Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

Potassium chlorate

EC Number: 223-289-7
CAS Number: 3811-04-9

CLH-O-0000007010-92-01/F

Adopted

10 June 2021

10 June 2021

CLH-O-0000007010-92-01/F

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: **Potassium chlorate**

EC Number: **223-289-7**

CAS Number: **3811-04-9**

The proposal was submitted by **Sweden** and received by RAC on **9 April 2020.**

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

PROCESS FOR ADOPTION OF THE OPINION

Sweden has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation/*** on **4 May 2020**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **3 July 2020**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Anca Oana Docea**

Co-Rapporteur, appointed by RAC: **Anja Menard Srpčič**

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The RAC opinion on the proposed harmonised classification and labelling was adopted on **10 June 2021** by **consensus**.

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	017-004-00-3	Potassium chlorate	223-289-7	3811-04-9	Ox. Sol. 1 Acute Tox. 4* Acute Tox. 4* Aquatic Chronic 2	H271 H302 H332 H411	GHS03 GHS07 GHS09 Dgr	H271 H302 H332 H411			
Dossier submitters proposal	017-004-00-3	Potassium chlorate	223-289-7	3811-04-9	**Remove** Acute Tox. 4 * Aquatic Chronic 2 **Modify** Acute Tox. 3	**Remove** H332 H411 **Modify** H301	**Remove** Dgr GHS09 **Modify** GHS06	**Remove** H332 H411 **Modify** H301		**Add** Oral; ATE = 100 mg/kg bw	
RAC opinion	017-004-00-3	Potassium chlorate	223-289-7	3811-04-9	**Remove** Acute Tox 4* Aquatic Chronic 2 **Modify** Acute Tox 3	**Remove** H332 H411 **Modify** H301	**Remove** GHS09 **Modify** GHS06	**Remove** H332 H411 **Modify** H301		**Add** Oral; ATE = 100 mg/kg bw	
Resulting Annex VI entry if agreed by COM	017-004-00-3	Potassium chlorate	223-289-7	3811-04-9	Ox. Sol. 1 Acute Tox 3	H271 H301	GHS03 GHS06 Dgr	H271 H301		Oral; ATE = 100 mg/kg bw	

GROUNDS FOR ADOPTION OF THE OPINION

RAC general comment

Potassium chlorate is used in the manufacture of potassium chlorate crystals, of pyrotechnics and matches, and in the formulation of cosmetics and personal care products. It has an existing entry to the CLP regulation as Ox. Sol. 1; H271, Acute Tox. 4*; H302, Acute Tox.4*; H332, and Aquatic Chronic 2; H411. The proposal from the dossier submitter (DS) was to remove Aquatic Chronic 2; H411 and Acute Tox. 4*; H332 and to modify the existing acute oral toxicity classification to Acute Tox. 3; H301. Potassium chlorate almost totally dissociates in water producing potassium cations and chlorate anions and therefore the read-across of data from sodium chlorate is justified to assess the acute toxicity when there is a lack of studies for potassium chlorate.

HUMAN HEALTH HAZARD EVALUATION

RAC evaluation of acute toxicity

ACUTE TOXICITY – ORAL ROUTE

Summary of the Dossier Submitter's proposal

Available animal studies on acute oral toxicity (cf. Table 8 of the CLH report):

Species	**LD_{50} (mg/kg bw)**	**Dosing (mg/kg bw)/Test substance**	**Results (mortality)**	**Reliability (DS)**	**Year of the study**	**Remarks**
Sprague-Dawley rat, 5 animals/sex/dose	>5000 mg/kg bw	2000/ sodium chlorate 5000/ sodium chlorate	2000: 0(M)/0(F)/5(M)/5(F) 5000: 0(M)/1(F)/5(M)/5(F)	1	1991	GLP study according to EPA OPP 81-1 (Acute Oral Toxicity)
CD rat, 2 animals/sex/dose – range finding study and 8 animals/sex/dose, except 10000 g where 8 males and 7 females were tested – main study	4950 (male) 6250 (female)	**Range study:** 1000;1500; 5000/ sodium chlorate **Main study**: 1470; 2150; 3160; 4640; 6810/ sodium chlorate (male) 2150; 3160; 4640; 6810; 10000/ sodium chlorate (female)	**Range study:** **Male**: 5000: 2/2 1500: 0/2 1000: 0/2 **Female**: 5000: 0/2 1500: 0/2 1000: 0/2 **Main study**: **Male**: 6810: 7/8 4640: 3/8 3160: 0/8 2150: 0/8 1470: 0/8 **Female**: 10000: 7/7 6810: 5/8 4640: 0/8 3160: 0/8 2150: 0/8	2	1981	OECD TG 401 (Acute Oral Toxicity) before 2002; No information on test substance purity, No GLP
Collie and boxer dog/ 1 or 2 animals/dose, sex not specify	No LD_{50} obtained	500; 1000; 2000; (gavage); 5000 (by slow i.v. injection)	500: 0/1 1000: 1(boxer)/2 2000: 1(collie)/1	3	1971	No GLP or according to a standard method
Not specified	1200-7000	Not specified	Not specified	4	1970	No GLP, no guideline specified
Rat, no further detail	7000-8000	Not specified	Not specified	4	1948	No specified
Rat, no further detail	1200	Not specified	Not specified	4	1960	No specified

In the records on the decision on the classification of sodium chlorate from the Technical Committee on Classification and Labelling (TC) C&L, 1989 a LD_{50} of 1200 mg/kg bw in rat was identified. However, the study report is not available to the dossier submitter. The 2015 EFSA scientific opinion (Risks for public health related to the presence of chlorate in food) also mention that "other publications" reported oral LD_{50} for sodium chlorate to be 1200 mg/kg bw (equivalent to 936 mg chlorate/kg bw) in rats (Lewis 1996, HSDB 2003, as cited in EFSA scientific opinion 2015) and the oral LD_{50} for potassium chlorate to be 1 870 mg/kg bw (equivalent to 1272 mg chlorate/kg bw) in rats (RTECS 1994, as cited in EFSA scientific opinion 2015). In the Registry of Toxic Effects of Chemical Substances from NIOSH the oral LD_{50} in rat was 1870 mg/kg. None of these rat studies is available to the DS to be able to assess quality and reliability.

