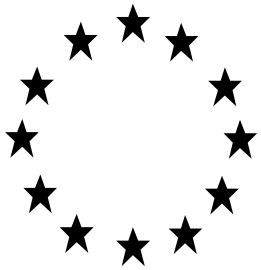
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Active chlorine released from chlorine

Product-type 2
(Disinfectants and algaecides not intended for direct application to humans or animals)

January 2017

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1 STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1 Procedure followed

This assessment report has been established as a result of the evaluation of the active substance active chlorine released from chlorine as product-type 2 (Disinfectants and algaecides not intended for direct application to humans or animals), carried out in the context of the work programme for the review of existing active substances provided for in Article 89 of Regulation (EU) No 528/2012[1], with a view to the possible approval of this substance.

Active chlorine released from chlorine (releaser CAS no.: 7782-50-5) was notified as an existing active substance, by the Euro Chlor Chlorine Registration Group at Euro Chlor, hereafter referred to as the applicant, in product-type 2.

Commission Regulation (EC) No 1062/2014 of 4 August 2014[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process.

On 31st July 2007, Italian competent authorities received a dossier from the Euro Chlor Chlorine Registration Group at Euro Chlor. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 2nd April 2008.

On 17th May 2010, the Rapporteur Member State submitted to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the "Agency" (ECHA). Revisions agreed upon were presented at the Biocidal Products Committee and its Working Groups meetings and the competent authority report was amended accordingly.

1.2 Purpose of the assessment report

The aim of the assessment report is to support the opinion of the Biocidal Products Committee and a decision on the approval of active chlorine released from chlorine for product-type 2, and, should it be approved, to facilitate the authorisation of individual biocidal products. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available from the Agency web-site shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Regulation (EU) No 528/2012, such conclusions may not be used to the benefit of another applicant, unless access to these data for that purpose has been granted to that applicant.

[1] Replace by Article 90(2) for a new active substance submitted under Article 11 of the BPD

[2] COMMISSION DELEGATED REGULATION (EU) No 1062/2014 of 4 August 2014 on the work programme for the systematic examination of all existing active substances contained in biocidal products referred to in Regulation (EU) No 528/2012 of the European Parliament and of the Council. OJ L 294, 10.10.2014, p. 1

2 OVERALL SUMMARY AND CONCLUSIONS

2.1 Presentation of the Active Substance

2.1.1 Identity, Physico-Chemical Properties & Methods of Analysis

The active substance covered by this assessment is 'active chlorine released from chlorine' ([3]).

Upon use for MAIN GROUP 1 – Disinfectants (PT2), chlorine releases 'active chlorine', *i.e.* efficacious chlorine or available/releasable chlorine that is disinfectant, algaecide, fungicide and microbiocide.

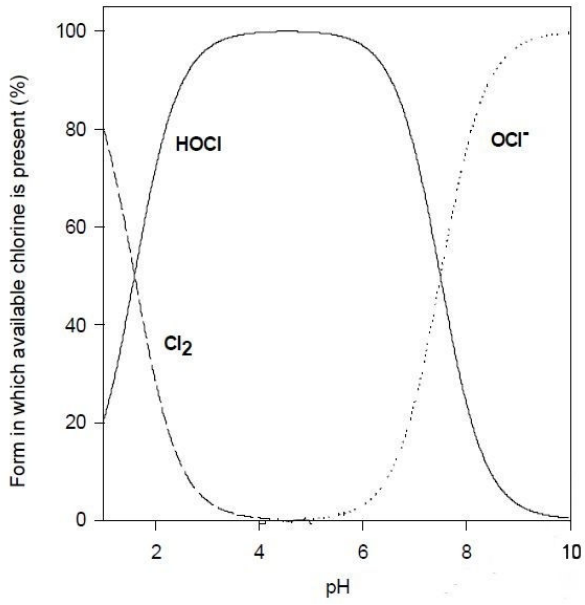
Namely, in water chlorine (Cl_2) disproportionates into hypochlorous acid (HClO) and hydrochloric acid (HCl) according to:

$Cl_2 + H_2O \leftrightarrow HClO + H^+Cl^-$ ([4])

Further, hypochlorous acid is a weak acid and it partially dissociates into hypochlorite anion (ClO^-) according to:

$HClO + H_2O \leftrightarrow ClO^- + H_3O^+$ ([5])

The ratio of Cl_2/HClO/ClO^- is pH and temperature dependent. The pH-dependence is displayed in the following figure, where the percentage of the different species at the equilibrium is showed as a function of pH. Hypochlorous acid is predominant in the pH range 4 to 5.5, whereas the hypochlorite anion predominates at pH >10. Chlorine can be present at pH < 4 only.



([3]) As in *CA-March15-Doc.5.1-Final, Revised on 23 June 2015, Annex II – Releasers*

([4]) $K_{hydrolysis}(Cl_2)$ = 3.2 x 10^{-4} mol/dm^3 at 20°C (Solvay, International Research Document, 1979)

([5]) K_a(HClO) = 3.5 x 10^{-8} mol/dm^3 at 20°C (Solvay, International Research Document, 1979)

Identification of the active substance releaser

The following information attains to the active substance releaser, i.e. chlorine.

Active substance releaser	
CAS-No.	7782-50-5
EINECS-No.	231-959-5
Other No.	017-001-00-7 (Index number)
IUPAC Name	Chlorine
CAS name	Chlorine
Common name, synonyma	Chlorine
Molecular formula	Cl2
Structural formula	Cl — Cl
Molecular weight	70.906 g/mol
Purity	≥ 99.5 % w/w (in compliance with European norm EN 937:2009)
Additives	None
Impurities	Non-relevant non-significant impurities are present, which are considered as confidential information and, hence, described in the Confidential Annex.

The manufacturing process described in the Euro Chlor dossier can be found in the Annex of Confidential Data.

Identification of the biocidal product

The biocidal product described in the dossier is chlorine as manufactured (≥ 99.5 % w/w, in compliance with EN 937:2009).

Biocidal product	
Trade name	Chlorine
Manufacturer's development code number(s)	None allocated
Active substance released	Active chlorine released from chlorine
Physical state of preparation	gaseous
Nature of preparation	GA (gas)

Physical-chemical properties of the active substance releaser (chlorine)

Chlorine is a very strong oxidizing agent. The standard redox potential of gaseous chlorine in neutral aqueous solution at 25°C and 101.3 mbar is:

$Cl_2(gas) + 2e^- \rightarrow 2Cl^- (aq) + H_2O$ E°Red = + 1.36 V

Chlorine can react violently with some gases such as hydrogen.

Chlorine is a well-characterised, basic chemical and, as a result, its physical-chemical properties were investigated and published several times. Accordingly, the data set presented by the applicant refers to literature data, while no additional studies were performed for the specific purpose of the approval.

