose. Clinical signs: No signs at 150 and 300 mg/kg bw. Reduced spontaneous activity at 600 mg/kg bw. At 750 mg/kg bw, reduced spontaneous activity after first administration, and reduction of spontaneous activity, prone position and ataxia after second administration. Body weight: Total body weight variation in the main experiment was 7.5 %. While control gained weight (4/5 animals), weight loss was noted after application of the test substance at all concentrations. Histopathology and comet assay: Liver, forestomach, glandular stomach and duodenum were investigated histopathologically and DNA breaks in those organs were analysed using the alkaline comet assay. Histopathology: The test item caused inflammatory and reactive lesions in a dose dependent		

			manner in the stomach at doses ≥ 300 mg/kg bw and in the duodenum at doses ≥ 600 mg/kg bw. In forestomach inflammation was observed in only one treated animal (at the dose of 600 mg/kg); in glandular stomach inflammation was observed in 3 out of 5 animals in the top dose of 750 mg/kg. Inflammation was scored as mild to slight. Comet assay: Results shown as tail intensity. Negative control was within historical negative control data. Positive control showed a significant increase in tail intensity in all organs analysed. Test item showed no increase in tail intensity in no organ.		

No human data on *in vivo* genotoxicity of KMPS is available.

A.3.8.2.1. Short summary and overall relevance of the provided information on germ cell mutagenicity

Bacterial reverse mutation test (Ames test)

A key study on mutagenicity in bacteria was with Oxone® Monopersulphate compound (KMPS) conducted on *Salmonella typhimurium* strains TA1535, TA1537, TA98, TA100 and *Escherichia coli* strain WP2 with and without a metabolic activation system. Cytotoxicity was observed in the definitive assay in all strains at the highest concentration of 5000 μg of Oxone® Monopersulphate Compound/plate with metabolic activation and in strains, TA1535, TA1537, TA98 and TA100 at 500 μg Oxone® Monopersulphate Compound/plate without metabolic activation. Under the test conditions of the study, Oxone® Monopersulphate Compound (KMPS) did not show mutagenic activity.

Mammalian chromosome aberration test

Oxone® Monopersulphate Compound (KMPS) was tested for structural and numerical chromosomal aberrations in human blood lymphocytes in the presence and absence of a metabolic activation system. The concentrations tested were: 312.5, 625 and 1250 µg of Oxone® Monopersulphate Compound/mL (first test), and 500, 1000 and 1250 µg of Oxone® Monopersulphate Compound /mL (second test) with and without S9 mix. Oxone® Monopersulphate Compound was found to have clastogenic activity at 1250 µg/mL when compared with control value in the presence and absence of metabolic activation that contained only vehicle.

In the first test, Oxone® Monopersulphate Compound caused a reduction in the mitotic index to 53% of the vehicle control, both in the presence and absence of S9 mix.

In the second test, a clastogenic activity was also found at 1250 µg of Oxone® Monopersulphate Compound/mL with and without S9 mix when compared with control value that contained only vehicle. Oxone® Monopersulphate Compound caused a reduction in the mitotic index to 52% of the vehicle control in the absence of S9 mix and 45% in the presence of S9 mix.

In both tests, Oxone® Monopersulphate Compound caused a significant increase in the proportions of cells with chromosomal aberrations at 1250 µg/mL (with and without S9 mix), when compared to the control (vehicle) value. Under these experimental conditions, Oxone® Monopersulphate Compound is found to have clastogenic activity *in vitro*, in both the presence and absence of S9 mix.

Both tests showed no statistically significant increase in the number of polyploid metaphase cells when compared with the solvent control, i.e. no increase in numerical chromosomal aberrations was noted for Oxone® Monopersulphate Compound.

Mammalian cell gene mutation assay

Oxone® Monopersulphate Compound (KMPS) was tested for mutagenicity potential in mouse lymphoma L5178Y cells ($TK^{+/-}$). Cells were exposed to different concentrations of the test substance in the presence and absence of S9 mix. S9 mix was prepared from liver cells pre-treated with Aroclor 1254. Concentrations of Oxone® Monopersulphate Compound ranged from 39-5000 µg/mL. After a period of time, cells were incubated with trifluorethymidine, a selective agent that monitors the loss of functional $TK^{+/-}$ enzyme. Cell deficient in TK locus are resistant to toxic effects of TFT and do proliferate in the presence of TFT, whereas the non-mutant cells are not able to proliferate. The highest dose tested was selected based on RS (relative survival) and not on RTG (relative total growth) which is a more reliable indicator of cytotoxicity.

In Test 1, mean mutant frequencies at 400 or 500 µg/mL Oxone® Monopersulphate Compound were significantly increased without S9 mix, compared to control. Mean mutant frequencies were also increased at 600 or 800 µg/mL Oxone® Monopersulphate Compound in the presence of S9 mix. Number of induced mutants exceeded the global evaluation factor (GEF), indicating positive response in line with the currently valid guidance.

Test 2 confirmed the results of Test 1. Again, the statistically significant increase in the mean mutant frequencies was reported at 400 – 600 µg/mL Oxone® Monopersulphate Compound when no S9 mix was used. In the presence of S9 mix, the mean mutant frequencies were significantly elevated at 700 or 800 µg/mL Oxone® Monopersulphate Compound. This study deviates from the currently valid OECD 490 (2016) also in frequency of spontaneous mutants, which is higher as recommended in the guidance. However, in test 1 the recommended frequency is only slightly higher as recommended. Colony sizing was not performed in any test or control group.

In the 2nd study in mouse lymphoma L5178Y cells ($TK^{+/-}$), cells were exposed to different concentrations of the test item in the presence and absence of metabolic activation (S9-mix prepared from male Wistar rats induced with phenobarbital and beta-naphthoflavone). Concentrations ranged from 50 to 2000 µg/mL. After a period of time, cells were incubated with trifluorethymidine, a selective agent that monitors the loss of functional TK+/- enzyme. Cell deficient in TK locus are resistant to toxic effects of TFT and do proliferate in the presence of TFT, whereas the non-mutant cells are not able to proliferate. The second study was conducted taking into consideration the colony sizes to differentiate between mutagenic and clastogenic responses.

No precipitation of the test item was noted. No growth inhibition was observed both in the presence and absence of metabolic activation. No biologically relevant increase of mutants was found after treatment with the test item both in the presence and absence of metabolic activation. The global evaluation factor (GEF defined as the mean of the negative / vehicle mutant frequency plus one standard deviation) was not exceeded by the induced mutant frequency at any concentration. The positive controls showed distinct and biologically relevant effects in mutation frequency and showed the ability of the test system to differentiate between mutagenic and clastogenic responses. Thus, the test item was considered to be non-mutagenic and non-clastogenic under the conditions of the study.

The second mouse lymphoma assay (Anonymous, 2019a) did not confirm the result of the first study (Anonymous, 2002b), even though higher concentrations were tested in the second, fully OECD 490 GD compliant, study. Results of both gene mutation studies might differ due to presence of impurities in the test material, however, this can not be supported by any evidence since identity of batch used in study by Anonymous (2002) is not known. Additionally, the different toxicity may have been observed due to the use of different cells and different test protocols. The chromosomal aberration test by Allais (2001) was done in human lymphocytes. This is another type of cells than the cells used in the MLA studies. The Voges study was done as per OECD 490 (2016) whereas the Clare study was done as per OECD 476 (from 1997). Therefore, the two studies were not done according to the same protocol and therefore direct comparison between those two studies should be avoided.

Mammalian Erythrocyte Mouse Micronucleus Test

Oxone® Monopersulphate Compound (KMPS) was tested *in vivo* in CD-1 mice for the induction of micronuclei formation. At the highest doses tested (males: 1750 mg/kg bw; females: 2000 mg/kg bw, corresponding to KMPS concentrations of 87.5 and 100 mg/mL, respectively) no mortalities were observed. Males showed fast and irregular respiration, flat and hunched posture, underactivity, abnormal gait, partially closed eyes, piloerection/ungroomed and incidence of weight loss, whereas females showed

fast respiration, flat and hunched posture, underactivity, abnormal gait, partially closed eyes and piloerection/ungroomed.

No statistically significant increases in the frequency of micronucleated immature (polychromatic) and mature (normochromatic) erythrocytes were observed in mice of both sexes treated with Oxone® Monopersulphate Compound and killed 24 or 48 hours later, compared to vehicle control values.

No statistically significant decrease in the proportion of immature erythrocytes was recorded at either sampling time in male mice. In female mice, a significant decrease was observed at the highest treatment dose 2000 mg/kg bw at the 24 hour sampling time only, while no such effect was evident at the 48 hour sampling time point.

Reduction in the PCE/(PCE+NCE)-ratio observed in female mice at the highest concentration level at the 24 hour sampling time point could be a direct consequence of the local (acute) toxicity of KMPS rather than related to systemic toxicity. The oral doses given to male and female mice were in the range of the LD_{50} observed in rats and although no mortalities occurred in mice, there were clinical signs of toxicity evident at the top dose levels. These signs were noted during the first 24 hours of treatment which is consistent with the observations made in the acute oral study in rats. This supports the conclusion above that the decreased PCE/(PCE+NCE)-ratio at the high dose level of female mice at the 24 hours sampling time point is related to the acute toxicity of KMPS. Moreover, oral gavage represents a bolus administration and the test concentration of 100 mg/mL (which is clearly above the threshold for irritation) leads to damage of the stomach and upper gastrointestinal tract. Even moderate tissue or organ damage is expected to lead to leakage of food ingredients and gastric acid as well as to compromise efficient uptake of nutrients. Any alterations in the PCE/(PCE+NCE)-ratio are therefore considered to be secondary to the sound local toxicity of KMPS after bolus administration. Due to the uncertainty with regard to the availability of the test substance at the target organ, the biological significance of this result is questionable.

***In vivo* Mammalian Alkaline Comet Assay**

Moreover, KMPS was tested *in vivo* in Crl: WI (Han) Wistar rats for the induction of DNA breaks. As identified in the dose-range finding experiment, the maximum tolerable dose was 750 mg/kg bw and no sex differences in toxicity were present. Therefore, only males were used for the main experiment. In dose range finding study animals were treated with 75, 125, 250, 500, 750, 1000 and 2000 mg/kg bw. At 2000 mg/kg bw reduced spontaneous activity and, piloerection, ataxia, half eyelid closure and lacrimation were observed. At 1000 mg/kg bw the same clinical signes were reported. Additionally, dark reddened stomach mucosa and stomach dilated with gas were seen. At next lower dose 750 mg/kg bw/d prone position, reduced spontaneous activity, ataxia, piloerection, half eyelid closure, moving the bedding and hunched posturewere reported. No difference between sexes were found. According to the histopathological analysis, the test item caused inflammatory and degenerative lesion in the stomach from 250 mg/kg bw onwards. The findings consisted of increased mixed inflammatory cell foci in the submucosa up to 500 mg/kg bw. Moreover, with increasing dose, from 750 mg/kg bw onwards, there were subacute submucosal inflammation associated with edema, erosion and/or ulceration in the stomach. The findings in the stomach at a dose of 750 mg/kg bw were considered adverse in nature. Based on these results doses selected for the main study were 150, 300, 600 and 750 mg/kg bw to demonstrate a dose-dependency in

histopathological findings and to induce clinical symptoms in the highest dose of 750 mg/kg bw.

Comet assay was performed on forestomach, duodenum and glandular stomach to observe genotoxicity at site of first contact and on liver cells as tissue indicative of systemic genotoxicity.
In the main test at the highest doses tested (750 mg/kg bw) no mortalities were observed. Animals treated with the test item showed reduced spontaneous activity at 600 mg/kg bw and 750 mg/kg bw. In addition, prone position and ataxia were observed at 750 mg/kg bw. Histopathology revealed inflammatory and reactive lesions caused by the test item in a dose dependent manner in the stomach at doses ≥ 300 mg/kg bw and in the duodenum at doses ≥ 600 mg/kg bw.

The alkaline comet assay detected no increases in DNA breaks in liver, forestomach, glandular stomach and duodenum after administration of the test item when compared to the vehicle control thereby demonstrating the lack of gene mutating and clastogenic potential of KMPS *in vivo* at site of first contact and systemically.

Other *in vivo* genotoxicity studies

No second *in vivo* genotoxicity study, studies investigating germ cell effects or further testing for genotoxicity of metabolites are necessary due to the local mode of action of KMPS and the rapid degradation to physiological potassium and sulphate ions which are non-genotoxic.

No human data on *in vivo* genotoxicity of KMPS is available.