Available human data on acute oral toxicity (cf. Table 9 of the CLH report for the full reference):

Type of data/report	**Test substance**	**Lethal dose in mg/kg bw[1]**	**Relevant information about the study (as applicable)**	**Limitation**	**Year of the study**
Review AFSSA (French poison center)[1]	Sodium chlorate	143-286 mg/kg bw (adult)	29 individuals had pathological methemoglobinemia (MetHb ⩾ 3%). The smallest doses causing a pathological MetHb (⩾ 3%) humans in this study were in the order of 10-20 grams of sodium chlorate orally ingested. 13 (45%) of the 29 individuals did not survive.	No data regarding the other comorbidities and pathologies of the individuals that can influence the toxicity of sodium chlorate	2011
Public literature/ Case report-accidental poisoning	Sodium chlorate	214 mg/kg bw (adult)	Outcome in 14 patients poisoned by sodium chlorate. Mortality was high (64%), and death invariably occurred, irrespective of treatment, when the amount of sodium chlorate ingested exceeded 100 g. In this study, the smallest lethal dose published was 15 g (214 mg of chlorate/kg body weight) and concerned a 46-year-old woman who died at medical care in intensive care. In this same series, another death occurred at a woman (unspecified age) following the intake of a 30 g dose (429 mg / kg chlorate despite treatment with methylene blue, hemodialysis and exsanguino-transfusion.	No data regarding the other comorbidities and pathologies of the individuals that can influence the toxicity of sodium chlorate for the 2 cases where the doses were lower than the average dose that produces high mortality (>100 g that is equivalent to 1428 mg/kg bw)	1979
Public literature/ Case report – accidental poisoning	Sodium chlorate	No death, survived 571 mg/kg	40 g sodium chlorate was taken by error instead of that amount of sodium chloride by a 28-year-old man and he survived.	No data regarding the other comorbidities and pathologies of the individuals that can	1962

Type of data/report	Test substance	Lethal dose in mg/kg bw[1]	Relevant information about the study (as applicable)	Limitation	Year of the study
		bw (adult)		influence the toxicity of sodium chlorate	
Public literature/ Case reports - accidental poisoning	Potassium chlorate	500 mg/kg bw (adult)	Cochran and Smith reported a case of Bright's disease in which potassium chlorate had mistakenly been given instead of potassium chloride. There was evidence that the patient took approximately 35 g over a period of 3 days. Death occurred on the 5th day after the last dose.	Bright's disease or glomerulonephritis can potentiate the direct toxic effect of chlorate on the proximal tubule of the kidney, preventing the elimination of the chlorate and prolonging the exposure of the erythrocytes increasing the toxicity compared to a healthy adult	1940
Public literature/ Case report – suicide attempt	Potassium chlorate	107 mg/kg bw (adult)	A mentally diseased army officer, aged 33, ate an entire tube of Pebeco Tooth Paste on an empty stomach, corresponding, in the opinion of the author, to 7.5 G of potassium chlorate and died.	No data regarding the other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate and if other substance was also involved taking into account that it was a mentally diseased individual.	1930
Public literature/ Case report – suicide attempt	Sodium chlorate	No death, survided 334 mg/kg bw (adult)	A 29 year old man ingested about 20 g of sodium chlorate (230 mg chlorate/kg body weight). He became cyanotic, and his hemoglobin dropped to 11 g/100 mL within 24 hr; methemoglobin and methemoalbumin were detected in his plasma. He was anuric for 14 days, then gradually improved, and he was released from the hospital after 6 wk.	No data regarding the other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate	1987; 1979
Public literature/ Case report – suicide attempt	Sodium chlorate	2143-2857 mg/kg bw (adult)	A case of severe sodium chlorate poisoning was observed within 5 h after suicidal ingestion of 150– 200 g of the herbicide. Methaemoglobinaemia was the early symptom of the intoxication.	No data regarding the other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate	1981
Public literature/ Case report	Sodium chlorate	71-143 mg/kg bw (adult) 133 mg/kg bw (child)	A dose of 5-10 g can prove fatal in adults, as can a dose of 2 g in small children.	No data regarding the other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate	1987

Type of data/report	Test substance	Lethal dose in mg/kg bw[1]	Relevant information about the study (as applicable)	Limitation	Year of the study
Public literature/ Case report – poisoning cases	Sodium chlorate	800 mg/kg bw (LD_{50} adult female)	The oral LD_{50} in adult women is reported to be 800 mg/kg bw	No data regarding the study and other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate	1996
Public literature/ Case report-poisoning cases	Potassium chlorate	No death, survided 600 mg/kg bw (infant)	A 3-month-old boy survived the ingestion of 3g sodium chlorate.	No more data regarding the study	1977
Public literature/ Case report – accidental poisoning	Potassium chlorate	100 mg/kg bw (adult)	A 76-year-old woman died after ingesting a tablespoon, about 7 g, of potassium chlorate.	No data regarding the other comorbidities/pathologies of the individual that can influence the toxicity of potassium chlorate	1970
Public literature/ Case reports-poisoning or suicide attempts	Sodium chlorate	No death, survided, 186 mg/kg bw (adult)	55 year old man swallowed 13 g	No data regarding other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate	1956
Public literature/ Case reports-poisoning or suicide attempts	Sodium chlorate	No death, survided, 200 mg/kg bw (adult)	Two cases of renal failure due to sodium chlorate poisoning. 67 year old female ingested 14 g of sodium chlorate and survived. In total 12 cases were reported (including the 10 reported by Derot 1948) in this publication and 8 were accidental poisonings.	No data regarding other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate	1962
Public literature/ Case reports-poisoning or suicide attempts	Sodium chlorate	200-429 mg/kg bw (adult)	6 out of 10 cases died, the fatal dose was about 30 g, one person died after 14 g.	No data regarding other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate	1948
Public literature/ Case report – suicide attempt	Potassium chlorate	1300 mg/kg bw (adult)	35 year old woman died after consuming tablets of potassium chlorate for 5 days, in total 91 g	No data regarding other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate	1950
Public literature/ Case report – accidental poisoning	Potassium chlorate	No death, survided 429-500 mg/kg bw (adult)	Patient received 30-35 g for 3 days.	No data regarding other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate	1940

Type of data/report	Test substance	Lethal dose in mg/kg bw[1]	Relevant information about the study (as applicable)	Limitation	Year of the study
Public literature/ Case report - suicide attempt	Potassium chlorate	571 mg/kg bw (adult)	48 year old woman drank 150-200 g of water with 40 g	No data regarding other comorbidities/pathologies of the individual that can influence the toxicity of potassium chlorate	1934
Public literature/ Case report - suicide attempt	Potassium chlorate	107 mg/kg bw (adult)	Man swallowed 7.5 g included in tooth paste.	No data regarding other comorbidities/pathologies of the individual that can influence the toxicity of potassium chlorate	1930
Public literature/ Case report - poisoning	Potassium chlorate	267-333 mg/kg bw (child)	8 year old boy was poisoned with an unknown amount, estimated 4-5 g	No data regarding other comorbidities/pathologies of the individual that can influence the toxicity of potassium chlorate	1934
Public literature/ Case report - poisoning	Sodium chlorate	333-667 mg/kg bw (child)	17 year old boy with down sydrome	No data regarding the other comorbidities/pathologies of the individual that can influence the toxicity of potassium chlorate	1969
Public literature/ Case report - poisoning	Sodium chlorate	No death, survided, 1071 mg/kg bw (adult) 1286 mg/kg bw (adult)	18 year old man 75 g chlorate in water, survived 78 year old man 90 g chlorate in water, died	No data regarding the other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate	1971
Public literature/ Case report – suicide attempt	Sodium chlorate	No death, survived, 714 mg/kg bw (adult)	23 year old woman consumed about 50 g and survived	No data regarding the other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate	1977
Public literature/ Case report – suicide attempt	Sodium chlorate	No death, survived, 571 mg/kg bw (adult)	22-year-old male ingested 40 g and survived. A 57-year-old male ingested an unknown amount and survived.	No data regarding the dose/or other comorbidities/pathologies of the individual that can influence the toxicity of sodium chlorate	1985

[1]Estimated intakes per kg bw were calculated with a default body weight assumption of 70 kg for adults, 10 kg for children and 5 kg for infants. Unknown means that the original article could not be retrieved.