Chlorine is a greenish-yellow gas at room temperature and ambient pressure (freezing point and boiling point at ambient pressure: -101.03 and -34.03 °C, respectively), with a characteristic stringent odour. One-litre chlorine gas weighs 3.169 g at 0 °C and 1 atm, whereas the density of compressed liquid chlorine is reported to be 1.413 kg/dm^3 at 20 °C (pressure: 10 kg/cm^2). Vapour pressure is 6.780 and 7.788 x 10^5 Pa at 20 and 25 °C, respectively (estimation by the Martin-Shin-Kapoor equation).

The Henry's law constant is calculated to be 6.5 x10^3 Pa m^3 mol^{-1} at 20 °C. However, for the purpose of risk assessment only, the Henry's law constant of hypochlorous acid (HClO) is also reported in the LoEPs as determined experimentally by Blatchley et al. (1992) ([6]) by the air stripping method, being hypochlorous acid the only volatile chlorine species present at the equilibrium at in-use pH values under PT2.

Chlorine absorbs above 290 nm, with an estimated ε_o^{max} of 70 at 333 nm and 0 K.

Only the molecule $^{35}Cl^{37}Cl$ absorbs in the IR region, namely at 551 cm^{-1} (18148 nm), 1100 cm^{-1} (9090 nm) and 1638 cm^{-1} (6105 nm). The MS spectra show that chlorine consists of two stable isotopes: ^{35}Cl and ^{37}Cl, with natural abundance of 75.8 and 24.2%, respectively.

Solubility of chlorine in pure water is reported to be 9.78 g/L (at 10 °C), 7.41 g/L (at 20 °C) and 5.91 g/L (at 30 °C). Solubility is complicated by either hydrolysis and formation of a hydrate which separates out at relatively low temperatures and at pressures near to atmospheric. The following data on selected polar and non-polar solvents are available: 121 g/kg (at 15 °C) in acetic acid; 159 g/kg (at 10 °C), 114 g/kg (at 20 °C) and 91 g/kg (at 30 °C) in tetrachloromethane; 290 g/kg (at 10 °C), 218 g/kg (at 20 °C) and 157 g/kg (at 30 °C) in benzene.

Viscosity of gaseous chlorine is calculated to be 12.4 x 10^{-3} and 13.3 x 10^{-3} Pa s at 0 and 20 °C, respectively. Whereas, viscosity of liquid chlorine is 0.385 x 10-^{3} Pa s at 0°C. Also surface tension was calculated for liquid chlorine (18.2 mN/m at 20 °C).

Chlorine is known to be stable at ambient temperature and pressure. Thermal dissociation into chlorine atoms occurs only at elevated temperatures (the degree of atomization of molecular chlorine is reported to be 0.019 at 1000 K).

Chlorine is known to be a non-flammable gas.

Harmonized classification was approved by EU for chlorine, which was inserted into Annex VI of CLP with ATP01corr. As regards physical hazards, chlorine is classified as Ox. Gas 1 (H270: may cause or intensify fire; oxidiser) and Press. Gas. Further, according to Note U, "*When put on the market gases have to be classified as 'Gases under pressure', in one of the groups compressed gas, liquefied gas, refrigerated liquefied gas or dissolved gas. The group depends on the physical state in which the gas is packaged and therefore has to be assigned case by case*."
Though harmonized classification exists, no evidence was provided by the applicant as regards the oxidizing properties of chlorine. A new test on oxidising gases according to the UN Recommendation on the Transport of Dangerous Goods, Manual of Tests and Criteria needs to

[6] Blatchley, E. R., III, R. W. Johnson, J. E. Alleman, and W. F. McCoy. Effective Henry's law constants for free chlorine and free bromine. Wat. Res., 26 , 99–106, 1992

be provided, at the latest six months before the date of approval.

Container materials must be chosen to suit the conditions under which chlorine is being handled. For dry chlorine gas (<20 mg H_2O/kg), steel is the usual material, whereas for liquid and cold dry chlorine gas, fine grain carbon steel should be used. For wet chlorine gas, the usual materials are titanium, rubber lined steel, glass reinforced polyester resins (GPR), PTFE lined steel, PVC externally reinforced with DRP and PVDF.

As described at the beginning of 2.1.1, upon dissolution of chlorine in water, active chlorine is released. For those physical-chemical properties determined in aqueous solution, read-across to the Euro Chlor data on 'active chlorine released from sodium hypochlorite' is made, since chlorine and sodium hypochlorite release the very same active substance (i.e. active chlorine).

Analytical methods for detection and identification

Analysis of the active substance releaser (chlorine)

An ISO method for the determination of chlorine content by volume in liquid chlorine for industrial use, after vaporization of the test item, is provided (ISO 2120, 1972, Liquid chlorine for industrial use - Determination of the content of chlorine by volume in the vaporized product). A known volume of chlorine is sampled (about 100 mL) obtained by gasification of liquid chlorine. The chlorine is absorbed by a 2% zinc amalgam in the presence of 1 mL saturated sodium chloride solution. The residual, non-condensable gases are also measured with this method.
No further validation data are needed, as the method was regarded to be well-established and concluded to be reliable and acceptable by WGII2016.

Since impurities of chlorine as manufactured are regarded as confidential information, analytical methods for the identification/quantification of impurities can be found in the Annex of Confidential Data.

Analysis of the active substance released (active chlorine)

As described at the beginning of 2.1.1, upon dissolution of chlorine in water, active chlorine is released. Thus, in principle, the same analytical method used for the analysis of another active chlorine releaser (i.e. sodium hypochlorite) will apply, upon dissolution of chlorine in water and appropriate dilution.

The method available in the CAR of 'active chlorine released from sodium hypochlorite' allows the determination of sodium hypochlorite in sodium hypochlorite aqueous solutions 1% w/w. Sodium hypochlorite reacts with potassium iodide to release iodine in the presence of acetic acid. The iodine is titrated with a sodium thiosulphate solution in the presence of starch indicator. Alternatively, titration can be carried out potentiometrically by means of titration automates, in which case the addition of soluble starch is unnecessary.
Linearity was investigated over the range 0.5 – 1.5 % w/w as sodium hypochlorite (corresponding to 0.48 – 1.43 % w/w as active chlorine):

R	0.9999
Slope	2.7492
Intercept	0.4040

The precision of the method was satisfactory. The % $RSD_{n=6}$ proved to be 0.51, below the acceptance criteria according the modified Horwitz equation (2.67). Specificity was tested against the blank only (i.e. water). A LOQ of 0.5% w/w as sodium hypochlorite (corresponding to 0.48% w/w as active chlorine) is proposed.

Formulation analysis

Chlorine as manufactured is also the representative product. The same analytical method described above for chlorine will apply.