A.3.8.2.2. Comparison with the CLP criteria

KMPS did not increase the number of revertant colonies in an in vitro bacterial reverse mutation assay (Ames test).

KMPS increased the formation of chromosomal aberrations in human peripheral blood lymphocytes and the number of gene mutations in mouse lymphoma cells *in vitro* in one assay. A more recent mouse lymphoma assay, fully guideline compliant and performed with higher dose of KMPS was also performed. Study result was clearly negative.

The positive findings in mammalian cell cytogenicity and gene mutation assay are considered to be a consequence of the oxidative nature of KMPS resulting in an impairment of the cellular physiology in *in vitro* systems. *In vitro*, the oxidizing KMPS has direct access to the DNA, resulting in mutations and chromosomal aberrations.

In an *in vivo* mouse micronucleus test performed with KMPS, no increase in micronucleated immature (PCE) or mature (NCE) erythrocytes was observed under study conditions. A significant decrease in PCE/(PCE+NCE)-ratio was reported in females at 24 hrs

post-application. Due to the local mode of action of KMPS it is questionable if decrease in PCE/(PCE+NCE)-ratio is a result of acute local toxicity of KMPS or a sporadic finding.

In order to demonstrate the lack of genotoxic activity of KMPS *in vivo*, at site of first contact and systemically, an in vivo rat Comet assay was conducted. In the in vivo Comet assay no indication of DNA-damage was observed in all four organs investigated (liver, forestomach, glandular stomach, and duodenum) covering both the first site of contact and the metabolism organs. The dose levels in this study were up to and including the maximum tolerated dose (MTD) of 750 mg/kg bw as determined by respective organ damage. For example, in the duodenum mucosal degeneration and mucosal hyperplasia were noted at the MTD and below. In the glandular stomach acute inflammation and mucosal necrosis together with bloody stomach were noted at the MTD. Likewise in the forestomach hyperkeratosis at the MTD and below. Negative result of Comet assay indicated that KMPS did not induce chromosomal aberrations or gene mutations *in vivo* under study conditions.

In vivo genotoxicity study investigating germ cell effects or further testing for genotoxicity of metabolites are not necessary due to the negative outcome of *in vivo* micronucleus assay and comet assay, local mode of action of KMPS and the rapid degradation to physiological potassium and sulphate ions which are non-genotoxic.

Conclusion on classification and labelling for germ cell mutagenicity

No classification of KMPS is warranted for genotoxicity according to CLP Regulation.

A.3.9. Carcinogenicity

No animal or human data on carcinogenicity is available for KMPS.

A.3.9.1. Short summary and overall relevance of the provided information on carcinogenicity

No animal or human data on carcinogenicity is available for KMPS. Based on the available data from the 14- and 90-day oral repeated dose toxicity studies in rats, the in vivo genotoxicity study in mice, and the in vivo Comet assay in rats, KMPS is considered to act via a local mode of action based on direct chemical reactivity only. Any potential systemic effects are considered to be secondary to the local irritation/corrosion caused by KMPS at the site of first contact. There is no indication for a carcinogenic potential of KMPS as shown in an *in vivo* genotoxicity studies.

In view of data from 90 day subchronic oral toxicity study (thickening of the forestomach and inflammation, oedema, haemorrhage in the mucosal and submucosal areas, epithelial necrosis, ulceration and hyperplasia were noted at the highest test concentration in

surviving animals) it is important to clarify possible non-genotoxic mode of action (MOA) of KMPS in relation to carcinogenic potential.

The corrosivity of a strong oxidizer like KPMS is different compared to strong acids and strong bases. KMPS releases reactive oxygen, which oxidizes macromolecules of the cell wall and membranes in unspecific manner leading to the cell wall disruption and loss of membrane integrity. In addition, after penetration into cells, intracellular molecules such as amino acids, polypeptides, RNA and DNA are also oxidized leading to the disruption of protein synthesis and cell death. KMPS shares a MOA with other approved peroxygen active substances, peracetic acid and hydrogen peroxide, which is the release of reactive oxygen species (ROS) and oxidation of organic material at the site of first contact leading to local corrosion/irritation. Many cancers arise from sites of chronic irritation, infection, or inflammation. Recent data have expanded the concept that inflammation is a critical component of tumour progression. ROS-sensitive signalling pathways are persistently elevated in many types of cancers, where they participate in cell growth/proliferation, differentiation, protein synthesis, glucose metabolism, cell survival and inflammation (Anonymous, 2010). ROS, particularly hydrogen peroxide, can act as second messengers in cellular signalling. A well-known MOA for non-genotoxic carcinogenesis is sustained cytotoxicity and related regenerative proliferation. Within the MOA sustained cytotoxicity, oxidative stress represents a central event.

To facilitate risk assessment, Anonymous (2018d) and Anonymous (2018b) have used the MOA for ethyl acrylate (EA) and forestomach tumours caused by non-genotoxic initiating events, to develop Adverse Outcome Pathways (AOPs). For EA, a pre-molecular initiating event (pre-MIE) of sustained glutathione depletion is probable. Especially relevant for EA is the assessment of the threshold leading to critical GSH depletion, followed by inflammation, cytotoxicity, and hyperplasia. These AOPs are applicable for hazard identification, risk assessment and human relevance assessment for other chemicals that also act by these AOP, possibly KMPS.

Indirect non-genotoxic MOAs of carcinogenicity by definition involve a precursor key event other than DNA reactivity i.e. a test substance dose below which the molecular initiating event is not triggered and/or the sequence of key events will not progress so that tumour formation is prevented (Anonymous, 2018c; Anonymous, 2021). In the 90-day oral toxicity study in rats at the highest concentration of KMPS, the initiating event after the reactive oxygen *in situ* was released from KMPS at the site of gavage dosing in the forestomach, may have been a depletion of glutathione (GSH) in the mucosal cell lining of the intestinal tract. The later than lead to an increase in epithelial damage, hyperplasia, and inflammation. Glutathione is known to be at the forefront in cell defense against oxidative stress that results from a free radical overload. It works with other antioxidants to preserve the functions of several vital proteins that are susceptible to oxidative damage, thereby rescuing cells from stress induced apoptosis. The enzymes involved in GSH redox cycling are important for both cellular free radical and non-radical detoxification (Anonymous, 2021b). Anonymous (1992) have shown that cells maintain the steady state balance of GSH as protective mechanism to prevent cytotoxicity and toxic responses in tissues remote from the dosing site.

An important topic of discussion, in particular in the area of carcinogenicity, is the human relevance of tumours observed in rodents.

To address this issue, the WHO International Programme on Chemical Safety developed a conceptual framework for assessment of species concordance. According to this framework, assessment of human relevance should address the plausibility of a hypothesized MOA based on a thorough weight-of-evidence evaluation including mode-of-action/species concordance analysis (Anonymous, 2020c). The utility of rodent forestomach tumour data for hazard and risk has been examined for decades because humans do not have a forestomach, and these tumours occur by varying modes of action (MOAs) (Anonymous, 2018b). Identification of non-genotoxic carcinogens (NGTXC) is difficult compared to genotoxic substances and has traditionally relied on rodent carcinogenicity assay, but there is considerable scientific doubt regarding the reliability of the model due to a high number of false positive results arising from long-term exposure of animals to high doses of the test substance and a low reproducibility making relevance to human risk assessment questionable (Anonymous, 2020b). Further supporting in this matter is the Guidance on BPR: Volume III Parts B+C (Version 4.0, December 2017, p. 241) where the relevance of the rat forestomach irritation for human risk assessment is questioned. There are differences in pH and epithelia structure between human stomach and rodent forestomach, but probably most important, the contact time between the oesophagus epithelium and ingested material is negligible in humans when compared to the rodents' forestomach, which functions as a storage organ. It was suggested that only those part of GI tract should be included in human risk assessment that have counterpart in humans, such as oral cavity, pharynx and oesophagus, glandular stomach, or intestine.

Leaving the forestomach out of consideration, which is the target organ in the 90-day rodent study, necrotic and inflammatory lesions of the glandular stomach and the small intestine were reported in the decedent animals exposed to 1000 mg/kg bw/day. These lesions were considered to be factors contributory to death. No pathological changes related to treatment were identified in animals receiving 200 mg/kg bw/day. The complete absence of any effect of treatment at this dose level indicates a steep dose-response curve between 200 and 1000 mg/kg bw/day. No treatment-related signs of inflammation, necrosis, and hyperplasia were reported in glandular stomach and the small intestine of the surviving animals. Therefore, a non-genotoxic MOA for carcinogenicity relevant to humans is not expected.

In view of the 90-day oral gavage study results discussed above, KMPS MOA, as well as the possible applicability of AOPs presented by substances with similar initiating events and adverse outcomes, a non-genotoxic MOA for KMPS for carcinogenicity is not expected to be relevant for human hazard and risk assessment.

A.3.9.2. Comparison with the CLP criteria

No carcinogenicity study has been performed with KMPS. KMPS is not considered carcinogenic based on weight of evidence approach.

A.3.9.3. Conclusion on classification and labelling for carcinogenicity

No classification of KMPS is warranted for carcinogenicity according to CLP Regulation.

A.3.10. Reproductive toxicity

A.3.10.1. Sexual function and fertility

No animal or human data on effects on fertility is available for KMPS.

A.3.10.1.1. Short summary and overall relevance of the provided information on adverse effects on sexual function and fertility

No animal or human data on effects on fertility is available for KMPS.
Due to its oxidative and corrosive/irritative properties, KMPS will cause destruction of skin and mucous membranes of the respiratory tract when applied topically or inhaled. These effects are considered to be of local nature due to the reaction of the substance with the surrounding tissue. Systemic toxicity would therefore occur only secondary to locally irritating effects. In the available studies there are no indications for any other mechanism of toxicity than the local corrosion/irritation. Since this mode of action is chemically driven, it is not species specific.
Moreover, breakdown products of KMPS are potassium and sulphate ions, which are both hydrophilic physiological metabolites. Bioaccumulation of the degradation products in the body is thus not expected. Application of KMPS in concentrations which do not cause irritation/corrosion, results in physiological concentrations of potassium and sulphate ions. Thus, no adverse effects besides the local corrosion/irritation are expected.
KMPS did not show any systemic effects in the two oral repeated dose studies in rats presented in chapters 3.5.1 and 3.6.1 and in the teratogenicity study in rats (chapter 3.10.1). Since KMPS is rapidly degraded to physiological metabolites (i.e. potassium and sulphate), it can be predicted that the embryo/foetus will not be exposed to any high levels of KMPS.
The predominant toxicological effect observed in the 14-day and 90-day studies in rats as well as in the teratology study in rats was local irritation/corrosion of the stomach. This mode of action is strictly concentration dependent, limited to the site of first contact, and not specific to any particular mammalian species or organ. Notably, it is not depend on toxicokinetic or toxicodynamic parameters. Thus, systemic exposure of the embryo/foetus does not occur and any potential systemic effects are considered to be only secondary to changes in the gastrointestinal tract.
Notably, the active substance is not genotoxic *in vivo* neither at the first site of contact nor systemically.

A.3.10.1.2. Comparison with the CLP criteria

KMPS is not considered to have adverse effects on sexual function and fertility.

A.3.10.2. Developmental toxicity

Table A.28 Summary table of animal studies on adverse effects on development

Summary table of animal studies on adverse effects on development							
Method, Duration of exposure, Route of exposure, Guideline, GLP status, Reliability, Key/supportive study	Species, Strain, Sex, No/ group	Test substance (including purity), Vehicle, Dose levels,	NOAELs, LOAELs (e.g. maternal, teratogenicity, embryotoxicity, offspring, parental, reproductive toxicity)	Results, maternal/parental (e.g. corrected body weight gain, for all dose levels)	Results, developmental (e.g. pup survival, structural abnormalities, altered growth, functional deficiencies, incidences and severity of the effects for all dose levels)	Remarks (e.g. major deviations)	Reference
Developmental Toxicity Study in Rats OECD 414 GLP: Yes Reliability: 1	Rat Crl:CD®(SD)IGS BR Females 22/dose	Oxone® Monopersulphate Compound Purity: 95.4% 0, 75, 250, 750 mg/kg bw/day (corresponding to¸0, 7.5, 25, 75 mg/mL)	Maternal NOAEL: 250 mg/kg bw/day (corresponding to NOAEC 25 mg/mL) Maternal LOAEL 750 mg/kg bw/day (corresponding to LOAEC 75 mg/mL); based on body weight gain, food consumption and	At 750 mg/kg bw/day: significant decrease in body weight gain and food consumption was noted as well as thickening of non-glandular stomach (4/22), red	The mean number of corpora lutea, implanation sites, resorptions, live foetuses and sex ratio were comparable across all groups. No teratogenic	/	Anonymous 2004

		Gestation day 6-20 Gavage	stomach findings. Developmental NOAEL ≥ 750 mg/kg bw/day (corresponding to NOAEC: ≥75 mg/mL) Developmental LOAEC was not determined	discolouration of glandular stomach (1/22) and intestine distention with fluids (1/22). <u>Clinical signs</u>: No test substance related findings.	effects were observed at any dose level.		