There is a key rat study (1991) performed in accordance with EPA Acute Toxicity Guideline, OPP 81-1 (equivalent to OECD Test Guideline TG 401) on sodium chlorate in compliance with GLP that showed that the LD_{50} of Sodium Chlorate Crystal is > 5000 mg/kg bw and supported by another two animal studis one in rats (1981) equivalent with OECD TG 401, (not GLP, no information on

test substance purity), that showed a LD_{50} of 4950 mg/kg bw in males and 6250 mg/kg bw in females and one dog study (1971) with limited reliability used only as supporting evidence. These studies showed that sodium chlorate show a low acute toxicity LD_{50} > 5000 mg/kg bw that does not meet the criteria of classification in Acute Tox. 4 for oral administration. The animal studies that have been used in the TC C&L from 1989 for classification according to which an LD_{50} of 1200 mg/kg bw rat was identified are not available to the DS. The studies reported in EFSA scientific opinion that state an LD_{50} for sodium chlorate of 1200 mg/kg bw in rats (Lewis 1996, HSDB 2003, as cited in EFSA scientific opinion 2015) are not available for assessment.

Several human case studies are describing accidental poisoning or suicide/homicide attempts with several limitations due to lack of robust summary reporting that doses of 5 to 10 grams (71-143 mg/kg bw) can be fatal in adults, and doses of 2 grams (0.2 g/kg bw) in children. But also multiple cases are described as surviving intakes ranging from 40 g (571 mg/kg bw3) to even 150-200 grams (2.1-2.9 g/kg bw). In many cases, the lethal dose in human is above 20 g (285 mg/kg bw) (Helliwell and Nunn 1979). The oral LD_{50} in adult women is reported to be 800 mg/kg (Lewis 1996).

Chlorate toxicity after ingestion in humans can be characterized primarily by gastrointestinal irritation, massive intravascular hemolysis, disseminated intravascular coagulation, cyanosis, and renal failure. Gastrointestinal irritation appears to be the result of a direct effect of the chlorate ion on the gastrointestinal mucosa. Intravascular hemolysis occurs after the formation of methemoglobin (MetHb) in exposed erythrocytes, eventually resulting in cyanosis. Besides, chlorate exerts a direct toxic effect on the proximal tubule of the kidney, causing necrosis and preventing the formation of urine and subsequent elimination of chlorate from the bloodstream, thus prolonging the exposure of the erythrocytes. Nephrotoxicity also seems mediated by MetHb catalysis. MetHb thus autocatalytically increases MetHb formation and destruction of the erythrocyte, which is shown in in vitro experiments. There are marked species differences in susceptibility to form MetHb where humans appear as more severely affected than rodent species.

The human poisoning incident reports demonstrate the lethal effect of sodium and potassium chlorate at concentration ranges that warrant classification.

The lowest lethal doses or ranges reported in this CLH proposal are the following:

- 71-142 mg/kg bw in adults (based on the assumption of default body weight 70 kg) and 133 mg/kg bw in children (Hartley and Kidd 1987)
- 100 mg/kg bw in a 76-year-old woman (based on the assumption of default bodyweight as 70 kg) (Fukomoto and Fukomoto 1970)
- 107 mg/kg bw in an adult man (based on the assumption of default bodyweight as 70 kg) (Bernstein cited in Klendshoj 1962)
- 125 mg/kg bw in a 43-year-old male (based on the assumption of default bodyweight as 70 kg) (AFSSA 2011).
- 214 mg/kg bw in a 46-year-old woman (based on the assumption of default bodyweight as 70 kg) (Helliwell and Nunn 1979)

Thus, based on a number of human case reports indicating the lowest lethal doses < 300 mg/kg bw the DS considers that a category 3 classification is justified rather than the current category 4 (minimum classification). In line with CLP guidance (to use the minimum dose or range shown or expected to cause mortality) for deriving a human ATE and considering that the available human data is quite incoherent, the DS proposes to use the converted Acute Toxicity point Estimate (cATpE), which is 100 mg/kg bw for category 3, to set the ATE.

Comments received during consultation

Four comments were received: 3 from the Member State Competent Authorities (MSCA) and 1 from industry (IND). 3 MSCAs agreed with the proposal as Acute Tox. 3; H301 with an ATE of 100 mg/kg bw.

One IND commented regarding the use of poisoning cases that occurred in the 60's and 70's (mostly suicide attempts) for the classification to Acute Tox. 3, that these studies are not controlled for underling illness or a history of other substance abuse. They did not agree with the use of 83 mg/kg bw as the basis for ATE derivation and suggested that 332 mg/kg bw equivalent to the ingestion of 20 g, as is stated in many cases, is more appropriate for deriving the ATE.

The DS responded that rats appear to have lower sensitivity to MetHb formation compared to humans and rat data are therefore not considered to be adequate for acute toxicity classification. Consequently, the assessment of acute toxicity needs to be based on the available human data. They agree that the evaluation of human data may be difficult due to various limitations, such as uncertainties relating to exposure assessment. However, according to the Guidance on the Application of the CLP Criteria v. 3.1.2.3.1 (CLP guidance) "*The minimum dose or concentration or range shown or expected to cause mortality after a single human exposure can be used to derive the human ATE directly, without any adjustments or uncertainty factors*". Following the CLP guidance 3.1.2.3.1 and the guidance example in 3.1.5.1.1 an ATE derived from the available data needs to be set despite the various limitations of human data. There are several cases available in the CLH proposal with human lethal doses (lowest lethal doses are summarised on page 17-18 in the CLH report, ranging from 71 mg/kg bw to 214 mg/kg bw) that support category 3 rather than category 4. An ATE needs to be set to protect also the most sensitive groups in the population. Therefore it may be considered justified to select the lowest dose or dose ranges. The DS finds that, by using a Weight of evidence approach and expert judgement, it is justified to use the converted Acute Toxicity point Estimate (cATpE), which is 100 mg/kg bw for category 3.

Assessment and comparison with the classification criteria

According to the CLP guidance, the preferred test species for evaluation of acute toxicity by the oral routes is the rat. When experimental data for acute toxicity are available in several animal species, scientific judgement shall be used in selecting the most appropriate LD_{50} values from among valid, well-performed tests.

There is a 1991 GLP study (regarded by the US EPA as a key animal study) with reliability 1 based on the DS assessment, a valid GLP supporting study from 1981, a non-GLP study with reliability 2 based on the DS assessment, and a non-GLP study with low reliability based on the DS assessment that supports no classification as the LD_{50} is 4950-6250 mg/kg bw. There are several studies from 1960 with low reliability due to lack of reported data that suggested the LD_{50} = 1200 mg/kg bw in rats that the DS does not have access to, and ECHA was unable to find, that supported the previous classification as Acute Tox. 4.

There are several human case studies of accidental poisoning or suicidal attempts evaluated by the DS, mainly because humans are more sensitive to methemoglobinemia produced by sodium chlorate compared to rodents. The main effects of chlorate toxicity after ingestion in humans is characterized primarily by gastrointestinal irritation, massive intravascular hemolysis, disseminated intravascular coagulation, cyanosis, and renal failure. Gastrointestinal irritation appears to be the result of a direct effect of the chlorate ion on the gastrointestinal mucosa. The intravascular hemolysis occurs subsequent to the formation of methemoglobin in exposed erythrocytes, eventually resulting in cyanosis. In addition, chlorate exerts a direct toxic effect on the proximal tubule of the kidney, causing necrosis and preventing the formation of urine and

subsequent elimination of chlorate from the bloodstream, thus prolonging the exposure of the erythrocytes. Nephrotoxicity also seems mediated by MetHb catalysis. MetHb thus autocatalytically increases MetHb formation and destruction of the erythrocyte, which is shown in *in vitro* experiments (Steffen, Wetzel 1993).