Residues analysis

The active substance is "active chlorine released from chlorine", which is thought to consist of chlorine (Cl_2), hypochlorous acid (HClO) and hypochlorite anion (ClO^-) in equilibrium. The predominant species will depend on pH value (chlorine is available only at pH < 4, hypochlorous acid is predominant in the range 4 to 5.5, whereas only hypochlorite anion is present at pH >10).

At the in-use pH values in PT2, chlorine is virtually non-present at the equilibrium, whereas the predominant species are the hypochlorite anion and the hypochlorous acid.

Analytical method for residues in air

Residue definition: Cl_2/HClO/ClO^-

Hypochlorite is a non-volatile species. Hypochlorous acid is volatile, but according to literature data, the Henry's Law constant is ≈ 0.1 Pa m^3 mol^{-1}, i.e. volatilization from the aqueous phase is expected to be slow. Furthermore, there are indications that the half life is only a few hours, i.e. much shorter than the value derived by Atkinson calculation. So occurrence in air is not probable for this species, either.
In PT2, chlorine is handled exclusively in closed systems and exposure to the gas is not expected, but during connecting/disconnecting of chlorine vessels.
Two analytical methods ([7],[8]) are available in the CAR to monitor human exposure, which allow the determination of chlorine in workplace air in the range 0.3-7.0 mg Cl_2/m^3. In principle, the range can be expanded. Though not validated, the two available methods are published methods, so they can still be concluded to be acceptable for the purpose (determination of chlorine in workplace air).

Analytical method for residues in soil

Residue definition: HClO/ClO^-

Not required. For none of the intended uses, soil is the first receiving compartment. Environmental exposure is expected *via* the facility drain into the STP or *via* the treated effluent directly into the surface water. Active chlorine (HClO/ClO^-) can reach the soil compartment only indirectly, *via* sewage sludge: rapid degradation occurs already with organic matter therein. In the event of contamination of soil, e.g. due to direct application of chlorinated water, active chlorine would react rapidly with organic matter in soil anyway.

Analytical method for residues in drinking water

Residue definition: HClO/ClO^- and relevant metabolite chlorate (ClO_3^-)

The analytical methods for active chlorine (HClO/ClO^-) as available in the original Euro Chlor dossier are not acceptable, since validation is not in accordance with the Additional Guidance on TNsG on analytical methods. Therefore, a fully-validated analytical method for active chlorine residues in drinking water is requested. A fully validated analytical method is also requested for the relevant metabolite chlorate (ClO_3^-). Methods, which are necessary for monitoring purposes, should be submitted at the latest six months before the date of approval of the active substance.

[7] Reference: OSHA Method «Chlorine in Work place Atmosphere» 05.01.83; Smith & Cochran Spectrophotometric determination of Free Chlorine in Air using Sulphamic acid/Tri-iodide procedure - Anal Chem 1986 Vol 58 pp 1591-1592

[8] Reference: OSHA Method «Chlorine in Work place Atmosphere» 05.01.83; NIOSH free chlorine in air 01.01.75; ISO 7392/2 Water quality – Determination of free and total chlorine Part 2 Colorimetric method using DPD for routine control purposes 15.10.85

Analytical method for residues in surface water

Residue definition: $HClO/ClO^-$

Not required. Environmental exposure is expected *via* the facility drain into the STP or *via* the treated effluent directly into the surface water, but rapid degradation occurs with organic matter therein. Rapid degradation occurs also with the organic matter in surface water ($DT_{50\ surface\ water}$= 56 min at environmental temperature).

Analytical method for residues in body fluids and tissues

Residue definition: $HClO/ClO^-$

Not required. Hypochlorite anion/hypochlorous acid are oxidizing agents and degrade rapidly with organic matter. Besides, due to corrosive properties, systemic toxicity would be secondary to local effects.

Nevertheless, in case of an accidental release of chlorine, the analytical methods available for the monitoring of chlorine in workplace air are meaningful for monitoring human exposure.

Analytical method for residues in food and feed

Not required under PT2.

2.1.2 Intended Uses and Efficacy

Chlorine, as releaser of active chlorine, has strong bactericidal, fungicidal, sporicidal and virucidal activity; it has also been reported to inactivate prions (Block 5th edition, Ch. 33, p. 659, S. Prusiner et al. - Decontamination procedures).

Field of use envisaged

The uses assessed belong to the product-type 2:

a) Treatment of sewage / waste water including municipal waste water; before receiving the waste water plant (pre-chlorination), after the waste water plant (post-chlorination) (5-40 mg/L active chlorine)

b) Treatment of public swimming pools; continuous flow and shock disinfection (3 and 50 mg/L active chlorine, respectively)

The "organism to be protected" is man. The aim of the treatments is to control infectious diseases or nuisance (smell generating) organisms.

Under PT2, chlorine is used in the protection of humans from pathogenic organisms which may result in spreading of contagious diseases due to contact with contaminated water (e.g. swimming pool). Professional use is envisaged. The concentrations to obtain efficacy on target organisms vary depending on the type of microorganism and the type of use of the substance. For PT2 the range is from 3 mg/L active chlorine (for pool continuous flow disinfection) to 50 mg/L active chlorine (for pool shock disinfection).

The active substance released from either chlorine, sodium hypochlorite or calcium hypochlorite in aqueous solutions is active chlorine. The hypochlorite ion is in equilibrium with hypochlorous acid and chlorine. The equilibrium depends on the pH value: chlorine is available only below pH 4, in the neutral pH range hypochlorous acid is the predominant species and at pH values higher than 10 the only species present is the hypochlorite ion (please, refer to the beginning of para. 2.1.1 of this document).

For the chemical reactivity in aqueous solution with the same active chlorine concentrations and the same pH conditions, it is irrelevant whether active chlorine is generated from chlorine gas, calcium hypochlorite or sodium hypochlorite. Therefore, all studies investigating hypochlorite aqueous solutions can be used for the evaluation and assessment of active chlorine released from any of the three releasers.

The disinfecting efficiency of hypochlorite aqueous solution is dependent on the active chlorine concentration and decreases with an increase in pH and vice versa, which is parallel to the concentration of un-dissociated hypochlorous acid.

It has to be stressed that the activity is strongly reduced by the presence of organic load and in general by the presence of particles. The chlorination and the oxidation reaction of active chlorine are unspecific. At low concentrations, at or in between the concentrations used in the Risk Assessment (3 mg/L for swimming pools), active chlorine is still able to maintain the concentration of pathogens below a critical level. In such conditions the proteins of the membrane are partly destroyed and the bacteria are not able to multiply.