No human data on developmental toxicity study is available for KMPS.

A.3.10.2.1. Short summary and overall relevance of the provided information on adverse effects on development

In the rat teratogenicity study, females received Oxone® Monopersulphate Compound (KMPS) from days 6 to 20 of gestation at doses of 0, 75, 250 or 750 mg/kg bw/day (corresponding to concentrations of 0, 7.5, 25, 75 mg/mL). One animal receiving KMPS at the highest dose 750 mg/kg bw/day was found dead on day 13 of gestation. Before death weight loss and decreased food consumption on days 8-10 of gestation were observed. Later the animal regained weight and food consumption was normal. Necropsy revealed no gross postmortem abnormalities.

On day 21 day of gestation, stomach abnormalities (like thickened nonglandular stomach, red discoloration of the glandular stomach, distension of the intestine with fluids) were observed in 4 dams receiving 750 mg/kg bw/day. Animals also gained less weight and consumed less food compared to control animals.

The number of corpora lutea, implantation sites, resorptions, number of live foetuses, and sex ratio were comparable across the groups. Mean fetal weight was 4% lower (statistically not significant) in the 75 mg/mL group.

The maternal and foetal NOAEL for Oxone® Monopersulphate Compound was derived at 250 mg/kg bw/day, based on decreased maternal weight gain, food consumption, mortality and stomach findings and based on the slightly lower foetal weight in the 750 mg/kg bw/day group. No teratogenic effects were observed at any concentration. Thus, the NOAEL for embryotoxic/teratogenic effects is ≥ 750 mg/kg bw/day. Thereafter it can be concluded that KMPS is not toxic for fetal development in the rat.

A.3.10.2.2. Comparison with the CLP criteria

In a teratogenicity study performed with KMPS in rats, no maternal and fetal toxic effects were observed at 250 mg/kg bw/d (corresponding to 25 mg/mL). No developmental effects were observed up to and including the highest tested dose of 750 mg/kg/bw/d (corresponding to a concentration of 75 mg/L). KMPS in not considered to adversely affect development of foetuses.

A.3.10.3. Effects on or via lactation

No animal or human data on effects on or via lactation is available for KMPS.

A.3.10.3.1. Short summary and overall relevance of the provided information on effects on or via lactation

Due to its oxidative and corrosive/irritative properties, KMPS will cause destruction of skin and mucous membranes of the respiratory tract when applied topically or inhaled. These effects are considered to be of local nature due to the reaction of the substance with the surrounding tissue. Systemic toxicity would therefore occur only secondary to locally irritating effects. In the available studies there are no indications for any other mechanism of toxicity than the local corrosion/irritation. Since this mode of action is chemically driven, it is not species specific.

Moreover, breakdown products of KMPS are potassium and sulphate ions, which are both hydrophilic physiological metabolites. Bioaccumulation of the degradation products in the body is thus not expected. Application of KMPS in concentrations which do not cause irritation/corrosion, results in physiological concentrations of potassium and sulphate ions. Thus, no adverse effects besides the local corrosion/irritation are expected.

Consequently, no influence of KMPS on or via lactation is expected.

A.3.10.3.2. Comparison with the CLP criteria

KMPS is not considered to have any effects on or via lactation.

A.3.10.4. Conclusion on classification and labelling for reproductive toxicity

No classification of KMPS is warranted for reprotoxicity or effects on or via lactation according to CLP Regulation.

A.3.11. Aspiration hazard

No data on aspiration hazard is available for KMPS.

A.3.12. Further Human data

Table A.29 Summary table of further human data

Summary table of further human data				
Type of data/ report, Reliability**, Key/supportive study	Test substance (including purity), Vehicle	Relevant information about the study	Main effects, Observations	Reference
Medical surveillance no guideline applicable	Caroat®	150 persons (males and females) were exposed daily towards KMPS. Exposure was continuously during production, analysis and application of KMPS. Neither exposure concentration nor overall time of exposure are stated. Workers of KMPS production were examined for health effects periodically within 6 years. Examinations included a hearing test, sight test, lung function test, ECG under exercise, blood and urine examinations.	No specific adverse effects of KMPS on health were observed within a period of 6 years.	Anonymous 2005b
Respiratory health surveillance	Oxone	33 active employees at Oxone manufacturing site, Memphis. Employees filled out Interval Health History and Wellness Appraisal or OSHA questionnaires including questions regarding respiratory health. Additionally pulmonary function test was performed to evaluate pulmonary obstructive disease.	No pulmonary symptoms were reported among the employees for the 2013-2016 calendar year.	Anonymous, 2016c

In a medical surveillance with 150 persons, no specific adverse effects were observed for KMPS. More recent surveillance of respiratory health of active employees in Oxone manufacturing facility showed no pulmonary symptoms among employees.

KMPS does not have adverse health effect on workers at the production site.

A.3.13. Other data

No further data is available.

A.4. Environmental effects assessment

A.4.1. Fate and distribution in the environment

A.4.1.1. Degradation

A4.1.1.1 Abiotic degradation

Hydrolysis and oxidation upon contact with oxidizable substances (organic and inorganic)

Table A.30 Summary table – Abiotic degradation

Summary table – Abiotic degradation							
Method, Guideline, GLP status, Reliability, Key/supportive study	Test medium	pH	Temp. [°C]	Initial TS conc., C_0 [g/L] [1]	Half-life, DT_{50} [h]	Rate constant k [h^{-1}]	Reference
Hydrolysis							
OECD 111 GLP Ri = 2 key study	buffer	4.0	20	3.0	> 800 [2]	n.d.	Anonymous, 2007a
			30		440 [2]	n.d.	
			50		n.d.	0.0066	
	buffer	7.0	20	3.0	145 [2]	n.d.	
			30		53 [2]	n.d.	
			50		n.d.	0.12	
	buffer	9.0	20	3.0	2.8 [2]	n.d.	
			30		n.d.	0.4	
			50		n.d.	0.68	
	seawater	8.0-8.2	20	3.0	5.6 [2]	n.d.	
			30		2.5 [2]	n.d.	
			50		1.4 [2]	n.d.	
	freshwater	7.8-8.2	20	3.0	215 [2]	n.d.	
			30		65 [2]	n.d.	
			50		8.7 [2]	n.d.	
Oxidation upon contact with oxidizable substances (organic and inorganic)							
No guideline mentioned Not GLP Ri = 2 key study	Synthetic pool water with Body Fluid Analogue	7.4-7.6	29±1	12	3 [3]	n.d.	Anonymous, 2007b
	Synthetic pool water without Body Fluid Analogue	7.4-7.6	29±1	12	120 [3] (extrapolated)	n.d.	
No guideline mentioned Not GLP Ri = 2 key study	Activated sludge	-	12	0.3	0.187 [4]	3.7	Anonymous, 2011
No guideline mentioned Not GLP Ri = 2 key study	Activated sludge	-	20	0.3	5.25E-03 [5] (rapid phase) 8.24 [5] (slow phase)	132.1 0.08413	Anonymous, 2012

No guideline mentioned Not GLP Ri = 2 key study	Activated sludge	-	16	0.3	1.13 [6] (Denny activated sludge) < 0.083 [6] (Drumnadrochit activated sludge)	0.611 (Denny activated sludge)	Anonymous, 2018
No guideline mentioned Not GLP Ri = 3	Soil	-	22	100 ppm	<1	-	Anonymous (2005) Doc. No. 721-002

1: nominal concentration
2: DT_{50} values were determined by visual examination of the plot 'ln (normalised % KMPS) vs time'
3: DT_{50} values were determined by visual examination of the plot 'concentration KMPS (ppm Oxone) vs time'
4: DT_{50} value was determined based on logarithmic diagram 'ln rate vs ln [Oxone]'
5: DT_{50} values were derived by CAKE v3.3 software using Double-First-Order in Parallel model (DFOP) fit
6: DT_{50} value was derived by CAKE v3.3 software using Single first-order kinetics (SFO) fit
n.d.: not determined

$KHSO_5$, the active ingredient in KMPS, can be degraded abiotically

a) by hydrolysis
b) by a disproportionation reaction
c) by an oxidation reaction upon contact with oxidizable substances (organic and inorganic)

a) In the **hydrolysis** study, the degradation of KMPS was measured by determining the loss of active oxygen by iodometric titration. The aqueous hydrolysis test was conducted according to test method OECD 111 with no deviations. KMPS was dissolved in buffer solutions of pH 4, 7 and 9 as well as in synthetic seawater and freshwater. The test solutions were incubated at 20, 30 and 50°C. The concentration of KMPS in the test solutions was determined at different time intervals by titration with sodium thiosulfate. It is actual decomposition via disproportionation that is being monitored by the analytical method used in the study.

The degradation of KMPS in aqueous solution is pH and temperature dependant. Degradation is accelerated with increasing temperature and increasing pH. While KMPS has a half-life of above 800 h (at 20 °C) in a buffered solution of pH 4, the half-life at pH 7 is 145 hours and only 2.8 hours at pH 9. The half-life at pH 7 and 20 °C corresponds at 12 °C to 275 hours or 11.5 days. Degradation in seawater is considerably faster (DT_{50} = 5.6 hours, pH 8.0-8.2, 20 °C) than in reconstituted freshwater (DT_{50} = 215 hours, pH 7.8-8.2, 20 °C).

Since the titration method would also detect other peroxide species and a loss of active oxygen was observed it can be concluded that no other peroxide species is built upon hydrolysis.

Furthermore, it was shown that the formation of hydrogen peroxide via hydrolysis occurs only after long time and results only in negligible amounts (Anonymous, 2016a and Anonymous, 2016b).

The reason for the faster degradation of KMPS in seawater is the so-called Haber-Will-Statter Reaction. In this, the sodium chloride of the seawater is oxidised by KMPS so that chlorine is released.

$$HSO_5^- + 2Cl^- + 2H^+ \rightarrow HSO_4^- + Cl_2 + H_2O$$

The chlorine reacts with water to form hypochlorous acid:

$Cl_2 + H_2O \rightarrow HOCl + HCl$

Hypochlorous acid (HOCl) is only of transient nature. As shown in Annex II (Kinetic model on the long term hypochlorite decay in the environment) to the ESD on drinking water disinfectants (EUBEES2)[1], hypochlorous acid is extremely rapidly eliminated in the environment due to reaction with ammonia and organic material which act as reductants.

b) The **disproportionation** reaction seems to occur spontaneously and slowly according to the following reaction scheme generating hydrogen sulphate and oxygen:

$2\ HSO_5^- \rightarrow 2\ HSO_4^- + O_2$

c) Oxidation reactions upon contact with oxidizable substances

1. In the study on the "Depletion of Potassium Monopersulfate in Synthetic Pool Water" (Anonymous, 2007b), it was shown that the decomposition of KMPS in water is very dependent on the presence of **oxidizable** contaminants. The addition of a 'body fluid analog' to the synthetic pool water used in this laboratory test reduced the half-life for decomposition of KMPS from ca. 120 hours (synthetic pool water without 'body fluid analog') to ca. 3 hours. This is explained by the consumption of $KHSO_5$ in many different oxidation reactions with reduced amine substrate components of the added 'body fluid analog', according to the general reaction:

$KHSO_5 + X \rightarrow KHSO_4 + X = O$

It can be assumed that KMPS is degraded at similar rates in natural waters, such as pond and river water. The higher the concentration of oxidizable organic substrate is in the water, the faster KMPS will be degraded.

Such oxidizing reactions can also occur in soil due to the high content of oxidizable agents in soil.

2. The degradation of KMPS by reactions upon contact with oxidizable substances was also determined in activated sludge, i.e. in a medium containing inorganic and organic oxidizable substances in abundance.

In order to check the design firstly a pre-study was performed (Anonymous, 2011). In the main study (Anonymous, 2012) this design was mostly applied (pre-study: test temperature 12 °C; main study: test temperature 20 °C). Since the sampling for both studies took place separately and at a different time, the investigated sewage sludges are considered as individual systems in the following.

The purity of the test substance Oxone (KMPS) was analysed at the beginning of the test.