The lowest lethal doses or ranges reported in the CLH proposal with in-depth analyses by RAC are the following:

- 71-142 mg/kg bw in adults (based on the assumption of default body weight 70 kg) and 133 mg/kg bw in children, no data available regarding the treatment applied or other comorbidities (Hartley and Kidd 1987)
- 100 mg/kg bw in a 76-year-old woman (based on the assumption of default bodyweight as 70 kg), no data regarding the treatment applied or other comorbidities (Fukomoto and Fukomoto 1970)
- 107 mg/kg bw in a 33-year-old man (based on the assumption of default bodyweight as 70 kg) that ate an entire tube of Pebeco Tooth Paste that contain the equivalent of 7.5 g of potassium chlorate on an empty stomach. No details regarding the treatment applied could be found (Bernstein cited in Klendshoj 1962)
- 125 mg/kg bw in a case of a 43 years-old-man that volunteer ingested an equivalent of 8.8 g sodium chlorate contained in 5 mL powder based on self-report. He denied exposure to other chemicals. He presented to the hospital with multiple clinical complications as renal insufficiency, hemolysis, deglobulinization, thrombocytopenia and respiratory distress requiring intubation, resulting in death from shock before 48 hours. The treatment applied was methylene blue and vitamin C (AFSSA 2011). Interesting is that in that case series the patients that survived as high doses as 4456 mg/kg bw; 2500 mg/kg bw, 1683 mg/kg bw or 933 mg/kg bw underwent treatment by hemodialysis (AFSSA 2011).
- 214 mg/kg bw in a case of a 46-year-old woman that accidentally ingested 15 g of sodium chlorate equivalent to 214 mg/kg bw based on the assumption of default bodyweight as 70 kg and treated with supportive measurements. In the same case reports of 14 accidental or deliberate ingestion of potassium chlorate the patients that survived doses 1428 mg/kg bw (100 g ingested) 642 mg/kg bw (45 g ingested) or 428.57 mg/kg bw (30 g ingested) based on the assumption of default bodyweight as 70 kg underwent treatment by hemodialysis or peritoneal dialysis (Helliwell and Nunn 1979).

The human case reports showed that the lowest lethal doses < 300 mg/kg bw support classification as Acute Tox. 3 according to the CLP criteria. These dose levels are observed in case reports where hemodialysis or peritoneal dialysis were not applied. New mechanistic studies showed that methylene blue, the antidote for methemoglobinemia produced by chlorate and used in 1960-1980 is not efficient in chlorate poisoning. It was shown *in vitro* that the chlorates induce concentration-dependent oxidation of haemoglobin. The methemoglobin formation is followed by denaturation of the globin, a cross-linking of erythrocyte membrane protein and inactivation of membrane enzymes. The high sensitivity of glucose-6-phosphate dehydrogenase to denaturation by chlorate explains the inefficacy of methylene blue to reduce MetHb formed, as the antidotal effect of methylene blue depends on NADPH formed mainly by the oxidation of glucose-6-phosphate. The observed changes occur only in the presence of MetHb which forms a destabilising complex with chlorate. MetHb thus autocatalytically increases MetHb formation and destruction of the erythrocyte (Steffen and Wetzel 1993). In chlorate poisoning, haemodialysis is recommended not only as renal replacement therapy but also for removal of the toxic agent and increase the survival of intoxicated patients.

Overall conclusion: Despite the limitations of the case reports reviewed, RAC cannot disregard the studies that showed mortality at doses below 300 mg/kg bw and that support classification as Acute Tox. 3; H301. The cases that showed survival at higher doses were treated by haemodialysis or peritoneal dialysis, i.e. the recommended treatment in chlorate poisoning both for preventing acute renal failure and for removal of the toxic agent.

In the view of these data, RAC agreed that potassium chlorate should be **classified as Acute Tox. 3; H301, with an ATE = 100 mg/kg bw** by using the converted Acute Toxicity point Estimate (cAtpE) for category 3 based on human case reports.

ACUTE TOXICITY – INHALATION ROUTE

Summary of the Dossier Submitter's proposal

Animal studies on acute inhalation toxicity of potassium chlorate:

Species	LC_{50} (mg/l)	Test substance, form and particle size (MMAD)	Type of exposure	Dosing (mg/l)/Duration of exposure	Results (mortality)	Reliability (DS)	Study	Remarks
Wistar rat, 3 animals/sex/dose, 11 week old	>5.1 ± 0.3 mg/L	Potassium chlorate/MMAD (mean mass aerodynamic diameter) 4µm and 4.4µm and the gsd (geometric standard deviation): 1.9 and 1.8	Nose only inhalation, with an average air flow of 1.4 L/min	5.1 mg/L/4 h and 8 minutes; the nominal concentration was 144 mg/L	No mortality, no gross pathology findings	1	2010	GLP study according to OECD TG 436 (Acute Inhalation Toxicity: Acute Toxic Class Method)

No human studies or other animal studies were reported for acute inhalation toxicity.

There is only one OECD TG and GLP compliant animal study with potassium chlorate in rats that shows low acute toxicity, LC_{50} (4 h) > 5.1 mg/L (2010c). The MMAD and gsd were determined twice during the experiment. The MMAD was 4.0 µm and 4.4 µm, and the gsd was 1.9 and 1.8. Agglomeration of the particles in aerosol could determine the high MMAD values for the second measurement outside the recommended range of 1-4 µm, but close to the upper limit, and due to the appropriate gsd it is assumed that the deposition in the lower respiratory tract had occurred.

Comparing these results with the CLP guidance values for Acute Tox. 4 (1,0 < ATE ≤ 5,0), the criteria for classification is not met and hence the DS proposed to remove the existing Acute Tox.4*; H332 for potassium chlorate.

Comments received during consultation

Three MSCAs commented during the consultations and all agreed with the DS's proposal to remove the existing Acute Tox.4*; H332 classification for potassium chlorate.

Assessment and comparison with the classification criteria

According to the CLP guidance, the preferred test species for evaluation of acute toxicity by inhalation routes is the rat. When experimental data for acute toxicity are available in several animal species, scientific judgement shall be used in selecting the most appropriate LD_{50} values from among valid, well-performed tests.

The available GLP, OECD TG 436 study in rats with reliability 1 based on the DS evaluation showed the LC_{50} (4 h) is above 5.1 mg/L in rats. The criteria for classification is therefore not met.

RAC concludes that potassium chlorate does not meet the criteria for classification for acute inhalation toxicity and proposed that **Acute Tox. 4* should be removed from CLP Annex VI**.

ENVIRONMENTAL HAZARD EVALUATION

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

General information

The substance is currently listed in Annex VI of Regulation (EC) No 1272/2008 with a classification for environment hazard as Aquatic Chronic 2 (H411). The mesocosm study used to classify both sodium and potassium chlorate was not considered valid as evaluated in the REACH registration dossier and by the DS. The available data that is considered valid for potassium chlorate, as presented in CLP report, do not support a classification for hazards to the aquatic environment.