A very large list of studies done by different methods in different conditions and on different groups of organisms have been reported in Doc. IIIA, but the key studies used for the evaluation are those presented in Doc. IIIB and IIB, correctly performed following EN Norms on bacteria, fungi, viruses, spores, in which a disinfectant activity was correctly demonstrated using Eau de Javel 12°Cl (about 3.6% active chlorine) and a product containing 2.74% active chlorine as product tests. According to such tests, the disinfectant activity is obtained with concentrations of active chlorine ranging from < 1000 mg/L (bacteria and fungi) to 3600 mg/L (viruses). Acceptable additional data from the literature demonstrate that active chlorine possesses disinfectant activity even at much lower concentration (<0.7 mg/L), depending on the condition of use. Although known to be effective also against mycobacteria and prions, such activity has not been demonstrated by targeted tests performed for the purpose of this dossier. As in-use conditions tests are not required for a.s. approval, the efficacy data package will have to be implemented at product authorization stage, and more information should be provided to demonstrate full efficacy against all claimed target organisms of the products.

Although different species vary in their sensitivity to active chlorine, development of acquired resistance is not expected since its multiple molecular sites of attack on the surface and within the microbial cells. Active chlorine is in fact regarded by experts [see IFH (International Scientific Forum on Home Hygiene) review October 2003 and Submission to SCENIHR, February 2008)] as one of the biocides where acquired resistance is least likely to develop. For the same reasons cross-resistance is not to be expected, nor has it been observed. Despite use for almost a century in purifying drinking water, where very low (sub ppm) concentrations are continuously maintained, the development of acquired resistance has not been observed. Adaptation of organisms to active chlorine can be determined by comparison of the Minimum Inhibitory Concentration (MIC), but this is not relevant in practice as the actual use concentrations are much higher and thus a sufficient margin of safety is provided.

No management strategies are necessary as acquired resistance to active chlorine has not developed nor will develop due to its reactive nature and unspecific mode of action. Some temporary adaptation giving modestly reduced susceptibility is sometimes observed in organisms exposed continuously at low concentrations (e.g. in water pipes through formation of biofilms) but this is readily managed e.g. by control / removal of the biofilm.

The assessment of the biocidal activity of the active substance demonstrates that active chlorine released from chlorine has a sufficient level of efficacy against the target organism(s) and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious.

In addition, in order to facilitate the work of Member States in granting or reviewing authorisations, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.3 Classification and Labelling

Active Chlorine is released from chlorine to give an equilibrium of chlorine, hypochlorous acid and hypochlorite anion in aqueous solution. The ratio of Cl_2/HClO/ClO^- is pH and temperature dependent and therefore, classification for active chlorine is not feasible.

Current classification

Chlorine is listed on Annex VI of Regulation (EU) No 758/2013 (Corrigendum to Annex VI to CLP Regulation, Index No 017-001-00-7).

Harmonized classification of chlorine according to Annex VI, Table 3.1 of Regulation (EC) 1272/2008 (CLP)

Classification	
Hazard Class and Category	Oxidising Gas 1 Press. Gas Acute Toxicity (inhal.) 3 * Eye Irritation 2 STOT SE 3 Skin Irritation 2 Aquatic Acute 1
Hazard Statement Codes	H270 H331 H319 H335 H315 H400
Labelling	
GHS Pictogram	GHS03 GHS04 GHS06 GHS09
Signal Word	Danger
Hazard Statement	H270: May cause or intensify fire; oxidiser H331: Toxic if inhaled H319: Causes serious eye irritation H335: May cause respiratory irritation H315: Causes skin irritation H400: Very toxic to aquatic life
M Factor	M factor=100

Proposed classification

Based on the results obtained in the acute inhalation study and taking into account the provisions laid down in Regulation (EC) No 1272/2008 (CLP), chlorine needs to be classified as acutely toxic by inhalation (Acute Tox. (inhal) 2; "Fatal if inhaled"; H330).

2.2 Summary of the Risk Assessment

2.2.1 Human Health Risk Assessment

2.2.1.1 Hazard identification and effects assessment

The active substance covered by this assessment is "active chlorine released from chlorine".
Chlorine gas is handled exclusively in closed systems and an exposure to the gas is only accidental. Due to its gaseous aggregate state, inhalation is the only possible exposure route.
In water, chlorine forms hypochlorous acid (HClO), which is in equilibrium with the hypochlorite ion (ClO^-) characterised by its well-known irritating/corrosive effects, and chlorine (Cl_2). In biological systems, characterised by pH values in the range 6-8, the most abundant species is HClO. At alkaline pH values, ClO^- is predominant, whilst Cl_2 is the main species only below pH 4.
Since in aqueous solutions, sodium hypochlorite (NaOCl) and chlorine share the same anion (ClO^-) and, thus, release the very same active substance (i.e. active chlorine, thought to consist of hypochlorite, hypochlorous acid and chlorine in equilibrium), read-across is possible for all the toxicological end-points.
Therefore, whenever specific data obtained with chlorine are not available, reference is made to the respective Euro Chlor data obtained with sodium hypochlorite. It shall be noted that the same approach was adopted for the physical-chemical properties determined in aqueous solution, as well as for the mode of action.
During BPC TOX-WGIII-2016, the members agreed that human health effects are primarily due to the local mode of action of chlorine gas and potential systemic effects are secondary to its direct irritating reactivity.

Absorption, distribution, metabolism and excretion

Inhalation route of exposure
Bolus inhalation measurements were performed in 10 volunteers during nasal and oral quiet breathing (Nodelmann, 1999). At a pre-determined time during inhalation, the data-acquisition system automatically injected a 10 mL Cl_2 bolus into the inspired airflow. Peak inhaled chlorine concentration (c_{max}) was 3.0 ppm for oral and nasal breathing and additional c_{max} of 0.5 ppm for nasal breathing. Additionally, anatomic measurements of the respiratory system were performed (forced vital capacity, dead space, nasal volume, oral volume and pharyngeal volume).

To summarise, the measurements indicated that more than 95% of inspired chlorine was absorbed in the upper airways of all subjects, whereas the dose delivered to the respiratory air spaces was negligible. Both the high absorptivity of chlorine in the upper airways and the domination of the gas-phase diffusion resistance were attributable to the rapid hydrolysis of chlorine in the mucosa.

However, inhalation absorption is considered as not relevant because chlorine-related toxicity is based on local effects only (with secondary systemic effects at high doses).

During BPC TOX-WGIII-2016, the members concluded that inhalation absorption values are not deemed necessary due to the lack of systemic effects.

Oral route of exposure
For ADME data after oral exposure, since the active chlorine releaser chlorine is a gas, read across is made to studies performed with sodium hypochlorite.

Two rat studies are available analysing ADME of [^{36}Cl]-HOCl (Abdel-Rahman, 1982 and 1983). These studies suggest that after exposure *via* oral route, HOCl is absorbed and excreted mainly through urine as chloride (36.43% + 5.67 of the administered dose after 96 h); a lesser extent of HO^{36}Cl-derived radioactivity not necessarily associated with absorption was detectable in the faeces 96h after exposure (14.8% + 3.7). The oral absorption is therefore considered around 35%.