A reaction mixture of Oxone (KMPS) and activated sludge was prepared by mixing activated sludge and Oxone (KMPS) solution with initial concentration of 300 ppm KMPS. Oxone concentration in activated sludge and deionized water was determined indirectly by the addition of Oxone containing sample to a known, excess concentration of FAS. As Oxone reacts rapidly with Fe(II) in a redox reaction and results in the formation of Fe(III) salts,

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subsequent titration of the remaining FAS with potassium dichromate determines the residual concentration of Fe(II) in the solution.

KMPS reacts immediately and extremely quickly upon contact with the diverse substances that can be oxidized and which are abundantly available in activated sludge. Therefore, it is absolutely impossible to measure the immediate initial concentration of 300 ppm KMPS in the reaction mixture.

The three measurements from the first sampling time in the main study showed all very similar KMPS values. For this reason and since the test substance purity was determined directly before starting the test, it can be concluded that no experimental mistake had occurred and that the initial concentration was equal 300 ppm, according to the mass of KMPS which was added to the system. Such rapid degradation behaviour is very well known also from other peroxides like hydrogen peroxide and peracetic acid, for which degradation half lives in activated sludge of 2 - 3 minutes have been determined (AR Hydrogen peroxide, 2015 and AR Peracetic acid, 2015).

These other peroxygen compounds have the same general spectrum of various different potential reaction partners for oxidation and decomposition as KMPS: organic material, inorganic material (such as halides and sulphides), transition and heavy metals (catalytic degradation), particle surfaces (heterogeneous catalytic decomposition).

These diverse reaction partners and reaction pathways explain why the reaction kinetics for the peroxides are not constant over the whole degradation time, as the observed degradation is the overall result of various decomposition pathways. This could also be seen for KMPS.

In pre-study (Anonymous, 2011) Oxone was degraded below 100 ppm very rapidly. A DT_{50} of 11.23 min (0.187 h) was determined using a logarithmic diagram for 300 ppm Oxone in the presence of activated sludge at 12 °C. In the main study (Anonymous, 2012), the pattern of degradation suggests that dissipation followed biphasic kinetics with very rapid degradation in the first minute, but slower degradation afterwards. Kinetic analysis using CAKE v3.3 software has shown that based on visual assessment, chi-square test and t-test, DFOP is providing best fit of the measured data. The following DT_{50} values were determined at 20°C:

Rapid phase: DT_{50} = 5.25E-03 h (k_1 = 132.1 h^{-1})
Slow phase: DT_{50} = 8.24 h (k_2 = 0.08413 h^{-1})

In order to obtain more profound information on degradation of KMPS in activated sludge, a further study was performed by Anonymous, 2018. The degradation of Oxone (KMPS) in activated sludge from two municipal STPs was determined via titration of ferrous ammonium sulphate (FAS). The initial Oxone concentration was 300 ppm, likewise in the study by Anonymous, 2011 and the study by Anonymous, 2012. Limit of quantification was determined to be ≥ 53.6 ppm. Oxone concentration was determined over 8 points at 0, 5, 10, 20, 40, 80, 140 and 240 minutes. Degradation tests of Oxone were performed at 16 °C. For the Drumnadrochit activated sludge, the results fell below the limit of quantification after 5 minutes. The results also show that Oxone concentration tends toward zero over time. Therefore, DT_{50} < 5 min at 16 °C (< 0.083 h) has been determined for the Drumnadrochit activated sludge. Kinetic analysis using CAKE v3.3 software has shown that degradation in Denny activated sludge follows single first order kinetics, with rate constant k = 0.611 h^{-1}. Determined DT_{50} was 1.13 h at 16 °C. The difference in half-lives for Drumnadrochit and Denny activated sludge can be attributed to the difference in organic loading of the sludge

samples as evidenced by the measurement of the COD (chemical oxygen demand). The Drumnadrochit activated sludge sample with 239.8 mg/L has a significantly higher COD value than the Denny activated sludge sample with COD of 27.2 mg/L. Since Oxone is consumed in the reaction with organic species, the Drumnadrochit activated sludge is expected to show faster degradation which is in agreement with obtained study results.

From the studies on degradation of KMPS in activated sludge, the following experimentally derived DT_{50} values at 12 °C were obtained by using the equation for temperature correction as indicated in item ENV182 in the TAB (Nov. 2021) but considering a molar activation energy of 54 KJ/mol for abiotic degradation processes as agreed in WG ENV I-2023:

Anonymous, 2011:	0.187 h
Anonymous, 2012:	15.34 h (slow phase)
Anonymous, 2018:	1.55 h (Denny activated sludge)
	< 0.114 h (Drumnadrochit activated sludge)

Since the half-lives determined in the different studies differ between <0.114 h and 8.24 h, a reliable DT_{50} value needs to be derived on the basis of the available experimental data. According to item ENV13 (TAB, Nov. 2021) a geometric mean value is to be used when more than three DT_{50} values are available. As the degradation of KMPS was tested in four sludge systems, it is appropriate to use the geomean DT50 for the risk assessment. In contrast to the other studies, in the sludge tested in the study by Anonymous, 2012, the degradation of KMPS could be described best with the DFOP kinetic model. Following discussion in WG ENV I 2023, it was agreed to use only the slow phase DT_{50} derived from the DFOP model for fate modelling and to include all timepoints in the fitting. This procedure is in line with guidance given in Figure 7-2 of the FOCUS degradation kinetics report (2014).
Thus, the four experimentally derived DT_{50} values in activated sludge were used to calculate the geometric mean value.

Geometric mean DT_{50} value in activated sludge is: 0.844 hour at 12 °C.

Results from tests simulating the conditions in a sewage treatment plant (STP) need to be carefully used for assessing the degradation in the aquatic environment. The main reasons for this are that the microbial biomass in a STP is significantly different from the biomass in the environment, that there is a considerably different composition of substrates.

It is very challenging, if not impossible, to obtain a reliable experimental DT_{50} in soil. A soil degradation study was submitted for KMPS (Annex point 7.2.1/01, Anonymous 2005, Doc. No. 721-002). Even if the submitted soil degradation study showed deficiencies (in the reporting and the difficulty in determining initial concentration due to rapid degradation), it could be shown, that after one hour, no KMPS remained in soil. This is in line with expectations as the peroxymonosulfate ion is kinetically more reactive than other oxidising substances such as hydrogen peroxide.

Phototransformation in water

KMPS does not absorb light in the relevant wavelength range (290 – 800 nm). Therefore, phototransformation of KMPS can be excluded.

Table A.31 Summary table – Photo-oxidation in air

Summary table – Photo-oxidation in air						
Model	Substance	Light protection (yes/no)	Estimated daily (24h) OH conc. [OH/cm³]	Overall OH rate constant [cm³/molecule sec]	Half-life [h]	Reference
AOPWIN Atkison calculation Ri = 1	Potassium peroxomonosulfate	n.d.	0.5×10^6	4.0000×10^{-12}	96.264	Anonymous, 2007c
	Caro's acid		0.5×10^6	4.1400×10^{-12}	93.009	

The DT_{50} of KMPS in air considering photochemical and oxidative decomposition was calculated according to Atkinson (programme used: AOPWIN) to be 4.011 days (24-hr day, corresponding to 96.264 hours).

For Caro's acid (peroxysulfuric acid), a DT_{50} in air of 3.875 days (24-hr day, corresponding to 93.009 hours) was determined.

As both substances contain no olefinic carbon-carbon double or acetylic triple bonds, they are not supposed to react with ozone.

A4.1.1.2 Biotic degradation

As KMPS is an inorganic compound, biodegradation tests are not applicable.

A4.1.1.3 Rate and route of degradation including identification of metabolites and degradation products

As KMPS is an inorganic compound, biodegradation tests to simulate biodegradation in environmental compartments are not applicable.

Biodegradation is not relevant for KMPS, but as explained in paragraph 4.1.1.1. KMPS can be decomposed abiotically. For $KHSO_5$, which is the active ingredient in KMPS, several abiotic decomposition pathways exist forming potassium ions, hydrogen sulphate ions, O_2 and oxidation products X=O.

A.4.1.1.3.1 Biological sewage treatment

Not applicable for CLH report.

A.4.1.2. Distribution

A4.1.2.1 Adsorption onto/desorption from soils

KMPS is an inorganic salt with ionic structure. It is readily soluble in water and dissociates completely in aqueous solution. Due to its high solubility in water, its low vapour pressure ($< 1.2 \times 10^{-4}$ Pa at 20 °C), resulting in a very low Henry's Law Constant (2.04×10^{-7} Pa x m³ x mol^{-1}), and due to its low partition coefficient n-octanol/water (log Pow < 0.30 measured at 20 °C and -3.90 calculated), KMPS can be expected to partition nearly exclusively into the water phase. Upon contact with soil, KMPS decomposes either by hydrolysis or disproportionation to potassium ions, hydrogen sulphate and oxygen. Furthermore, very fast decomposition of KMPS in soil can be expected, due to the ubiquitous presence of oxidizable organic substrate. Leaching of KMPS in the soil profile to groundwater can therefore be excluded.

A4.1.2.2 Higher tier soil adsorption studies

No higher tier studies are required, see paragraph 4.1.2.1.

A4.1.2.3 Volatilisation

Regarding volatilisation, please see Part A, section 1.3 Physical and chemical properties of the active substance.

A.4.1.3. Bioaccumulation

Measured aquatic bioconcentration
No data available.

Estimated aquatic bioconcentration
The low log Pow (< 0.30 measured at 20 °C and -3.90 calculated) indicate that KMPS has a low potential for bioconcentration and bioaccumulation (according to guideline OECD 117, log Pow values below 4 are regarded to be indicators of low accumulation potential). Moreover, KMPS dissipates rapidly in the environment (hydrolysis DT50 at pH 7 corrected to 12 °C 275 hours or 11.5 days). Considering these facts, it can be concluded that KMPS has no potential for bioaccumulation.

A.4.1.3.1 Short summary and overall relevance of the provided information on bioaccumulation and conclusion on bioaccumulation potential for classification and labelling purposes

The low log Pow (< 0.30 measured at 20 °C and -3.90 calculated) indicate that KMPS has a low potential for bioconcentration and bioaccumulation (according to guideline OECD 117, log Pow values below 4 are regarded to be indicators of low accumulation potential). Moreover, KMPS dissipates rapidly in the environment (hydrolysis DT50 at pH 7 corrected to 12 °C 275 hours or 11.5 days). Considering these facts, it can be concluded that KMPS has no potential for bioaccumulation.

A.4.1.4. Monitoring data

No monitoring data are available.

A.4.2. Effects on environmental organisms

A.4.2.1. Atmosphere

Not applicable for CLH report.

A.4.2.2. Toxicity to sewage treatment plant (STP) microorganisms

Inhibition of microbial activity (aquatic)

Table A.32 Summary table – inhibition of microbial activity

Summary table – inhibition of microbial activity								
Method, Guideline, GLP status, Reliability, Key/supportive study	Species/ Inoculum	Endpoint	Exposure		Results [mg KMPS/L]			Reference
			Design	Duration	NOEC	EC_{10}	EC_{50}	
OECD 209 GLP Ri = 1 key study	Activated sludge	Respiration rate	Static	3 h	> 100	> 100	> 100	Anonymous, 2001d

Inhibition of microbial activity of KMPS was tested in a 3-hour respiration inhibition test with activated sludge. The EC_{50} from the study is > 100 mg a.i./L based on nominal concentrations.