Read across justification

In water, sodium and potassium are naturally present and the amounts added with the test substance in experimental scenarios are not considered to have an impact on the test result. Sodium is the fifth most abundant alkali metal in the Earth's crust (22.700 mg/kg) and the principal cation in sea water (10.500 mg/L). Sodium values in stream water are from 0.23 to 1284 mg/ L (median value: 6.58 mg/L). Potassium occurs in various minerals, from which it may be dissolved through weathering processes. Sea water contains about 400 mg/L potassium. It tends to settle, and consequently ends up mostly in sediment. Rivers generally contains about 2-3 mg/L potassium. The counter ion present is therefore not relevant for the test results and will not contribute to the effects caused by the substance.

Water solubility was measured for both substances and has shown that both substances are highly soluble in water (see Table below).

There is also limited aquatic ecotoxicity data available for potassium chlorate. In the CLH report, studies with marine algae were available for both sodium and potassium chlorate. Based on these studies the DS concluded that both substances share toxicological profile, being non-toxic to marine algae with NOEC values greater than 100 mg/L (see Table below).

Both sodium and potassium chlorate strongly dissociate with pKa values in the range of -1 to -3 (theoretical range), meaning that both substances almost totally dissociate in water, producing sodium/potassium cations and chlorate anions.

***Table**: A brief comparison of sodium and potassium chlorate*

Measure	Sodium chlorate	Potassium chlorate
Water solubility (g/L at 20 °C)	696 - 736	69.9
Toxicity values (mg/L) for marine algae	*Skeletonema costatum* E_rC_{50} > 1000 NOE_rC > 1000	*Dunaliella tertiolecta* E_rC_{50} > 1469 (15 mg NO3-/L) NOE_rC = 735 (15 mg NO3-/L) *Nitzschia closterium* E_rC_{50} > 735 (15 mg NO3-/L) NOE_rC = 147 (15 mg NO3-/L)

Based on the above, the DS concluded that study outcomes drawn for sodium chlorate are also valid for potassium chlorate and vice versa.

Degradation

Potassium chlorate is highly soluble in water (69.9 g/L at 20°C).

Potassium chlorate in aqueous solutions is known for its chemical stability under environmental conditions (Urbanski 1998).

Based on the chemical structure it is expected that potassium chlorate is resistant to hydrolysis and is considered as stable in sterile water across the pH range. There are no relevant metabolites, degradation, or reaction products.

In the CLH report, the DS indicated that biotic conversions of potassium chlorate should not be assessed in standard OECD TG 301 tests for ready biodegradability and OECD TG 302 tests for inherent biodegradability because these tests only detect biodegradation of organic compounds under aerobic conditions.

Degradation of sodium chlorate in the Sturm test (OECD TG 301 B) using a specific analysis of chlorate was thought to be possible by L'Haridon (2003) because of the existence of anaerobic niches within the sludge particles used as inoculum. These anaerobic niches do occur in properly operated biological wastewater treatment plants (high activated sludge concentrations and low oxygen levels of~2 mg/L) but not under OECD TG 301 test conditions (low level of activated sludge and oxygen levels of >>9 mg/L). Moreover, the amount of biodegradable reducing agents in a standard OECD TG 301 test also limits preventing chlorate reduction.

Ready biodegradability of sodium chlorate transformation can be demonstrated using the methodology of the Closed Bottle test (OECD TG 301 D) with one major modification (van Ginkel *et al*., 1995). The test was modified by adding excess amounts of reducing agents (fatty acids, amino acids, carbohydrates). A minor part of the reducing agent was oxidized with the molecular oxygen present in the bottles thereby creating anaerobic conditions. The test was inoculated with low concentrations of activated sludge, soil, digested sludge or dilutions of river and ditch water in line with the OECD TG 301. Complete removal of chlorate was achieved within 28 days with all inocula tested and most reducing agents.

The ease with which chlorate reduction occurs naturally is also demonstrated by Bryan and Rohlich (1954). The authors have used the chlorate reduction as a measure for the Biological Oxygen Demand (BOD). The study has shown that chlorate is rapidly reduced by microorganisms using organic compounds as carbon and energy source present in sewage.

The DS indicated that a valid ready biodegradability test result is not available for potassium chlorate because chlorate is an electron acceptor like molecular oxygen. Nevertheless, all aspects important for achieving a ready biodegradability test result *i.e*. ultimate (complete) biodegradation, rate of biodegradation and number and occurrence of competent micro-organisms present in "unacclimated" ecosystems and biological treatment plants have been investigated (see above).

Microorganisms are capable of growth on potassium chlorate in the presence of reducing agents under anaerobic conditions. The biodegradation pathway proves that chlorate is reduced completely to chloride. The biodegradation kinetics of chlorate have been determined with mixed and pure cultures. The maximum growth rates of chlorate reducing microorganisms range from 0.04 to 0.56 h^{-1}, which is comparable or much higher than growth rates of nitrifying bacteria. Ammonium is oxidized readily in OECD TG 301 tests due to these nitrifying bacteria.

Painter and King (1983) used a model based on the Monod equation to interpret the biodegradation curves in ready biodegradability tests. According to this model, growth rates of competent microorganisms of 0.01 h^{-1} or higher do result in a ready biodegradation of the test substance. Reduction of chlorate has been detected in terrestrial ecosystems, fresh water, marine environment, compost, and aquifers.

Up to recently, perchlorate and chlorate presence in the environment was thought to be primarily anthropogenic. Recent evidence makes a strong case for the more widespread natural occurrence of perchlorate, outside of the long-established occurrence in caliches of the Atacama Desert in. Improved sensitivity of perchlorate detection techniques shows widespread existence of ppb levels of perchlorate. Not all perchlorate detected could be traced to anthropogenic sources. Natural perchlorate in soils is rare but occurs in other arid environments at levels up to 0.6 weight %. In the southern high plains groundwater, perchlorate is better correlated with iodate, known to be of atmospheric origin, compared to any other species (Dasgupta *et al*., 2005).

Natural perchlorate may be formed from chloride aerosol by electrical discharge and by exposing aqueous chloride to high concentrations of ozone (Bao and Gu, 2004; Bohlke *et al*., 2005). Information regarding the perchlorate formation process is, however, still largely unknown. Perchloric acid is the stable end product of the atmospheric chemistry because of its resistance to photolysis (Simonaitis and Heicklen, 1975) and occurs in aerosols in stratosphere of the earth at 0.5 to 5 parts per trillion (Murphy and Thomson, 2000). Perchlorate was also detected in rain and snow samples. This strongly suggests that some perchlorate is formed in the atmosphere and a natural perchlorate background of atmospheric origin should exist. In soils and surface waters perchlorate is reduced via chlorate. Chlorate is therefore part of natural chloro-oxy acid cycle. The existence of a chloro-oxy acid cycle does explain the enormous potential for chlorate reduction in the environment.