However, oral absorption is considered as not relevant because chlorine-related toxicity is based on local effects only (with secondary systemic effects at high doses).

During BPC TOX-WGIII-2016, the members considered that the oral absorption values should be removed from the CAR due to the lack of systemic effects.

Dermal route of exposure
No data is available on ADME after dermal exposure towards chlorine or sodium hypochlorite.

However, the potential of hypochlorite solutions to penetrate the skin is low given its reactivity to proteinaceous material at the site of first contact. In addition, the investigation of the dermal penetration using hypochlorite at non-irritant concentrations would be poorly informative, since concentrations in the physiological range would have to be applied.

Dermal absorption is considered as not relevant because chlorine-related toxicity is based on local effects only (with secondary systemic effects at high doses).

In the absence of clear systemic effects, the BPC TOX-WGIII-2016 concluded that dermal absorption values are not deemed necessary.

Other metabolism study
In an *in vitro* study (Scully, 1990), the chlorination of amino acids present in stomach fluids of fasted rats was investigated. Rats were starved for 8, 24 and 48 h. 3 mL deionised water was administered by gavage. Stomach fluid was recovered from each rat, pooled and chlorinated by addition of 3.4 mL sodium hypochlorite solution (1011 mg/mL as Cl_2). The solution was incubated at room temperature in the dark for 15 min. The concentrations of the free amino acids in the stomach fluid varied with the fasting time. Concentrations are highest in animals fasted for 24 h. HPLC analysis of the chlorinated and dansyl sulfinic acid derivatised contents revealed a number of compounds suspected of being chloramine derivatives. Three chloramino acids, N-chloroglycine, either N-chloroleucine or N-chloroisoleucine and N-chlorophenylalanine, were identified by GC/MS. Formation of N-chlorovaline and N-chloroserine was suggested by their HPLC retention times, but their identification could not be confirmed by GC/MS.

Acute Toxicity

Chlorine gas is handled exclusively in closed systems and an exposure to the gas is only accidentally. Due to its gaseous aggregate state, dermal and oral exposure towards chlorine gas is not relevant. However, skin contact with aqueous solutions of chlorine gas may occur.

In an acute **inhalation** toxicity study in Wistar rats ([redacted] 1987) conducted with chlorine, restlessness during exposure, eyes mostly being closed and often irritated, dyspnea during and following exposure, wet nares, bubble formation and nasal discharge (mainly in the highest concentration group) were evident. The LC_{50} value for 60 min exposure was derived at 1321 mg/m^3 (corresponding to 448 ppmV based on a mole volume of 24.055 L/mol at 20°C). No 4-hour inhalation LC_{50} is available. The harmonized CLP classification for chlorine for acute toxicity by inhalation is Acute Tox. (inhal.) 3, "Toxic if inhaled" (H331).

Many other studies on chlorine acute toxicity by inhalation are available in the literature carried out on several species, although most of them quite dated and have been revised in the EU RAR for chlorine (2007). The EU RAR on chlorine (2007) also identified an overall 60 minutes LC_{50} of 448 ppm (1.3 mg/L, 1344 mg/m^3) in rats.

Formally, Regulation (EC) 1272/2008 (CLP) requires conversion of existing inhalation toxicity data which have been generated using a 1-hour testing exposure to 4-hour exposures (division by a factor of 2 for gases according to Annex I, notes to Table 1.1, paragraph c). However, in the case of chlorine which only exerts local effects at the side of first contact, it is expected that local irritative effects are rather concentration than time dependent. Hence, findings for 4-h exposure durations are expected to be similar to those observed after 1-h exposures.
Consequently, due to the lack of systemic effects, time extrapolation is not considered relevant and the 4-h LC_{50} be expected in the same range as the 1-h LC_{50}, i.e. 1321 mg/m^3 (corresponding to 448 ppmV). Nevertheless, and irrespective of time extrapolation, chlorine warrants classification as Acute Tox. (inhal.) 2, "Fatal if inhaled" (H330).

For acute **oral and dermal** toxicity studies, since the active chlorine releaser chlorine is a gas, read across is made to studies performed with sodium hypochlorite.

Sodium hypochlorite has been demonstrated to be of low toxicity in acute studies in the rat by the oral and dermal route of exposure (Anonymous, 1970). In the acute oral and dermal studies, the LD_{50} was determined to be greater than 2000 mg avCl/kg bw. Signs of toxicity were evident in the oral study characterised by hypoactivity, muscular weakness, haemorrhagic rhinitis and emaciation and in the dermal study by moderate to severe erythema.
These data on NaOCl are supported by many data found in the literature, as described in the EU-RAR on sodium hypochlorite (2007).

Conclusion on acute toxicity
The harmonized CLP classification for chlorine for acute toxicity by inhalation is Acute Tox. (inhal.) 3, "Toxic if inhaled" (H331).
Based on the results obtained in the acute inhalation toxicity study and taking into account the provisions laid down in Regulation (EC) No 1272/2008 (CLP), chlorine rather warrants classification as Acute Tox. (inhal.) 2, "Fatal if inhaled" (H330).

Results for acute oral and dermal toxicity studies with aqueous solutions of active chlorine were provided for sake of completeness. However, they are not relevant for classification and labelling of chlorine gas (which does not warrant classification for neither acute oral nor acute dermal toxicity according to Regulation (EC) No 1272/2008).

Irritation and corrosivity

No irritation and corrosivity studies are available for the active chlorine releaser chlorine (chlorine gas) and read-across is made to data obtained with sodium hypochlorite.

Skin irritation
A study to investigate the skin irritating potential of sodium hypochlorite (Nixon, 1975) was performed. The results indicate that sodium hypochlorite, 5.25%, was slightly irritant in rabbits and guinea pigs under the conditions described in the study. The mean score obtained from intact skin (sum of mean erythema and edema scores at 4, 24 and 48 hours) was 1.0 for rabbits and 0.3 for guinea pigs. All findings were reversible.

Eye irritation
Two eye irritation studies in rabbits and monkeys are available (Pashley, 1985,; Carter, 1965) indicating eye irritating properties for concentrations of 5.25 and 5.5% avCl, respectively.

Conclusion on skin and eye irritation
The results of the studies performed with sodium hypochlorite are in line with the harmonised classification of chlorine as Skin Irrit. 2 ("Causes skin irritation"; H315), Eye Irrit. 2 ("Causes serious eye irritation"; H319) and STOT SE 3 ("May cause respiratory irritation"; H335) according to Annex VI, Regulation (EU) No 1272/2008.