A.4.2.3. Aquatic compartment

A4.2.3.1 Freshwater compartment

Acute/short-term toxicity (freshwater)

Table A.33 Summary table – acute/short-term aquatic toxicity

Summary table – acute/short-term aquatic toxicity										
Method, Guideline, GLP status, Reliability, Key/supportive study	Species	Endpoint/ Type of test	Test material	Exposure		Results [mg KMPS/L]			Remarks	Reference
				Design	Duration	LC/EC_0	LC/EC_{50}	LC/EC_{100}		
Fish										
Directive 92/69/EEC, Part C.1, OECD 203 GLP Ri = 1 key study	*Oncorhynchus mykiss* (Rainbow trout)	Mortality	KMPS	Semi-static	96 h	27	53	101	Nominal concentrations	Anonymous, 2001a
Invertebrates										
Directive 92/69/EEC, Part C.2, OECD 202 GLP Ri = 3	*Daphnia magna*	Immobility	KMPS	Semi-static	48 h	1.4	1.98	2.6	Mean measured concentrations	Anonymous, 2001b

Algae (growth inhibition)							72-h E_bC_{50}[1]	72-h E_rC_{50}[2]		
Directive 92/69/EEC, Part C.3, OECD 201 Ri = 2 key study	*Pseudokierchneriella subcapitata*	Growth inhibition	KMPS	Static	96 h	0.43	0.84	> 0.87	Mean measured concentrations	Anonymous, 2001c
[1] calculated from the area under the growth curve; [2] calculated from growth rate										

Acute/short-term toxicity to fish

Acute toxicity of KMPS on Rainbow trout (*Oncorhynchus mykiss*) was studied in a 96 hour semi-static test system according to Directive 92/69/EEC, Part C.1 and OECD 203 guideline. The study was conducted at nominal exposure concentrations of 6.25, 12.5, 25.0, 50.2, 100 mg KMPS/L, based on the results of preliminary range finding study. Temperature, pH, and dissolved oxygen were monitored for control as well as for test item during the entire study at 0, 24, 48, 72 and 96 hours. The test item concentrations were monitored for freshly prepared media at 0 and 72 hours and for old test media at 24 and 96 hours. Analytical concentrations were 100 - 107 % of nominal. The 96 hour LC_{50} toxicity value was determined to be 53 mg/L. The highest concentration at which no mortality occurred was 27 mg/L. The lowest concentration at which 100 % mortality occurred was 101 mg/L.

Acute/short-term toxicity to invertebrates

The acute toxicity of KMPS in *Daphnia magna* was determined in a 48 hour semi-static test system conducted according to Directive 92/69/EEC, Part C.2 and OECD 202 guideline. Nominal test concentrations of KMPS used were 0.625, 0.125, 0.25, 0.50, 10 mg/L, based on the results of preliminary range finding study. Temperature, pH, and dissolved oxygen were monitored for control as well as for test item for freshly prepared media at 0 and 24 hours and for old test media at 24 and 48 hours. The stock solution concentrations were analysed at 0 and 24 hours. In addition, the highest test concentration of 10 mg/L was analysed at 0 (fresh media) and 24 hours (old media) resulting in concentrations of 7.8 mg/L and 4.0 mg/L, respectively. These results are below the stated LOQ for the analytical method of 10 mg/L.

The validity criterion in OECD 202 guideline that the initial concentrations of the test substance are ≥ 80 % of nominal is not met in this test. Despite measured stock solution concentrations are above LOQ, it is not clear whether the stock solutions were kept under similar conditions as the test media. Stability of the test substance in a stock solution that is kept in a refrigerator in the dark does not prove stability under the test conditions. Analytical measurements in the highest test concentration resulted in an initial concentration of 78 % of nominal and a concentration of 40 % of nominal after 24 hours, indicating a low stability under the conditions of the test. The pH of the test media was around 8. The hydrolysis study resulted in DT_{50} values (20 °C) of 145 hours at pH 7 and 2.6 hours at pH 9, so some dissipation at a pH of 8 seems likely. The geometric mean measured concentration in the highest test concentration was 5.6 mg/L which corresponds to 56 % of nominal. As best estimate, RMS recalculated the EC_{50} with the trimmed Spearman-Karber method assuming a geometric mean concentration of 56 % of nominal for all test concentrations.

This results in the following endpoints based on mean measured concentration:

48 h EC_{50} = 1.98 mg/L
48 h EC_0 = 1.4 mg/L
48 h EC_{100} = 2.6 mg/L

The highest test concentration is however below the limit of quantification and the analytical results cannot be relied upon. In BPC-ENV WG I-2023 it was agreed to change the RI to 3, not reliable, in particular because of the high LOD of the analytical method in this study compared to the other studies.

Acute/short-term toxicity to algae

The effects of KMPS on the growth of the alga *Pseudokierchneriella subcapitata* was determined in accordance with Directive 92/69/EEC, Part C.3 and OECD 201 guideline in a static 96 hour test. Algal cultures were exposed to 5 test concentrations (0.0625, 0.125, 0.25, 0.50 and 1.0 mg/L nominal), based on the results of preliminary range finding study. These cultures, together with one untreated control group of six replicates, were incubated under continuous illumination of approximately 4000 lux at 23 ± 1 °C for 96 hours. The OECD and EU guideline recommend a 72 hour study under a 6000 - 10000 lux lighting regime. This deviation from the OECD and EU guideline recommendations is not considered to have affected the validity of this study with respect to the outcome of the OECD and EU guidelines or the outcome of the study, because a 32 fold increase in cell numbers was achieved in the control cultures after a 72 hour exposure period. This rate of cell growth therefore satisfies the validity criteria of the OECD and EU guidelines.

The analytical method was insufficiently sensitive to analyse the test concentration due to the LOQ of 1.5 mg/L. Therefore, only the concentrated aqueous stock solutions were analysed. Initial concentrations of the stock solutions were not verified as the test substance was not stable in the stock solutions and dissipation may have occurred before dosing of the test media. This is assumed to be without influence on the plausibility of the results according to the OECD 201 guideline updated in 2006 (the study was performed following the older OECD 201 guideline dated 1984) which states that analytical verification of the test concentrations is not mandatory, if an analytical method for determination of the test substance in the concentration range used is not available.

Considering the updated OECD 201 guideline, its validity criteria are met, as based on the cell count data in the study report, the calculations resulted in mean coefficients of variation of 3.09 for day 0-1, 7.85 for day 1-2, 2.77 for day 2-3 and 5.08 for day 3-4. The coefficient of variation of average specific growth rate during the whole test period was calculated as 2.87.

The following endpoints are derived from this study based on mean measured concentrations:

72 h NOEC = 0.43 mg/L
72 h E_bC_{50} = 0.84 mg/L
72 h E_rC_{50} > 0.87 mg/L

Chronic/long-term toxicity (freshwater)

Table A.34 Summary table – chronic aquatic toxicity

Summary table – chronic/long-term aquatic toxicity								
Method, Guideline, GLP status, Reliability, Key/supportive study	Species	Endpoint/ Type of test	Test material	Exposure		Results [mg KMPS/L]	Remarks	Reference
				Design	Duration	LOEC / NOEC / EC_{10}		
Algae (growth inhibition)								
US EPA 850.5400 GLP Ri = 2 key study	*Pseudokierchneriella subcapitata*	Growth inhibition	KMPS	Static	96 h	0.87 / 0.43 / n.d. (biomass, growth rate)	Mean measured concentrations	Anonymous 2007c

The available data demonstrate a higher toxicity to marine species compared to freshwater species. Therefore, no further chronic data for KMPS on freshwater species were submitted.

A4.2.3.2 Sediment compartment

The physico-chemical properties of KMPS (calculated log Kow = -3.90) suggest that the active substance is not likely to partition into sediment to a significant extent. With regard to the negligible exposure, toxicity tests with sediment organisms are not deemed to be relevant and necessary.

4.2.3.3 Marine compartment

Acute/short-term toxicity (seawater)

Table A.35 Summary table – acute/short-term aquatic toxicity

Summary table – acute/short-term aquatic toxicity										
Method, Guideline, GLP status, Reliability, Key/supportive study	Species	Endpoint/ Type of test	Test material	Exposure		Results			Remarks	Reference
				Design	Duration	LC/EC_0	LC/EC_{50}	LC/EC_{100}		
Fish										
US EPA 850.1075, 1996 GLP Ri = 2 key study	*Cyprinodon variegatus* (Sheepshead minnow)	Mortality	KMPS	Static	96 h	0.190	0.467	0.762	Mean measured concentrations	Anonymous, 2007d
Invertebrates										
US EPA 850.1035 (1996), draft GLP Ri = 2 key study	*Americamysis bahia* (Mysid shrimp)	Mortality	KMPS	Static-renewal	96 h	0.193	0.513	0.774	Mean measured concentrations	Anonymous, 2007e
Algae (growth inhibition)							96-h E_bC_{50}[1]	96-h E_rC_{50}[2]		
US EPA 850.5400 GLP Ri = 2 key study	*Skeletonema costatum*	Growth inhibition	KMPS	Static	96 h		0.325	0.370	Nominal concentrations	Anonymous, 2007f
[1] calculated from the area under the growth curve; [2] calculated from growth rate										

Acute/short-term toxicity to fish

The acute toxicity of KMPS to marine species *Cyprinodon variegatus* (Sheepshead minnow) was determined in a static, 96 hour test. The test was conducted in accordance with the US EPA 850.1035 guideline. Nominal test concentrations of KMPS used were 222, 444, 889, 1780 and 3560 µg/L, based on the results of preliminary range finding study. Dissolved oxygen concentration, pH,

temperature and salinity were monitored for control as well as for test item during the entire study at 0, 24, 48, 72 and 96 hours.

The stock solution concentrations were analysed at 0 hours. In addition, control and the two highest test concentrations of 1780 and 3560 µg KMPS/L were analysed at 0 and 96 hours. The concentration of the test substance in the stock solution was determined to be 93 - 108 % of nominal, while in the two highest solutions tested KMPS recoveries were from 78 - 86 % at test start and decreased below the LOQ at test end. This is a major deviation from the US EPA 850.1035 guideline, as the study was not performed with a flow-through design, although concentrations after 96 hours were below the LOQ in this static test. In BPC-ENV WG I-2023, it was agreed that the endpoints should be corrected to mean measured concentrations 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 of the initial measured concentration and ½ LOQ equals 0.686 mg $KHSO_5$/L, corresponding to 42.8% of nominal. This may be extrapolated to all test concentrations resulting in nominal endpoints to be corrected by a factor 0.428.

Mortality of sheepshead minnow was 0, 0, 20, 100 and 100 % at 222, 444, 889, 1780, 3560 µg KMPS/L, respectively, at the end of 96 hours. The 96 h LC_{50} was determined to be 0.468 mg/L, based on mean measured concentrations. The highest mean measuredl concentration causing no mortality at test end was 0.190 mg/L. The lowest mean measured concentration causing 100 % mortality at test end was 0.762 mg/L.

Acute/short-term toxicity to invertebrates

The acute toxicity of KMPS to marine species *Americamysis bahia* (Mysid shrimp), was determined in a 96 hour static-renewal test. The test was conducted in accordance with the US EPA 850.1035 guideline. Nominal test concentrations of KMPS used were 222, 444, 889, 1780 and 3560 µg/L, based on the results of preliminary range finding study. Dissolved oxygen concentration, pH, temperature and salinity were monitored for control as well as for test item for freshly prepared media at 0, 24, 48, 72 and 96 hours and for old test media at 24, 48 and 72 hours.

The stock solution concentrations were analysed at 0 and 72 hours. In addition, control and the highest test concentration of 3560 µg KMPS/L were analysed at 0 and 72 hours in new solutions and at 24 and 96 hours in old solutions. The concentration of the test substance in the stock solution was determined to be 83 to 91 % of nominal at 0 hours and 85 to 97 % of nominal at 72 hours, while in the highest solution tested KMPS recoveries were 61 - 81 % at 0 hours and 96 - 102 % at 72 hours. Concentrations in the old solutions were below the LOQ after 24 hours. In BPC-ENV WG I-2023, it was agreed that the endpoints should be corrected to mean measured concentrations 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 aritmetric mean of initial measured concentration and ½ LOQ equals 0.696 mg $KHSO_5$/L, corresponding to 43.5% of nominal. This may be extrapolated to all test concentrations resulting in nominal endpoints to be corrected by a factor 0.435.

Mortality of mysid shrimp was 0, 0, 10, 100 and 100 % at 222, 444, 889, 1780, 3560 µg KMPS/L, respectively, at the end of 96 hours. The 96-h LC_{50} was determined to be 0.513 mg KMPS/L, based on mean measured concentrations. The highest mean measured concentration causing no mortality at test end was 0.193 mg KMPS/L. The lowest nominal concentration causing 100 % mortality at

test end was 0.774 mg KMPS/L.

Acute/short-term toxicity to algae

The toxicity of KMPS to marine algae *Skeletonema costatum*, was determined in a 96 hour, static toxicity test. The test was conducted in accordance with US EPA 850.5400 guideline. Nominal test concentrations of KMPS used were 55.6, 111, 222, 444, 889 and 1780 µg/L, based on the results of preliminary range finding study. pH and temperature were monitored for control as well as for test item at 0 and 96 hours.