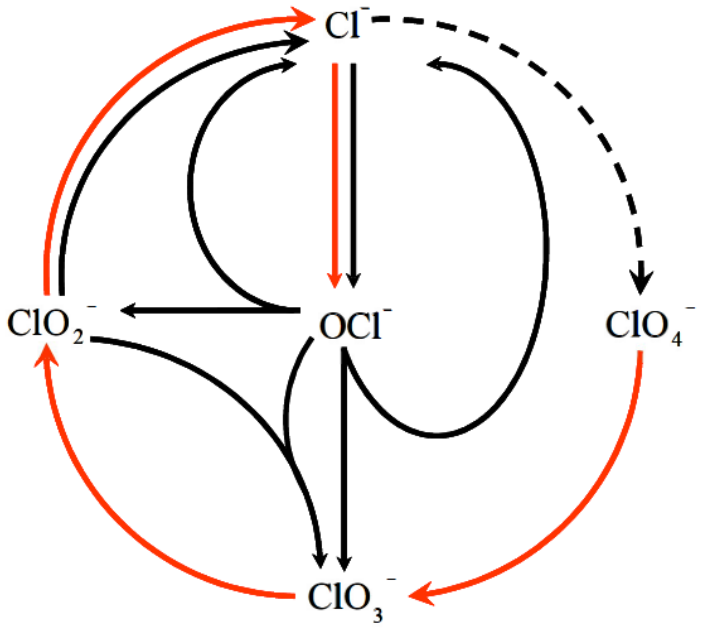

Figure 1: Chloro-oxo acid cycle. The dashed arrow represents the recent findings of perchlorate formation in aerosols. The red arrow are reactions catalysed by enzymes present in (per)chlorate respiring bacteria, nitrate reductases and peroxidases (formation of hypochlorite). The black arrows indicate chemical reactions occurring under ambient environmental temperatures.

In conclusion, the DS pointed out that these findings demonstrate the wide distribution of chlorate-reducing micro-organisms and that potassium chlorate is rapidly biodegradable. Tests only deviating from OECD TG 301 methodology with respect to the absence of oxygen (van Ginkel *et al*., 1995) do indicate potassium chlorate is readily biodegradable. Hence, in applying a weight of evidence approach to this specific case it can be concluded that the substance should be considered as rapidly degradable for classification purposes.

Bioaccumulation

No measured data on bioaccumulation were identified by the DS. The DS concluded that based on the environmental fate and behaviour of the substance (the complete dissociation in water due to low dissociation constant and high water solubility) no significant bioaccumulation is expected.

Aquatic Toxicity

Due to the limited aquatic ecotoxicity data available for potassium chlorate, the data on sodium chlorate was used by the DS. In addition to aquatic toxicity studies on marine algae using potassium chlorate, studies on fish, invertebrates, algae, and aquatic plants using sodium chlorate are presented in the CLP report. Only relevant studies from each trophic level with the most conservative endpoint expressed as test substance (Na- or $KClO_3$) and as chlorate ion are summarized in the table below for acute and chronic aquatic toxicity (key endpoints used in hazard classification are highlighted in bold). The toxicity values were adjusted by the DS for the molecular weight of the test substance or chlorate ion. All toxicity values are expressed as nominal values.

***Table**: Summary of relevant studies from each trophic level expressed as test substance and as chlorate anion for acute and chronic toxicity. Toxicity endpoint values are converted to potassium chlorate where necessary to complete the data set.*

Method/Test material	**Species**	**Endpoint**	**Toxicity value (mg/L)**			**Reference**
			$NaClO_3$	**$KClO_3$**	**ClO_3^-**	
Short-term toxicity						
EPA OPP 72-1 Sodium chlorate	*Oncorhynchus mykiss*	96h LC_{50}	>1000	>1151	>784	Study report (1991a) Key study
EPA OPP 72-1 Sodium chlorate	*Lepomis macrochirus*	96h LC_{50}	>1000	>1151	>784	Study report (1991b) Supporting study
OECD TG 203 Sodium chlorate	*Brachydanio rerio*	96h LC_{50}	>1000	>1151	>784	Study report (1991h) Supporting study
OECD TG 203 Sodium chlorate	*Pimephales promelas*	96h LC_{50}	>1000	>1151	>784	Study report (1993) Supporting study
In house protocol Sodium chlorate	*Oryzias latipes*	96h LC_{50}	2585	n.a	2027	Study report (1993) Supporting study
EPA OPP 72-3 Sodium chlorate	*Cyprinodon variegatus*	96h LC_{50}	>1000	>1151	>784	Study report (1991c) Key study
EPA OPP 72-2 Sodium chlorate	*Daphnia magna*	48h EC_{50}	>1000	>1151	>784	Study report (1991d) Key study
EPA OPP 72-2 Sodium chlorate	*Daphnia magna*	48h EC_{50}	1172	n.a.	919.3	Study report (1995) Supporting study
In-house method Sodium chlorate	*Mysidopsis bahia*	96h LC_{50}	>1000	>1151	784	Study report (1991f) Key study
EPA OPP 122-2 Sodium chlorate	*Pseudokirchneriella subcapitata#*	72h E_bC_{50} 96h E_bC_{50}	129 133	148 n.a.	101 104	Study report (1991e) Supporting study
ISO 10253 guideline Sodium chlorate	*Skeletonema costatum*	72h EC_{50}	>1000	n.a.	>784	Study report (2010a) Supporting study
OECD TG 201 Sodium chlorate	*Scenedesmus subspicatus*	72h E_bC_{50}	> 1592.3	n.a.	> 1248.4	Study report (2004c) Supporting study
According to own protocol Potassium chlorate	*Dunaliella tertiolecta*	15mg NO_3^- /L 72h E_rC_{50}	/	>1469	>1000	Stauber J.L. (1998b) Supporting study
According to own protocol Potassium chlorate	*Nitzschia closterium*	15mg NO_3^- /L 72h E_rC_{50}	/	>735	>500	Stauber J.L. (1998) Key study
OECD TG 221 Sodium chlorate	*Lemna minor*	7d EC_{50} (biomass growth) 7d EC_{50} (growth rate)	**73.7** 134 128	**84.8** n.a. n.a.	**57.5** 105 100	Study report (2003) Key study

		7d EC_{50} (biomass dry weight)				
U.S. EPA-FIFRA, Guideline 72-3 Sodium chlorate	*Crassostrea virginica*	96h EC_{50} 96h LC_{50}	1000 1000	n.a. n.a.	784 784	Study report (1991g) Other information
ISO/DC 20666 Sodium chlorate	*Brachionus plicatilis*	96 EC_{50}	596	n.a.	467	Study report (2010b) Supporting study
Long-term toxicity						
OECD TG 210 Sodium chlorate	*Danio rerio*	36d NOEC	≥ 500	≥ 575	≥ 392	Study report (2004a) Key study
OECD TG 211 Sodium chlorate	*Daphnia magna*	21d NOEC	≥ 500	≥ 575	≥ 392	Study report (2004b) Key study
EPA OPP 122-2 Sodium chlorate	*Pseudokirchneriella subcapitata #*	96h NOEC (cell growth)	62.5	71.9	49.0	Study report (1991e) Supporting study
OECD TG 201 Sodium chlorate	*Scenedesmus subspicatus*	72h NOEC (biomass) 72h NOEC (growth rate)	396.9 1592.3	n.a. n.a.	311 1248.4	Study report (2004c) Supporting study
OECD TG 201 Sodium chlorate	*Scenedesmus subspicatus*	72h NOEC	2001	n.a.	1569	Study report (1994a) Supporting study
ISO 10253 guideline Sodium chlorate	*Skeletonema costatum*	72h NOEC	≥ 1000	n.a.	≥ 784	Study report (2010a) Supporting study
72 hours test according to own protocol based in ISO Sodium chlorate	*Phaeodactylum tricornutum*	NOE_bC NOE_rC	64 128	n.a. n.a.	50 100	Study report (1994b) Supporting study
According to own protocol Potassium chlorate	*Dunaliella tertiolecta*	15mg NO_3^- /L NOE_rC	/	735	500	Stauber J.L. (1998b) Key study
72 hours test according to own protocol Potassium chlorate	*Nitzschia closterium*	15mg NO_3^- /L NOE_rC	/	147	100	Stauber J.L. (1998a) Key study
OECD TG 221 Sodium chlorate	*Lemna minor*	7d NOEC (biomass growth, growth rate, biomass dry weight)	**10**	**11.5**	**7.8**	Study report (2003) Key study
ISO/DC 20666 Sodium chlorate	*Brachionus plicatilis*	96h EC_{10} 96 NOEC	21 46	24 n.a.	16.5 36	Study report (2010b) Supporting study