Sensitisation

No sensitisation studies are available for the active chlorine releaser chlorine (chlorine gas) and read-across is made to data obtained with sodium hypochlorite.

Three skin sensitisation studies were conducted in guinea pigs with sodium hypochlorite ([redacted] 1982; [redacted] 1985a and 1985b). The studies showed no sensitising effects.

Conclusion on skin sensitisation
On the basis of the weight-of-evidence from read across to sodium hypochlorite studies, it can be considered that chlorine is not a skin sensitizer. Moreover, chlorine is not classified as skin sensitizer according to the harmonised classification as provided in Annex VI of Regulation (EC) No 1272/2008.

Repeated dose toxicity

Oral administration of sodium hypochlorite

No oral repeated dose studies are available for the active chlorine releaser chlorine (chlorine gas) and read-across is made to data obtained with sodium hypochlorite.

The subacute oral repeated dose toxicity of sodium hypochlorite has been investigated in a 28 day rat study (Anonymous, 1970). A NOAEC of >7500 ppm avCl was determined.

Three subchronic repeated dose toxicity drinking water studies of sodium hypochlorite are available for rats and mice (Hasegawa, 1986; Daniel, 1990; Daniel, 1991). NOAECs derived were 0.1% avCl, ≥0.025% avCl (highest dose tested) and ≥0.02% avCl (highest dose tested), respectively.

Data on chronic repeated dose toxicity is available from four chronic toxicity/carcinogenicity drinking water studies in rats and mice (Hasegawa, 1986; NTP, 1992; Soffritti, 1997; Kurokawa, 1986). The NOAECs derived lay between >0.0275% and 0.1% avCl.

Overall, no systemic effects or morphological changes on microscopic examination could be observed with the exception of body weight and liver effects. As a consequence of these results, the eCA presented before BPC TOX-WGIII-2016 the statement "Chlorine-related toxicity is based on local effects (with few secondary systemic effects at high doses)" detailing that based on the weight of evidence, sodium hypochlorite acts via a pure local mode of action (with secondary systemic effects at high doses only). In particular, effects on body and liver weight observed in the 90-day and 104-week studies were discussed in detail and considered as secondary to the local toxicity of sodium hypochlorite.

A potential mode of action underlying the reduced body and liver weights could be that the gut mucosa and microflora may be destroyed even below irritant concentrations since it is more sensitive than e.g. skin.

Since sodium or calcium hypochlorite decompose rapidly after "port of entry" contact, only sodium chloride will become systemically available.

Taking into account that sodium as well as chloride are broadly distributed nutrients no toxicological hazard arises.

Dermal administration of chlorine

The conduct of a dermal repeated dose/subacute toxicity study with the active chlorine releaser chlorine (chlorine gas) is considered to be unnecessary for the following reasons:

1. Chlorine is exclusively handled in closed systems and an exposure to the gas is only accidentally.
2. Since chlorine is a gas, the most relevant exposure is via inhalation. There are several inhalation studies (acute, repeated dose, subchronic and chronic) in animals available.
3. The relevant chlorine species in water are hypochlorous acid and hypochlorite anion. Due to its oxidative and corrosive nature, hypochlorous acid will cause skin destructions. These effects are considered to be of local nature only 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.
4. The irritant effect of aqueous solutions of chlorine is caused by their oxidative property and basic nature of hypochlorite ions, which create a high-pH environment on exposed body tissues. Concentrated hypochlorous acid solutions are set at pH values above 11. According to OECD 404 no tests should be performed with substances having a pH of 11.5 or higher which is the case for solutions with high contents in hypochlorite/hypochlorous acid. The testing of more diluted solutions will not yield other results as those obtained from the oral studies.

Consequently based on information available on effects following other routes of exposure, a repeated dermal toxicity test with aqueous solutions of chlorine is not required for animal welfare reasons. In addition, some human data exist (see in the following) from which is possible to derive a NOAEC.

Administration of chlorine via inhalation
Several repeated dose inhalation studies are available for the active chlorine releaser chlorine (chlorine gas).

In a subacute inhalation repeated dose toxicity study (Barrow, 1979) Fischer 344 rats were exposed to chlorine gas for 6 h a day for 6 weeks. The results of this study indicated that unequivocal upper and lower respiratory tract changes were produced in rats exposed to 9 ppm of chlorine. The respiratory tract effects found in animals exposed to 3 or 1 ppm chlorine were very similar and much less severe than those seen at 9 ppm. The result of the current study may have been affected by the presence of chloramines (generated from reaction of chlorine with ammonia from urine and faeces). The NOAEC in this study was set at 1.0 ppm equivalent to 3.0 mg/m^3.

A subchronic study in Rhesus monkeys was performed with exposures of 6 h per day for 52 weeks towards nominal concentrations of 0, 0.1, 0.5 and 2.5 ppm Cl_2 ([redacted] 1987). In this study, treatment-related responses were confined to ocular and respiratory tract irritation. Histopathological examinations revealed that treatment-induced lesions were limited to the respiratory epithelium of the nose and trachea. Nasal and tracheal lesions were induced by exposure to 2.3 ppm chlorine, while less distinct but similar changes were also present in the nasal passages of some animals in the 0.5 and 0.1 ppm groups in the absence of tracheal lesions, indicating a concentration-related response relationship for chlorine-induced airway toxicity. No histological lesions were observed in this study at sites other than the nasal cavity and trachea. The NOAEC was considered to be 0.5 ppm equivalent to 1.5 mg/m^3.

In a chronic toxicity/carcinogenicity study with mice and rats (Wolf, 1995), it could be demonstrated that chlorine is non-carcinogenic. Regarding non-cancer endpoints, Chlorine was clearly a nasal toxicant that affected all airway epithelial types in the nose, but no response was observed in the larynx or lower respiratory tract. A NOAEC of <0.4 ppm (<1.2 mg/m^3) was determined for both species.

Conclusion on repeated dose toxicity
Overall, no systemic effects or morphological changes on microscopic examination could be observed after oral administration of sodium hypochlorite solutions to rats and mice, with the exception of body weight and liver effects. However, these changes were considered secondary to the local toxicity of sodium hypochlorite. The NOAECs derived in chronic studies lay between >0.0275% and 0.1% avCl.

For the dermal route of exposure, no repeated dose toxicity studies are available, and are not deemed necessary, based on the gaseous state and information available on effects following other routes of exposure as well as for animal welfare reasons. In addition, some human data exist (for sodium hypochlorite, see in the following) from which it is possible to derive a dermal NOAEC.

The repeated dose toxicity studies performed with chlorine gas indicated respiratory tract irritation due to the local chemical reactivity of chlorine (i.e. irritation at first site of contact). NOAECs in the range of <0.4 ppm to 1.0 ppm (<1.2 mg/m^3 to 3.0 mg/m^3) were derived from the rat and mice studies, whereas a NOAEC 0.5 ppm (1.5 mg/m^3) was derived from the monkey study.