The stock solution concentrations were analysed at test initiation. In addition, control and the highest test concentration of 1780 µg KMPS/L were analysed at 0 and 96 hours. Measured concentrations in the stock solution samples ranged from 88 - 100 % of nominal concentrations, while in the highest solution tested the measured concentrations of KMPS at 0 and 96 hours were less than the LOQ, which was determined to be 700 µg/L. Moreover, the test substance was not stable in the stock solutions and dissipation may have occurred before dosing of the test media. Dissipation of the test substance was demonstrated to be very fast in the presence of chloride (seawater) and at high pH. Both conditions apply to the test medium for the marine algae test. In BPC-ENV WG I-2023, it was agreed that the endpoints should be corrected to mean measured concentrations 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 0.529 mg $KHSO_5$/L, corresponding to 66.5% of nominal. This may be extrapolated to all test concentrations resulting in nominal endpoints to be corrected by a factor 0.665.

Considering the updated OECD 201 guideline (the study was performed following the older OECD 201 guideline dated 1984), its validity criteria are met, as based on the cell count data in the study report, the calculations resulted in mean coefficients of variation of 22.21 for day 0-1, 28.52 for day 1-2, 21.14 for day 2-3 and 50.30 for day 3-4. The coefficient of variation of average specific growth rate during the whole test period was calculated as 4.10. Conclusion is that control behaviour becomes too variable after 96 hours, because exponential growth is not maintained. Therefore, the validity criteria are met during the first 72 hours in this test.

The following endpoints are derived from this study based on mean measured concentrations:

96 h NOE_bC = 0.074 mg/L
96 h NOE_rC = 0.295 mg/L
96 h E_bC_{50} = 0.325 mg/L
96 h E_rC_{50} = 0.370 mg/L

Chronic/long-term toxicity (seawater)

Table A.36 Summary table – chronic aquatic toxicity

Summary table – chronic/long-term aquatic toxicity								
Method, Guideline, GLP status, Reliability, Key/supportive study	Species	Endpoint/ Type of test	Test material	Exposure		Results [mg KMPS/L]	Remarks	Reference
				Design	Duration	LOEC / NOEC / EC_{10}		
Fish								
US EPA 850.1400 GLP Ri = 1 key study	*Cyprinodon variegatus* (Sheepshead minnow)	Egg hatchability	KMPS	Flow-through	37 d	> 0.889 / 0.889 / n.d.	Nominal concentrations	Anonymous, 2007g
		Fry survival				0.889 / 0.444 / n.d.		
		Standard length				> 0.444 / 0.444 / n.d.		
		Blotted wet weight				0.444 / 0.222 / n.d.		
Invertebrates								
US EPA 850.135 ASTM E1191-970 GLP Ri = 2 key study	*Americamysis bahia* (Mysid shrimp)	Adult survival	KMPS	Flow-through	28 d	0.533 / 0.267 / n.d.	Nominal concentrations	Anonymous, 2007h
		96 h juvenile survival				> 0.267 / 0.267 / n.d.		
		Length				> 0.267 / 0.267 / n.d.		
		Young / female				> 0.267 / 0.267 / n.d.		
Algae (growth inhibition)								
US EPA 850.5400 GLP Ri = 2 key study	***Skeletonema costatum***	**Growth inhibition**	**KMPS**	**Static**	**96 h**	**0.222 / 0.111 / n.d. (biomass)** **0.889 / 0.444 / n.d. (growth rate)**	**Nominal concentrations**	Anonymous 2007f

Chronic/long-term toxicity to fish

The early-life stage toxicity of KMPS to *Cyprinodon variegatus* (Sheepshead minnow), was determined under flow-through conditions where organisms were exposed to the test substance for a total of 37 days, which resulted in an exposure of 28 days post-hatch. The

test was conducted in accordance with the US EPA 850.1400 guideline. Nominal test concentrations of KMPS used were 28.9, 55.6, 111, 222, 444 and 889 µg/L, based on the results of preliminary range finding study. Temperature, dissolved oxygen concentration, pH and salinity were monitored for control as well as for test item at 0, 7, 14, 21, 28, 35 and 37 days.

The concentration of $KHSO_5$ in the control and stock solution containing 1.540 mg $KHSO_5$/L were determined one day prior test initiation and on study days 0, 7, 14, 21, 28, 35 and 37. The measured concentrations of the stock solution ranged from 92 to 120 % of the nominal concentration. According to the raw data, stock solutions were prepared on the following days: 1, 8, 15, 23, 31 and 36. Stock solutions were added to the test system daily (aside from D19 and D21). Analytical samples were taken on the following days: 0, 7, 14, 21, 28, 35 and 37. Given these data, it appears that KMPS was stable in the system. For example, stock solution prepared on D8 of the study was added to the test system daily, but were not sampled analytically until D14 (i.e., the stock was 6 days old), at which time the analytical recovery was 118%.

Hatching success in the control was 89 % and ranged from 85 to 93 % in the test item treatments without significant differences to the control. Based on hatching success, the NOEC was 0.889 mg/L and the LOEC was estimated to be > 0.889 mg/L. Post hatch survival of fry in the control was 97 % and ranged from 2 to 96 % in the test item treatments, with significant effects in the highest tested concentration of 889 µg/L. Based on post-hatch survival, the NOEC was 0.444 mg/L and the LOEC was 0.889 mg/L. Blotted wet weight was significantly reduced at 0.444 mg/L, while mean length was not significantly different compared to the control considering the 0.889 mg/L treatment was not included in the analysis due to survival effects. Therefore, NOEC values for standard length and blotted wet weight were 0.444 and 0.222 mg/L, respectively. The LOEC values for standard length and blotted wet weight were > 0.444 and 0.444 mg/L, respectively.

Chronic/long-term toxicity to invertebrates

The life-cycle toxicity of KMPS to the *Americamysis bahia* (Mysid shrimp), was determined under flow-through test conditions where the organisms were exposed to the test substance for a total of 28 days. The test was conducted in accordance with US EPA 850.135 ASTM E1191-970 guideline. Nominal test concentrations of KMPS used were 33.3, 66.7, 133, 267, 533 µg/L, based on the results of preliminary range finding study. Temperature, dissolved oxygen concentration, pH and salinity were monitored for control as well as for test item at 0, 8, 14, 21 and 28 days.

The concentration of $KHSO_5$ in the control and stock solution containing 1.870 mg $KHSO_5$/L were determined one day prior test initiation and on study days 0, 7, 14, 21 and 28. The measured concentrations of the stock solution ranged from 96 to 116 % of the nominal concentration. According to the raw data, stock solutions were prepared on days 1, 9, 17 and 24. Stock solutions were added to the test system daily. Analytical samples were taken on days 0, 7, 14, 21 and 28. Based on this information it appears that KMPS is stable in this study as well. For example, stock solution prepared on D9 was added to the test system daily yet not analysed until D14, at which time the analytical recovery was 98%.

Mean % survival of the adult population was statistically reduced only at 0.533 mg/L (i.e. 0 %) on test day 7 through day 28 as compared to the negative control survival. Therefore, the NOEC and LOEC were 0.267 and 0.533 mg/L, respectively. The 96 hour

survival of the juvenile mysids ranged from 94 to 98 % in all treatment replicates and was 91 % in the controls. The average 96 hour juvenile survival in KMPS treatments was not statistically different as compared to the negative control survival. Since there was not a concentration dependent response, the 96 hour NOEC and LOEC for juvenile survival were 0.267 and > 0.267 mg/L, respectively.

The NOEC and LOEC values for adult male and female body lengths (day 14 and 28) were 0.267 and > 0.267 mg/L, respectively, due to the lack of statistically significant reduction in this parameter in comparison to the mean control male and female body length data.
The total young per female was not statistically reduced in any treatment as compared to the total young per female of the negative controls. Therefore, the NOEC and LOEC values for this parameter were 0.267 and > 0.267 mg/L, respectively.

The available data demonstrate a higher toxicity to marine species compared to freshwater species. This difference might be due to:

1. Formation of active chlorine in seawater;
2. An intrinsic higher toxicity of $KHSO_5$, the active ingredient in KMPS, to marine species compared to freshwater species. There is no theoretical or experimental basis to assume that this is generally the case and hence cause 1, the oxidation of halide ions in sea water is the reason for the greater sensitivity of marine species to KMPS.

Overall, the study results for aquatic organisms demonstrate a rapid toxic mode of action.

A4.2.3.4 Sea sediment compartment

The physico-chemical properties of KMPS (calculated log K_{OW} = -3.90) and its rapid degradation in seawater suggest that the active substance is not likely to partition into sediment to a significant extent. With regard to the negligible exposure, toxicity tests with sediment organisms are not deemed to be relevant and necessary.

A4.2.3.5 Higher tier studies on aquatic organisms

No data available.

A.4.2.4. Terrestrial compartment

Not applicable for CLH report.

A.4.2.5. Groundwater

Not applicable for CLH report

A.4.2.6. Birds and mammals

Not applicable for CLH report.

A.4.2.7. Primary and secondary poisoning

Not applicable for CLH report.

A.4.3. Endocrine disruption

Not applicable for CLH report.

A.4.4. Derivation of PNECs

Not applicable for CLH report.

A.4.4.1. Overall summary of acute and chronic aquatic toxicity data and Comparison with the CLP criteria

A.4.4.1. Short-term (acute) aquatic hazard

Table A.37 Summary of key information on acute/ short-term aquatic toxicity relevant for acute classification

Method	Species	Test material	Results [mg KMPS/L]	Remarks	Reference
Algae					
Directive 92/69/EEC, Part C.3, OECD 201	*Pseudokierchneriella subcapitata*	KMPS	72-h E_rC_{50} >0.87	Mean measured concentrations	Anonymous, 2001c
US EPA 850.5400	*Skeletonema costatum*	KMPS	96-h E_rC_{50} 0.370	Mean measured concentrations	Anonymous, 2007f

In the acute aquatic tests, a higher toxicity to marine species compared to freshwater species was observed. Based on available data, algae were found to be the most sensitive trophic level with E_rC_{50} of 0.370 mg KMPS/L obtained for the marine alga *Skeletonema costatum*.

A.4.4.2. Chronic/ long-term aquatic hazard (including information on bioaccumulation and degradation)

Table A.38 Summary of key information on chronic/ long-term aquatic toxicity relevant for chronic classification

Method	Species	Test material	Endpoint	NOEC [mg KMPS/L]	Remarks	Reference
Fish						
US EPA 850.1400	*Cyprinodon variegatus* (Sheepshead	KMPS	Egg hatchability	0.889	Nominal concentrations	Anonymous, 2007g
			Fry survival	0.444		

	minnow)		Standard length	0.444		
			Blotted wet weight	0.222		
Invertebrates						
US EPA 850.135 ASTM E1191-970	*Americamysis bahia* (Mysid shrimp)	KMPS	Adult survival	0.267	Nominal concentrations	Anonymous, 2007h
			96 h juvenile survival	0.267		
			Length	0.267		
			Young / female	0.267		
US EPA 850.5400	*Skeletonema costatum*	KMPS	Growth rate	0.444	Nominal concentrations	Anonymous, 2007f

Degradation

$KHSO_5$, the active ingredient in KMPS, can be degraded abiotically

a) by hydrolysis
b) by a disproportionation reaction
c) by an oxidation reaction upon contact with oxidizable substances (organic and inorganic)

Inorganic substances are considered rapidly degradable if convincing evidence is available that the substance can be degraded in the aquatic environment to a level >70 % within a 28–day period corresponding to a hydrolysis half-life < 16 days and it can be demonstrated that the degradation products do not fulfill the criteria for classification as hazardous to the aquatic environment.
The hydrolysis DT50 of KMPS in freshwater at pH 7 and 20 °C of 215 hours is extrapolated to 275 hours or 11.5 days at 12 °C. The reaction products hydrogen sulphate and oxygen formed following the disproportionation reaction are not of environmental concern. The DT50 of KMPS in seawater at pH 7 and 20 °C of 5.6 hours is extrapolated to 10.6 hours at 12 °C. The Haber-Will-Statter Reaction in the presence of chloride results in chlorine being formed. Chlorine reacts with water to form hypochlorous acid that is extremely rapidly eliminated in the environment due to reaction with ammonia and organic material which act as reductants.

Taking into consideration the available information based on a weight of evidence approach, KMPS can be considered as rapidly degradable for classification purposes according to the Annex I: 4.1.2.9.5 of the CLP GD (2017).

Bioaccumulation

The low log Pow (< 0.30 measured at 20 °C and -3.90 calculated) indicate that KMPS has a low potential for bioconcentration and bioaccumulation (according to guideline OECD 117, log Pow values below 4 are regarded to be indicators of low accumulation potential). Moreover, KMPS dissipates rapidly in the environment. Considering these facts, it can be concluded that KMPS has no potential for bioaccumulation.

Chronic aquatic toxicity

Two chronic toxicity studies on marine species and a study with a marine algal species are available for KMPS. Considering these data, fish were the most sensitive trophic group with a NOEC of 0.222 mg KMPS/L obtained for *Cyprinodon variegatus* (Sheepshead minnow).