Note:
n.a. – Recalculated value for potassium chlorate base on a molecular weight is not available in the CLH report.
#- In the CLH Report the freshwater green algae *Selenastrum capricornutum* is cited, which is formerly known as *Pseudokirchneriella subcapitata*.
/ - study was performed with potassium chlorate

Acute toxicity

For fish, six studies with six different fish species were available for sodium chlorate. The studies using freshwater fish followed EPA OPP 72-1 guideline for the rainbow trout (*Oncorhynchus mykiss*) and bluegill (*Lepomis macrochirus*), OECD TG 203 for zebrafish (*Brachydanio rerio*) and fathead minnow (*Pimephales promelas*) and in house protocol for Japanese rice fish (*Oryzias latipes*). The test using marine fish *Cyprinodon variegatus* was performed according to EPA OPP 72-3. In all six studies 96-h LC_{50} values of > 1000 mg/L were reported for sodium chlorate. On a molecular weight basis this would be > 1151 mg/L for potassium chlorate.

For sodium chlorate, two acute toxicity studies with *Daphnia magna* following EPA OPP 72-2 and one study for marine crustacea *Mysidopsis bahia* following in-house method were available. In all three studies, a 48-h EC/LC_{50} value of >1000 mg/L were reported. for sodium chlorate. On a molecular weight basis this would be > 1151 mg/L for potassium chlorate.

Three acute toxicity studies with three different algae species using sodium chlorate and two studies with two different marine algae species using potassium chlorate were available. For sodium chlorate, the studies using fresh water green algae followed EPA OPP 122-2 for *Pseudokirchneriella subcapitata* and OECD TG 201 for *Scenedesmus subspicatus*, while the test using marine algae *S. costatum* was carried out according to ISO 10253 guideline. For the potassium chlorate, both tests followed an in-house protocol but using different marine algae, *Dunaliella tertiolecta* and *Nitzschia closterium*. The lowest acute endpoint for algae is 72h E_bC_{50} of 129 mg/L for *P. subcapitata* using sodium chlorate (148 mg/L for potassium chlorate based on a molecular weight), while for potassium chlorate the lowest endpoint for algae is a 72h E_rC_{50} of 147 mg/L for *N. closterium*.

There was only one study following OECD TG 221 available using sodium chlorate for aquatic plants with the lowest value for acute toxicity to freshwater plant of 7-d EC_{50} value of 73.7 mg/L (84.8 mg/L for potassium chlorate based on a molecular weight) based on biomass growth for *Lemna minor*.

There were data available for other aquatic organisms, i.e. a 96-h LC/EC_{50} of > 1000 mg/L for eastern oyster (*Crassostrea virginica*) and a 96-h EC_{50} of 596 mg/L for marine rotatoria (*Brachionus plicatilis*).

From the available aquatic toxicity data, the DS concluded that aquatic plants are the most acutely sensitive taxonomic group. The lowest acute toxicity value is 7d EC_{50} of 73.7 mg/L (biomass growth) for duck weed *L. minor* for sodium chlorate, which corresponds to 84.4 mg/L potassium chlorate. This value is above the classification threshold value of 1 mg/L, therefore the classification of potassium chlorate as Aquatic Acute 1 is not warranted.

Chronic toxicity

There is one long-term toxicity study following OECD TG 210 for zebrafish (*Danio rerio*) available with 36-d NOEC value of ≥ 500 mg/L for sodium chlorate, which is ≥ 575 mg/L for potassium chlorate based on a molecular weight.

There was only one chronic study according to OECD TG 211 available using sodium chlorate for aquatic invertebrates with 21-d NOEC value of ≥500 mg/L for *D. magna*. On a molecular basis this would be ≥ 575 mg/L for potassium chlorate.

Five toxicity studies with four different algae species using sodium chlorate and two studies with two different algae species using potassium chlorate were available. For sodium chlorate, the studies using fresh water green algae followed EPA OPP 122-2 for *P. subcapitata* and OECD TG 201 for *S. subspicatus*, while the studies using marine algae followed ISO 10253 guideline for *Skeletonema costatum* and own protocol based in ISO for *Phaeodactylum tricornutum*. In case

of potassium chlorate, both tests followed in-house protocols but using different marine algae, *D. tertiolecta* and *N. closterium*. The lowest endpoint for algae is a 96-h NOEC of 62.5 mg/L based on cell growth for *P. subcapitata* using sodium chlorate (71.9 mg/L for potassium chlorate based on a molecular weight), while in the case of potassium chlorate the lowest endpoint for algae is 72-h NOE_rC_{50} of 147 mg/L for *N. closterium*.

A mesocosm study with macro brown algae *Fucus vesiculosus* using sodium chlorate is available (Lehtinen *et al*., 1988) which was the basis for chronic aquatic hazard classification of the substance under the Dangerous Substance Directive (Directive 67/548/EEC). The study was considered not valid by the DS because the study was not performed according to standard laboratory methods and not in compliance with GLP. Several study deficiencies regarding method and materials (replicates, test organisms, seawater) were pointed out by the DS. In the study, 6-month EC_{50} value of 80 µg ClO_3^-/L and 6m LOEC value of 15 - 20 µg ClO_3^-/L for *F. vesiculosus* were reported. As the study was not performed according to standard laboratory methods and the duration of the study was much longer than standard duration, the results are difficult to compare to test results from contemporary standardised laboratory test guidelines.

There was only one study following OECD TG 221 available using sodium chlorate for aquatic plants with the lowest value for chronic toxicity to freshwater plant 7-d NOEC value of 10 mg/L for *L. minor*. On a molecular weight basis this would be 11.5 mg/L for potassium chlorate.

There were data available for other aquatic organisms, i.e. 96-h EC_{10} of 21 mg/L for marine rotatoria (*B. plicatilis*) using sodium chlorate. On a molecular weight basis this would be 24 mg/L for potassium chlorate.

Based on the results from the long-term aquatic toxicity studies, the DS concluded that aquatic plants are the most sensitive taxonomic group. The lowest chronic toxicity value is 7d NOEC of 10 mg/L for duck weed *L. minor* for sodium chlorate, which corresponds to 11.5 mg/L potassium chlorate. This value is above the classification threshold value of 1 mg/L along with the understanding that the substance is rapidly degradable. Therefore, the substance does not warrant a classification for chronic toxicity. The DS pointed out that even if the substance would be considered as non-rapidly degradable this would not lead to classification for chronic aquatic hazard.