Genotoxicity

No genotoxicity studies are available for the active chlorine releaser chlorine (chlorine gas) and read-across is made to data obtained with sodium hypochlorite.

In vitro
Three Ames test studies are available for sodium hypochlorite (Ishidate, 1984; Kawachi, 1980; LeCurieux, 1993). These studies showed sporadic positive results when sodium hypochlorite was applied with metabolic activation.
One *in vitro* cytogenetic assay in mammalian cells (Ishidate, 1984) is available showing positive results only at a toxic dosage of sodium hypochlorite applied without metabolic activation.

In vivo
Two micronucleus tests (Hayashi, 1988; Meier, 1985) reported no mutagenic potential of sodium hypochlorite *in vivo*. An *in vivo* bone marrow aberration assay and a non-standard DNA damage assay in renal tissue (Meier, 1985; Kasai 1987) showed likewise negative results. Germ cell effects were studied in male mice (Meier, 1985), showing sporadically increased sperm-head abnormalities, however, with a non-guideline assay. Therefore, its biological significance is unclear. In four out of the five *in vivo* tests, no information on bone marrow toxicity was reported.
However, due to the local mode of action, the biological relevance of any result from an *in vivo* study is questionable in view of uncertainty of the availability of the test substance at the target organ.

Conclusion on genotoxicity
Overall, the results of the *in vitro* assays are consistent with the ability of hypochlorite to generate reactive oxygen species. Reactive oxygen species have the ability to induce sporadically DNA damage through an indirect mechanism, dependently on the ability of the cell to cope with oxidative stress. Negative results in the *in vivo* studies are considered sufficient to reassure about the absence of a mutagenic potential of hypochlorite *in vivo*.

Based on the available data on sodium hypochlorite, no genotoxic potential of chlorine is expected.

Carcinogenicity

Oral route
No oral carcinogenicity studies are available for the active chlorine releaser chlorine (chlorine gas) and read-across is made to data obtained with sodium hypochlorite.

Sodium hypochlorite was tested for carcinogenicity by the oral route in several studies (Hasegawa, 1986; NTP, 1992; Soffritti, 1997; Kurokawa, 1986). The NOAECs derived lay between >0.0275% and 0.1% avCl.

There were no treatment-related increases in non-neoplastic lesions or tumour incidence observed in the studies by Hasegawa, NTP and Kurokawa. In the Soffritti study, increased incidence of lymphomas and leukaemias were observed in females which were, however, within the historical control data.

Inhalation route
Two chronic toxicity/carcinogenicity studies were performed with chlorine.

The chronic toxicity and carcinogenic potential of chlorine was examined in Fischer 344 rats and in B6C3F1 mice in a 104 weeks inhalation study (Wolf, 1995). The animals were exposed to chlorine concentrations of 0, 0.4, 1.0 and 2.5 ppm.

General: Chlorine exposure resulted in decreased body weight gain. Survival to the scheduled termination of the study was not different between chlorine exposed and control animals. There were no biological or statistically significant increases in neoplasms related chlorine exposure. Chlorine-induced lesions were found only in nasal passages. No lesions were found in the remainder of the respiratory tract. The nasal lesions were generally site-specific within the nose, but their severity and incidence were not always concentration-dependent. Most of the nasal responses exhibited a clear anterior-to-posterior severity gradient and only rarely extended to the nasopharyngeal meatus.

Cancer endpoints: In this study it could be demonstrated that chlorine is not a carcinogen.
Non-cancer endpoints: Chlorine was clearly a nasal toxicant that affected all airway epithelial types in the nose, but no response was observed in the larynx or lower respiratory tract. Examination of the nasal lesion data reveals that the majority of lesions associated with chlorine exposure were also present in control animals, but with a lesser incidence or severity or both. This observation suggests that chlorine exacerbated the development of these background lesions.

The development of eosinophilic proteinaceous accumulation was associated with varying

degrees of mucous cell metaplasia and hyperplasia. This observation is consistent with the proposal that eosinophilic proteinaceous accumulations are composed of a protein associated with aberrant or excessive mucus synthesis. Mice exhibited sex differences in response to comparable concentrations of chlorine. Male mice had an equivalent incidence of septal fenestration at all exposure concentrations, whereas female mice only had increased incidences at the mid and high concentrations, suggesting that male mice are more sensitive than female mice to chlorine exposure. In all cases the specific localisation of the rodent lesions was in the upper respiratory tract. This observation may reflect regional airway dosimetry, regional tissue susceptibility, or a combination of these factors.

In the rat study, a NOAEC of <0.4 ppm (<1.2 mg/m³) was determined based on significantly increased incidence and severity in goblet cell hyperplasia and olfactory epithelium eosinophilic proteinaceous accumulation.

In the mouse study, a NOAEC of <0.4 ppm (<1.2 mg/m³) was determined based on significantly increased incidence in squamous epithelium eosinophilic proteinaceous accumulation (males) respiratory epithelium hyperplasia (males and females), and olfactory epithelium atrophy (females).

Conclusion on carcinogenicity
Based on the available data on chlorine itself (inhalation route) or sodium hypochlorite (oral route), no carcinogenic potential of chlorine is expected.

Reproductive toxicity

No prenatal development toxicity and reproductive toxicity studies are available for the active chlorine releaser chlorine (chlorine gas) and read-across is made to data obtained with sodium hypochlorite and chlorinated water.

Prenatal developmental toxicity
In a prenatal developmental toxicity study (Abdel-Rahman, 1982), rats were exposed to concentrations of 0, 1, 10 and 100 mg/L hypochlorite in drinking water for 2½ months prior to and throughout gestation. There were no signs of maternal toxicity nor treatment-related changes in viability, foetal weights and external appearance of all foetuses in all dose groups. The NOAEC for prenatal developmental effects was considered to be greater than 100 mg/L.

However, the rat study provided has been performed at too low concentration levels (1/10 of relevant NOAEC) and its statistical power is impaired by limited group size; therefore the study cannot be used to draw any firm conclusion on prenatal developmental hazard.
Nevertheless, it has been shown that sodium hypochlorite is rapidly degraded in the body to physiological metabolites (sodium, chloride and hydroxide ions). Therefore, it can be predicted that the embryo/foetus will not be exposed due to the fast degradation of sodium hypochlorite in blood and other body fluids before becoming systemically available.

Due to the local mechanism of action of sodium hypochlorite it can be assumed that the same results as seen in the rat prenatal developmental toxicity study would also be observed in the second study performed with another mammalian species (rabbit). Therefore, performance of a prenatal developmental toxicity study in rabbits is not considered justified for animal welfare reasons.