A.4.5.3 Conclusion on classification and labelling for environmental hazards and comparison with the CLP criteria

KMPS fulfils the CLP criteria for classification as Acute aquatic Category 1, H400 (Very toxic to aquatic life) with an M-factor of 1, based on the E_rC_{50} equal to 0.370 mg KMPS/L for

Skeletonema costatum in the range 0.1 < L(E)C_{50} ≤ 1 mg/L.

As the worst case chronic endpoint is ≤ 1 mg/L based on marine data and considering substance is rapidly degradable in seawater, KMPS shall be classified as Chronic aquatic Category 3, H412 (Harmful to aquatic life with long lasting effects) with no M factor assigned based on the NOEC equal to 0.222 mg/L for *Cypronodon variegatus*.

Aquatic Acute 1, H400 (M=1)

Aquatic Chronic 3, H412

Hazard statement on the label: Very toxic to aquatic life with long lasting effects (H410)

A.5. Assessment of additional hazards

A.5.1. Hazardous to the ozone layer

A.5.1.1. Short summary and overall relevance of the provided information on ozone layer hazard

Stratospheric ozone depletion can be excluded due to the short half-life in air. KMPS is predicted to have an atmospheric half-life of 96 hours. Additionally, as the molecule does not contain olefinic carbon-carbon double or acetylenic (triple) bonds, KMPS is not expected to react with ozone.

A.5.1.2. Comparation with the CLP criteria

The half-life of KMPS in air is relatively short and is therefore not considered to be involved in ozone depletion. KMPS does not fulfil the CLP criteria for classification.

A.5.1.3. Conclusion on classification and labelling for ozone layer hazard

No classification is proposed for KMPS regarding ozone layer hazard according to the criteria of the CLP Regulation.

A.6. Additional Labelling

Not relevant.

A.7. Assessment of exclusion criteria, substitution criteria and POP

Not applicable for CLH report.

D. Appendices

APPENDIX V: OVERALL REFERENCE LIST (INCLUDING DATA OWNER AND CONFIDENTIALITY CLAIM)

Author(s)	Year	Section No./ Reference No.	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data protection Claimed (Yes/No)	Owner
			Physical Properties and Hazards		
Anonymous	2002a	A3.1/01	OXONE MONOPERSULFATE COMPOUND - PHYSICOCHEMICAL PROPERTIES Source: Huntingdon Life Science Report No.: DPT 557/012940 GLP; (unpublished) Doc. No.: 119-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2007c	A3.1/02	PHYSICAL AND CHEMICAL CHARACTERISTICS OF OXONE:UV/VISIBLE ABSORPTION, CHARACTERIZATION SPECTRUM (IR), DISSOCIATION CONSTANT, MELTING POINT, FLAMMABILITY (SOLIDS), FLAMMABILITY (CONTACT WITH WATER) AND PYROPHORIC PROPERTIES Source: Case Consulting Laboratories, Inc., Whippany, N.J., United States Report No.: 3280-38 Antec International Ltd-24458 GLP; (unpublished) Doc. No.: 119-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2007e	A3.2/01	CALCULATION OF THE HENRY´S LAW CONSTANT - PENTAPOTASSIUM BIS (PEROXYMONOSULPHATE) BIS (SULPHATE) Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: 115-001 Not GLP; (unpublished) Doc. No.: 115-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	KMPS Registration Group
Anonymous	2007a	A3.3/01	PHYSICAL AND CHEMICAL CHARACTERISTICS OF KMPS P-16 - APPEARANCE, EFFECT OF PH ON	Yes (Data on existing a.s.	KMPS Registration Group

			SOLUBILITY, HYDROLYSIS AS A FUNCTION OF PH, SURFACE TENSION AND ACCELERATED STORAGE STABILITY Source: Case Consulting Laboratories, Inc., Whippany, N.J., United States Report No.: 3280-27 Antec International Ltd-21226 Not GLP; (unpublished) Doc. No.: 119-003	submitted for the first time for entry into Annex I.)	
Anonymous	2001	A3.3/02	FRENCH/EUROPEAN STANDARD NF EN 12678 - AFNOR 2001 - CHEMICALS USED FOR TREATMENT OF WATER INTENDED FOR HUMAN CONSUMPTION - POTASSIUM PEROXOMONSULFATE Source: Associoation Francaise de Normalisation Report No.: NF EN 12678 N-20040401-063271-T Not GLP; (unpublished) Doc. No.: 989-001	No	n.a.
Anonymous	2008b	A3.11.5/01	KMPS - LABORATORY STUDY OF RELATIVE SELF-IGNITION TEMPERATURE Source: E.I. DuPont de Nemours and Company DuPont Haskell laboratory Report No.: DuPont 24463 GLP; (unpublished) Doc. No.: 142-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2007d	A3.15/01	KMPS - LABORATORY STUDY OF EXPLOSIVE PROPERTIES Source: E.I. DuPont de Nemours and Company Agricultural Products Report No.: DuPont 22465 GLP; (unpublished) Doc. No.: 141-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	KMPS Registration Group
Anonymous	2003	A3.16/01	OXONE MONOPERSULFAE COMPOUND - OXIDISING PROPERTIES (SOLIDS) Source: Huntingdon Life Science Report No.: DPT636/024171 GLP; (unpublished) Doc. No.: 143-003	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2002b	A3.16/02	OXONE - UN TEST 0.1: TEST FOR OXIDISING SOLIDS	Yes (Data on existing a.s.	Lanxess Deutschland GmbH

			Source: Huntingdon Life Science Report No.: DPT630/023228 GLP; (unpublished) Doc. No.: 143-001	submitted for the first time for entry into Annex I.)	
Anonymous	2008a	A3.17/01	Physical and Chemical Properties of Oxone PS-16; Storage Stability OPPTS TEST GUIDELINES, SERIES 830, PRODUCT PROPERTIES: 830.6317 Source: Case Consulting Laboratories, Inc., Whippany, N.J., United States Report No.: 3280-28 Not GLP; (unpublished) Doc. No.: 145-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	KMPS Registration Group
Assessment of effects on Human Health					
Anonymous	2001a	A6.1.1/01	OXONE MONOPERSULFATE COMPOUND - ACUTE ORAL TOXICITY TO THE RAT (ACUTE TOXIC CLASS METHOD) Source: Huntingdon Life Science Report No.: DPT 567/012276/AC DuPont-5763 GLP; (unpublished) Doc. No.: 521-003	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2001b	A6.1.2/01	OXONE MONOPERSULFATE COMPOUND - ACUTE DERMAL TOXICITY TO THE RAT Source: Huntingdon Life Science Report No.: DPT 568/012277/AC DuPont-5762 GLP; (unpublished) Doc. No.: 522-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	1995	A6.1.3/01	INHALATION MEDIAN LETHAL CONCENTRATION (LC50) STUDY WITH H-20981 IN RATS Source: Haskell Laboratory Report No.: DuPont HLR 284-95 10143-001 GLP; (unpublished) Doc. No.: 528-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	1980	A6.1.3/02	INHALATION LETHAL CONCENTRATION (LC50) Source: Haskell Laboratory, Report No. 1043-80; 3840-001 Not GLP; (unpublished) Doc. No. 523-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	1983b	A6.1.4/01	BERICHT ÜBER DIE PRÜFUNG DER LOKALEN	Yes	United Initiators

			REIZWIRKUNG VON CAROAT NACH EINMALIGER APPLIKATION AN DER HAUT DES KANINCHENS (PATCH TEST) - INCLUDING ENGLISH TRANSLATION Source: ASTA-Werke, Bielefeld Report No.: TOX-364-83/84 83 0061 DKT Not GLP; (unpublished) Doc. No.: 565-001	(Data on existing a.s. submitted for the first time for entry into Annex I.)	
Anonymous	1985	A6.1.4/02	RD/1/85: ACUTE EYE IRRITATION/CORROSION TEST IN THE RABBIT Source: Life Science Research Report No.: 85/LAP013/307 Not GLP; (unpublished) Doc. No.: 566-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	United Initiators
Anonymous	2001c	A6.1.5/01	OXONE MONOPERSULFATE COMPOUND - SKIN SENSITIZATION TO THE GUINA-PIG (MAGNUSSON & KLIGMAN METHOD) Source: Huntingdon Life Science Report No.: DPT 571/013150/SS DuPont-5761 GLP; (unpublished) Doc. No.: 567-007	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2020	A6.1.5/03	LOCAL LYMPH NODE ASSAY IN MICE (LLNA-BRDU ELISA) Source: MB Research Laboratories, Spinnerstown, USA Report No.: MB 20-27954.26 GLP; (unpublished) Doc. No.: 567-009	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	United Initiators
Anonymous	2016a	C_A.6.1.5/02	Overview of sensitisation data on Oxone. Doc. 581-006 /	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	KMPS Registration Group
Anonymous	1983a	A6.2.1	ABSORPTION OF SULFATE FROM ORALLY ADMINISTERED MAGENSIUM SULFATE IN MAN Source: J. Toxicol-Clin. Toxicol., 1983, 20, (2), 107-114 Not GLP; (published) Doc. No. 592-002	No	N.R.

Anonymous	2010	A4.1.1	EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS); Scientific Opinion on the use of potassium sulphate and sodium sulphate as sources of respectively potassium and sodium added for nutritional purposes to food supplements. EFSA Journal 2010;8(12):1940 [12 pp.]. doi:10.2903/j.efsa.2010.1940.	No	EFSA
Anonymous	2008	A4.1.1	Scientific Opinion of the Panel on Food Additives and Nutrient Sources added to Food on a request from the Commission on Calcium sulphate for use as a source of calcium in food supplements. The EFSA Journal (2008) 814, 1-9.	No	EFSA
Anonymous	2004a	A4.5.1	Potassium peroxymonosulfate-induced contact dermatitis. Contact Dermatitis; 51:89-90.	No	N.R.
Anonymous	2016b	A4.5.1	Retrieved from CDC - POTASSIUM DICHROMATE - International Chemical Safety Cards - NIOSH (iiab.me) (accessed on 25.07.2022)	No	N.R.
Anonymous	2016c	A4.5.1	Respiratory Health History of Active Employees at Oxone™ Manufacturing Facility, Memphis Site (U.S.) Epidemiology Report EPI-060022016-HQL	No	N.R.
Anonymous	2005a	A6.2.1	OPINION OF THE SCIENTIFIC PANEL ON DIETETIC PRODUCTS; NUTRITION AND ALLERGIES ON A REQUEST FROM THE COMMISSION RELATED TO THE TOLERABLE UPPER INTAKE LEVEL OF POTASSIUM Source. The EFSA Journal, 2005, 193, 1-19 Not GLP; (published) Doc. No. 592-003	No	N.R.
Anonymous	2001d	A6.3.1/01	OXONE MONOPERSULFATE COMPOUND - PRELIMINARY TOXICITY STUDY BY ORAL ADMINISTRATION TO CD RATS FOR 14 DAYS Source: Huntingdon Life Science Report No.: DPT 577/012784 DuPont 5764 GLP; (unpublished) Doc. No.: 531-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH

Anonymous	1981	A6.3.3/01	SUBACUTE INHALATION TOXICITY OF OXONE Source: Haskell Laboratory Report No.: 431-81 3840-001 Not GLP; (unpublished) Doc. No.: 531-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2019a	A6.6.3/02	In vitro Mammalian Cell Gene Mutation Assay (Thymidine Kinase Locus/TK+/-) in Mouse Lymphoma L5178Y Cells with KMPS (technical) Source: Eurofins BioPharma Product Testing Munich GmbH Report No.: 192142 GLP; (unpublished) Doc. No.:	Yes (Data on existing active substance (a.s.) submitted for the first time for approval of the a.s.)	LANXESS Deutschland GmbH, United Initiators GmbH
Anonymous	2002a	A6.4.1/01	OXONE MONOPERSULFATE COMPOUND - TOXICITY STUDY BY ORAL ADMINISTRATION TO CD RATS FOR 13 WEEKS (VOLUME 1 AND 2) Source: Huntingdon Life Science Report No.: DPT 578/013232 DuPont 5765 GLP; (unpublished) Doc. No.: 533-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2001e	A6.6.1/01	OXONE MONOPERSULFATE COMPOUND - BACTERIAL REVERSE MUTATION ASSAY WITH AN INDEPENDENT REPEAT ASSAY Source: Huntingdon Life Science Report No.: DPT 572/012909 DuPont-5758 GLP; (unpublished) Doc. No.: 557-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2001f	A6.6.2/01	OXONE MONOPERSULFATE COMPOUND - IN VITRO MAMMALIAN CHROMOSOME ABERRATION TEST IN HUMAN LYMPHOCYTES (AMENDED FINAL REPORT) Source: Huntingdon Life Science Report No.: DPT 573/013219 Antec International Ltd-5759 GLP; (unpublished) Doc. No.: 557-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2002b	A6.6.3/01	OXONE MONOPERSULFATE COMPOUND - MAMMALIAN CELL MUTATION ASSAY	Yes (Data on existing a.s.	Lanxess Deutschland GmbH