Comments received during consultation

Two Member States (MS) and one company-manufacturer provided comments. With the exception of one MS, all commenters agreed with the proposals of the DS. One MS pointed out that more evidence is needed to justify that the substance is rapidly degradable and has a low bioaccumulation potential, although this will not impact the proposed classification for the environment. For the MS it is unclear how relevant the non-standard ready biodegradability study using excess reducing agents is to determine whether the substance is rapidly degradable. The MS also pointed out that fate and essentiality of the metal ion (and counter ion) were not fully considered in determination of the bioaccumulation potential of the substance.

Assessment and comparison with the classification criteria

Read across assessment

RAC agrees with DS that data for sodium chlorate and potassium chlorate could be considered together for evaluation of environmental hazard of potassium chlorate based on the following:

- Sodium and potassium chlorate have the same molecular and structural formula except for the alkali metal;

- Both sodium and potassium chlorate dissociate in water to form the identical base structure and their respective counter-ions;
- Both substances are readily soluble in water;
- For aquatic chronic toxicity, a comparison of the available marine algae studies does not indicate a marked difference in the ecotoxicological profile (see toxicity values in table). There is a lack of toxicity of both substances to marine algae.

RAC agrees with DS that toxicity of the test substance is expected to be related to the chlorate anion and not to the sodium or potassium ion.

Degradation

Potassium chlorate is highly soluble in water and is chemically stable in aqueous solutions under environmental conditions (hydrolytically stable).

According to the CLP Guidance, Section II.4 (version 5.0, July 2017) for a purely inorganic compound such as potassium chlorate the concept of degradability as applied to organic compounds has limited or no meaning. Additionally, the degradation decision scheme as in the CLP Guideline is not directly applicable for inorganic substances, as is it was primarily developed for organics. Potassium chlorate is an inorganic substance and therefore the ready biodegradability and simulation testing from the decision scheme are not considered relevant because these tests only detect biodegradation of organic compounds under aerobic conditions. Furthermore, no valid standard ready biodegradability test result is available for potassium chlorate in the CLH dossier because chlorate is an electron acceptor like molecular oxygen.

No degradation of sodium chlorate was observed under experimental conditions (aerobic) in the Sturm test (OECD TG 301B). RAC notes that this method is not applicable for inorganic substances like sodium or potassium chlorate.

Modified (adding excess amounts of reducing agents) Closed Bottle test (OECD TG 301D) indicated complete removal of chlorate within 28 days under anaerobic conditions (van Ginkel *et al*., 1995). The chlorate was reduced completely to chloride. The test show that microorganisms carrying out chlorate reduction inhabit a variety of environments including rivers, sediments, soils and WWTP. However, significant biodegradation of chlorate by these microorganisms did not take place under aerobic conditions. The environmental fate of chlorate therefore depends on several factors, including the availability of suitable substrates and the absence of molecular oxygen and nitrate (oxygen and nitrate are utilized prior to chlorate by microorganisms). As a consequence, microbial reduction of chlorate will mainly occur in soils and sediments.

The study by Bryan and Rohlich (1954) demonstrated rapid reduction of chlorate by microorganism using organic compounds as carbon and energy source present in sewage under conditions that exclude atmospheric oxygen.

Two tests (OECD TG 301D and the study by Bryan and Rohlich (1954)) were performed under anaerobic conditions. According to the CLP guidancesection II.2.3.7) data regarding anaerobic degradation cannot be used in relation to deciding whether a substance should be regarded as rapidly degradable, because the aquatic environment is generally regarded as the aerobic compartment where the aquatic organisms, such as those employed for aquatic hazard classification, are found.

Consequently, RAC considers the substance to be not rapidly degradable for the purposes of environmental classification.

Bioaccumulation

RAC agrees with DS that based on fate and behaviour of the substance (high aqueous solubility, complete dissociation in an aqueous solution) no significant bioaccumulation is expected.

Aquatic toxicity

Taking into account that toxicity of the test substance is expected to be related to the chlorate anion, RAC agrees that data from sodium chlorate for aquatic toxicity endpoints could be considered for the classification of the potassium chlorate. There are reliable data on acute and chronic toxicity for all three trophic levels based on sodium chlorate and these data are used to complete the data set for potassium chlorate. Reliable potassium chlorate data is only available for marine algae.

Acute aquatic toxicity

Aquatic plants are the most sensitive group. The lowest value being for sodium chlorate with duckweed *L. minor* is 7-d EC_{50} value of 73.7 mg/L which corresponds to 84.8 mg/L for potassium chlorate. RAC notes that all EC_{50}s/LC_{50}s for fish, invertebrates, algae, and aquatic plants (see Table) are above the threshold value of 1 mg/L. **Therefore, the substance does not warrant classification for acute aquatic hazard**. This is consistent with the conclusion of the DS.

Chronic aquatic toxicity

RAC considers that the mesocosm study with *F. vesiculosus* using sodium chlorate should not be taken into account for classification purposes due to study deficiencies pointed out by the DS. In addition, RAC acknowledge that REACH guidance (Chapter R.7b: Endpoint specific guidance, Version 4.0–June 2017, p. 33) indicates the number of potentially conflicting elements in mesocosm study designs which could affect the reliability of the results. Therefore, RAC is of the opinion that this data should not be considered for the classification of potassium chlorate. The remaining data available in the CLH dossier is considered as relevant and reliable by RAC.

Aquatic plants are the most sensitive group, and the lowest result is a 7-d NOEC value of 10 mg/L for sodium chlorate (11.5 mg/L for potassium chlorate) for duckweed *L. minor*. RAC notes that all NOECs/EC_{10} for fish, invertebrates, algae, and aquatic plants (see Table) are above the threshold value of ≤ 1 mg/L for all three trophic levels. Potassium chlorate is considered not rapidly degradable and had a low potential for bioaccumulation. Consequently, RAC concluded that potassium chlorate does not warrant classification for chronic aquatic hazard.

RAC notes that for some species with acute toxicity data, chronic toxicity data is not available. However, although potassium chlorate is considered not rapidly degradable all toxicity endpoints for species with no chronic toxicity data are well in excess of 100 mg/L. Consequently, following CLP table 4.1.0(b)(iii), no chronic classification is derived via the surrogate approach.

Overall, although RAC takes the contrary view to that of the DS in that potassium chlorate should be considered as not rapidly degradable based on the available data, RAC agrees with the DS that **potassium chlorate does not warrant classification for hazards to the aquatic environment.**

Additional references

Lehtinen, K.-J., Notini, M., Mattsson, J. & Landner, L. (1988): Disappearance of Bladder-Wrack (*Fucus vesiculosus* L.) in the Baltic Sea: relation to pulp-mill chlorate. – Ambio 17 (6): 387-393.

ANNEXES:

Annex 1 The Background Document (BD) gives the detailed scientific grounds for the opinion. The BD is based on the CLH report prepared by the Dossier Submitter; the evaluation performed by RAC is contained in 'RAC boxes'.

Annex 2 Comments received on the CLH report, response to comments provided by the Dossier Submitter and RAC (excluding confidential information).