			Source: Huntingdon Life Science Report No.: DPT 574/013360 DuPont-5851 GLP; (unpublished) Doc. No.: 557-004	submitted for the first time for entry into Annex I.)	
Anonymous	2001g	A6.6.4/01	OXONE MONOPERSULFATE COMPOUND - MAMMALIAN ERYTHROCYTE MOUSE MICRONUCLEUS TEST Source: Huntingdon Life Science Report No.: DPT 575/013538 DuPont-5760 GLP; (unpublished) Doc. No.: 557-003	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2021	A6.6.5/01	*In vivo* Mammalian Alkaline Comet Assay of (Liver, Forestomach, Glandular Stomach and Duodenum) Cells in Rats with KMPS Triple Salt [CAS No. 70693-62-8] Administered on 2 consecutive Days. Source: Report No.: STUGC20AA2882-3 GLP; (unpublished) Doc. No. 557-006	Yes (Data on existing active substance (a.s.) submitted for the first time for approval of the a.s.)	LANXESS Deutschland GmbH, United Initiators GmbH
Anonymous	2004	A6.8.1/01	OXONE MONOPERSULFATE COMPOUND - DEVELOPMENT TOXICITY STUDY IN RATS Source: Haskell Laboratory Report No.: DuPont-14174 15034 841 GLP; (unpublished) Doc. No.: 551-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2005	A6.12.1/01	POTASSIUMPEROXOMONOSULFATE - OCCUPATIONAL MEDICAL STATEMENT Source: Not relevant Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 574-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	United Initiators
Anonymous	1992a	A6.12.2/01	100-PERSON HUMAN PATCH TEST WITH AMMONIUM PERSULFATE, SODIUM PERSULFATE, AND IMPACT Source: Haskell Laboratory Report No.: Du Pont HLO 400-92	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH

			9222-001 Not GLP; (unpublished) Doc. No.: 572-001		
Anonymous	1992b	A6.12.2/02	EVALUATION OF DERMAL SENSITIZATION POTENTIAL OF IMPACT IN HUMANS Source: Haskell Laboratory Report No.: Du Pont HLO 498-92 Not GLP; (unpublished) Doc. No.: 572-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2016		Scientific opinion on dietary reference values for potassium. EFSA Journal 2016; 14(10):4592, 56 pp.(Published)	No	EFSA
Anonymous	2018a		Potassium - friend or foe? Pediatr Nephrol. 2017 Jul; 32(7): 1109–1121 (Published)	No	N.R.
Anonymous	2023		Hyperkalemia: Prevalence, Predictors and Emerging Treatments. Cardiol Ther 2023; 12,35-63. https://doi.org/10.1007/s40119-022-00289-z (Published)	No	N.R.
Anonymous	2021a		Potassium Metabolism and Management in Patients with CKD. Nutrients. 2021 May 21;13(6):1751 (Published)	No	N.R.
Anonymous	2019b		Scientific Opinion on the re-evaluation of sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, 514 (i), 514 (ii), 515 (i), 515 (ii), 516 and 517) as food additive. *EFSA Journal* 2019;17(10):5868, 38 pp. (Published)	No	EFSA
Anonymous	2020a		The Cellular and Physiological Basis for Lung Repair and Regeneration: Past, Present, and Future. Cell Stem Cell 26, April 2, 2020 (Published)	No	N.R.
Anonymous	1992		A Physiologically Based Pharmacokinetic and Pharmacodynamic Model to Describe the Oral Dosing of Rats with Ethyl Acrylate and Its Implications for Risk Assessment. Free Radic Res. 2010 May; 44(5) (Published)	No	N.R.
Anonymous	2018b		An Ad. verse Outcome Pathway (AOP) for forestomach tumors induced by non-genotoxic initiating events.	No	N.R.

			Regulatory Toxicology and Pharmacology 96 (2018) 30–40 (Published)		
Anonymous	2020b		A comprehensive view on mechanistic approaches for cancer risk assessment of non-genotoxic agrochemicals. Regulatory Toxicology and Pharmacology 118 (2020) 104789 (Published)	No	N.R.
Anonymous	2018c		Thresholds of Genotoxic and Non-Genotoxic Carcinogens. Toxicol. Res. Vol. 34, No. 4, pp. 281-290 (2018) (Published)	No	N.R.
Anonymous	2021b		Assessing chemical carcinogenicity: hazard identification, classification, and risk assessment. Insight from a Toxicology Forum state-of-the science Workshop. Critical Reviews in Toxicology, 51:8, 653-694 (Published)	No	N.R.
Anonymous	2018d		The role of ethyl acrylate induced GSH depletion in the rodent forestomach and its impact on MTD and in vivo genotoxicity in developing an adverse outcome pathway (AOP). Regulatory Toxicology and Pharmacology 92 (173-181 (Published)	No	N.R.
Anonymous	2010		Reactive oxygen species in cancer. Free Radic Res. 2010 May; 44(5) (Published)	No	N.R.
Anonymous	2020c		Towards a mechanism-based approach for the prediction of nongenotoxic carcinogenic potential of agrochemicals. CRITICAL REVIEWS IN TOXICOLOGY 2020, VOL. 50, NO. 9, 725–739 (Published)	No	N.R.
Anonymous	1994		Synchronous appearance of fibronectin, integrin alpha 5 beta 1, vinculin and actin in epithelial cells and fibroblasts during rat tracheal wound healing Virchows Arch 1994;425(4):425-34	No	N.R.
Anonymous	2021c		Review: Glutathione: Role in Oxidative/Nitrosative Stress, Antioxidant Defense, and Treatments. Volume6, Issue18, 2021, pp 4566-4590. Graphical Abstract, https://doi.org/10.1002/slct.202100773	No	N.R.

			(Published)		
Anonymous	2011		Guidelines for Drinking-water Quality, Fourth Edition, World Health Organization, Geneva, ISBN 978 92 4 154815 1 (Published)	No	WHO
Anonymous	2012		Guideline: Potassium intake for adults and children, World Health Organization, Geneva, ISBN 978 92 4 150482 9	No	WHO
Anonymous	2020d		Impact of Dietary Potassium Restrictions in CKD on Clinical Outcomes: Benefits of Plant-Based diet. Kidney Med. 2020 Jun 15;2(4):476-487. (Published)	No	N.R.
Environmental effects assessment					
Anonymous	2007a	A7.1.1.1.1/01	PHYSICAL AND CHEMICAL CHARACTERISTICS OF KMPS P-16 - APPEARANCE, EFFECT OF PH ON SOLUBILITY, HYDROLYSIS AS A FUNCTION OF PH, SURFACE TENSION AND ACCELERATED STORAGE STABILITY Source: Case Consulting Laboratories, Inc., Whippany, N.J., United States Report No.: 3280-27 Dupont-21226 Not GLP; (unpublished) Doc. No.: 119-003	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	KMPS Registration Group
Anonymous	2007b	A7.1.1.1.1/02	DEPLETION OF POTASSIUM MONOPERSULFATE IN SYNTHETIC POOL WATER Source: DuPont Chemical Solutions Enterprise Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 711-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2016a	A.7.1.1.1.1/03	LONG-TERM DATA ON DEGRADATION OF KMPS IN AQEOUS SOLUTION Source: DuPont Chemical Solutions Enterprise, Sudbury, UK Report No.: Not applicable GLP; (unpublished) Doc. No.: 711-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2016b	A.7.1.1.1.1/04	STUDY ON OXONE™ IN SOLUTION: IS HYDROGEN PEROXIDE RELEASED?	Yes (Data on existing a.s.	

			Source: Chemours Chemical Solutions, Sudbury UK Report No: Not applicable Not GLP; (unpublished) Doc. No. 711-005	submitted for the first time for entry into Annex I.)	
Anonymous	2012	A.7.1.1.1/01	DECOMPOSITION OF OXONE® IN ACTIVATED SLUDGE FROM STP Source: E.I. du Pont de Nemours and Company DuPont Chemicals & Fluoroproducts, experimental Station E402/5220 Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 713-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	KMPS Registration Group
Anonymous	2011	A.7.1.1.1/02	ANALYSIS OF KMPS DEGRADATION IN ACTIVATED SLUDGE AT 12°C. Source: DuPont Chemical Solutions Enterprise Laboratory Notebook. Report No.: Not applicable Not GLP; (unpublished) Doc. No. 713-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2018	A.7.1.1.1/03	ANALYSIS OF KMPS DEGRADATION IN ACTIVATED SLUDGE AT 12°C. Source: DuPont Chemical Solutions Enterprise Laboratory Notebook. Report No.: Not applicable Not GLP; (unpublished) Doc. No. 713-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2007c	A7.3.1/01	ESTIMATION OF THE ATMOSPHERIC RESIDENCE TIME OF POTASSIUM PEROXOMONOSULFATE USING THE ATKINSON METHOD Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: 743-001 Not GLP; (unpublished) Doc. No.: 743-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	KMPS Registration Group
Anonymous	2001a	A7.4.1.1/01	OXONE MONOPERSULFATE COMPOUND - ACUTE TOXICITY TO FISH Source: Huntingdon Life Science Report No.: DPT 579/013090 DuPont-5755 GLP; (unpublished)	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH

			Doc. No.: 821-003		
Anonymous	2007d	A7.4.1.1/02	KMPS: ACUTE TOXICITY WITH THE SHEEPHEAD MINNOW, *CYPRINODON VARIEGATUS*, DETERMINED UNDER STATIC TEST CONDITIONS Source: ABC Laboratories, USA Report No.: 61455 16918 261 GLP; (unpublished) Doc. No.: 821-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2001b	A7.4.1.2/01	OXONE MONOPERSULFATE COMPOUND - ACUTE TOXICITY TO *DAPHNIA MAGNA* Source: Huntingdon Life Science Report No.: DPT 580/013091 DuPont-5756 GLP; (unpublished) Doc. No.: 822-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2007e	A7.4.1.2/02	KMPS - ACUTE TOXICITY WITH MYSID SHRIMP, *AMERICAMYSIS BAHIA*, DETERMINED UNDER STATIC-RENEWAL TEST CONDITIONS Source: ABC Laboratories, USA Report No.: 61456 16918 260 GLP; (unpublished) Doc. No.: 825-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	KMPS Registration Group
Anonymous	2001c	A7.4.1.3/01	OXONE MONOPERSULFATE COMPOUND - ALGAL GROWTH INHIBITION ASSAY Source: Huntingdon Life Science Report No.: DPT 581/013092 DuPont-5757 GLP; (unpublished) Doc. No.: 823-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2007f	A7.4.1.3/02	KMPS: STATIC GROWTH INHIBITION TEST WITH THE MARINE DIATOM, *SKELETONEMA COSTATUM* Source: ABC Laboratories, USA Report No.: 61457 16918 323 GLP; (unpublished) Doc. No.: 823-003	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	KMPS Registration Group

Anonymous	2001d	A7.4.1.4/01	OXONE MONOPERSULFATE COMPOUND - ACTIVATED SLUDGE - RESPIRATION TEST Source: Huntingdon Life Science Report No.: DPT 558/012378 GLP; (unpublished) Doc. No.: 842-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	Lanxess Deutschland GmbH
Anonymous	2007g	A7.4.3.2/01	KMPS: EARLY LIFE-STAGE TOXICITY TEST WITH THE SHEEPSHEAD MINNOW, *CYPRINODON VARIEGATUS*, UNDER FLOW-THROUGH CONDITIONS Source: ABC Laboratories, USA Report No.: 61459 16918 215 GLP; (unpublished) Doc. No.: 826-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	KMPS Registration Group
Anonymous	2007h	A7.4.3.4/01	KMPS -- LIFE-CYCLE TOXICITY TEST OF THE SALTWATER MYSID SHRIMP, *AMERICAMYSIS BAHIA*, CONDUCTED UNDER FLOW-THROUGH TEST CONDITIONS Source: ABC Laboratories, USA Report No.: 61458 16918 290 GLP; (unpublished) Doc. No.: 829-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I.)	KMPS Registration Group