Reproductive toxicity
The reproductive effects of chlorinated water have been examined in a one-generation gavage study in rats (Carlton, 1986). No differences were observed between control rats and those rats exposed to up to 5 mg avCl/kg bw/d of the test material when fertility, viability, litter size, day of eye opening or day of vaginal patency were evaluated. No alterations in sperm count, sperm direct progressive movement, percent motility or sperm morphology were observed among adult male rats. In addition, male and female reproductive organ weights were comparable to the control groups and no significant histopathological changes were observed among treated male and female rats. No NOAEC could be determined since concentrations of aqueous chlorine solutions were not indicated in the study report.

In a multi-generation study (Druckrey, 1968) highly chlorinated water, containing available

chlorine at a level of 100 mg/L was administered daily as drinking water to rats over seven consecutive generations. There were no significant differences between control and treated animals with respect to lifetime, fertility, breeding outcome, clinical signs, organ weights, haematological parameters, histopathology, and neoplastic lesions. Based on this finding the parental, reproductive and developmental NOAEC is considered to be ≥0.01% avCl (only dose tested).

To examine the effects on the reproductive performance, mice were treated with chlorinated water at 10 ppm acidified with hydrochloric acid (pH 2.5) over a period of 6 months (Les, 1968). There was no detrimental effect on the reproduction of treated mice; on the contrary, reproductive performance in treated animals was statistically significantly increased when compared to control. The NOAEC is considered to be ≥10 ppm avCl (only dose tested).

Conclusion on prenatal developmental and reproductive toxicity
Prenatal developmental toxicity and reproductive toxicity studies performed did not show any effect on the prenatal development and reproductive cycle of both rats and mice.
However, these studies have been performed at too low concentration levels (1/10 of relevant NOAEC); therefore the studies cannot be used to draw any firm conclusion on prenatal developmental and reproductive toxicity hazard.
Nevertheless, in the absence of primary systemic effects and based on the available data on sodium hypochlorite, no prenatal developmental and reproductive toxicity potential of chlorine is expected.

Neurotoxicity

Special neurotoxicity studies were not performed. There is no evidence of a neurotoxic effect from other acute, subacute, subchronic and chronic studies performed with chlorine or sodium hypochlorite.
Studies investigating delayed neurotoxicity are not required as the structure of chlorine, hypochlorite or hypochlorous acid is not related to known neurotoxic substances as organophosphates.

Human data
Aqueous solutions of sodium hypochlorite, calcium hypochlorite and chlorine share the same mode of action (i.e. release of active chlorine), thus read-across is possible between these three active chlorine releasers.
A huge set of human data on "hypochlorite bleaches" and chlorine gas is available and is shortly summarized in the following:

Oral exposure towards hypochlorite solutions
Accidental human data are reported for ingestion and parenteral route: it can be concluded that the effects of accidental ingestion of domestic sodium hypochlorite bleaches are not expected to lead to severe or permanent damage of the gastro intestinal tract as recovery is rapid and without any permanent health consequences.

No indications of chronic toxicity in humans following exposure to sodium hypochlorite are reported in the literature. Although some studies reported small relative risks for colon and bladder cancer incidence for population consuming chlorinated drinking water for long periods of time, they refer to DBPs, are equivocal or insufficient to establish a causal relationship, considering the quality and the completeness of the studies and the interpretation of the available data and of the confounding factors.

Dermal exposure towards hypochlorite solutions
The human skin irritation potential of hypochlorite bleaches has been investigated under occluded patch test conditions and/ or prolonged contact times. These studies have been used to derive reference values for local effects, when animal data were not sufficiently reliable.

Nixon et al. (1975) reported that a hypochlorite solution at 5-5.25% available chlorine (pH 10.7) was found to be severely irritating to intact human skin after 4 h exposure under occluded patch conditions. In this study a clear evidence of irritating effects above 5% is identified.

Weak to moderate irritation was observed in 15 of 69 dermatitis patients patch tested (48 h, patch conditions not specified, reported as "covered contact") with 2% NaOCl. No irritation was observed in 20 persons from the same group after additional patch testing (48 h "covered contact") with 1% NaOCl (Habets 1986).

Accidental spillage of hypochlorite bleach into the eyes is expected to cause slight, temporary discomfort, which subsides within a short period of time or after rinsing with water. The available data from human exposure (Poison Control Centers) support Pashley's observation (1985), in which irritant effects in the human eye are less severe than in rabbits. Rinsing with water shows a reduction in the irritant effects both in animals and humans.

Reports from dermatological case studies indicate that there have been a few isolated cases of allergic contact sensitization. However, these isolated cases are poorly reported and not fully conclusive. Based on the systematic animal and human study data as well as on the scarcity of alleged sensitization cases reported from the market it is concluded that sodium hypochlorite does not pose a skin sensitization hazard.

Inhalation of chlorine gas

Several reports on accidental exposure to chlorine are available (Shroff, 1988; Mryos, 1991; Charan, 1985; Agabiti, 2001; Weill, 1969). Depending on chlorine concentrations, signs of toxicity ranged from dyspnea and coughing, irritation of the throat and eyes, headache, to temporary changes in lung function, cytopathological features and tracheobronchial congestions.

There are two relevant studies reported in which human volunteers have been exposed to chlorine:

A group of 8 volunteers were exposed on a single occasion to either 0.5 or 1.0 ppm (1.5 or 3.0 mg/m^3) chlorine gas for either 4 or 8 hours. Sensory irritation and a transient impairment in lung function were seen in those exposed to 1 ppm (3 mg/m^3), resolving within 1 day. Exposure to 0.5 ppm (1.5 mg/m^3) chlorine gas resulted in only trivial changes of lung function parameters, therefore the NOAEC was derived at 0.5 ppm (1.5 mg/m^3) (Rotman, 1983).

A group of 8 male volunteers were exposed to 0, 0.1, 0.3 or 0.5 ppm (0, 0.3. 0.9 or 1.5 mg/m^3) chlorine gas for 6 h/d on 3 consecutive days. Each individual was exposed to each of the four exposure scenarios in a double-blind fashion. A range of respiratory function parameters was measured and, in addition, nasal lavage fluid was analysed for a number of indicators of inflammatory cell damage. No significant effects were seen in parameters measured, and a NOAEC of 0.5 ppm (1.5 mg/m^3) was derived in the study (Schins, 2000).

Other tests

Data from other tests is available for the active chlorine releaser sodium hypochlorite, which are summarised in the following:

Tissue toxicity of sodium hypochlorite solutions was analysed in female guinea pigs (Cotter, 1985). On the shaved skin of the upper dorsum, a gauze pad was placed and soaked at 8-hour intervals with 0.1 or 0.5% sodium hypochlorite solution freshly prepared each day by dilution of Clorox bleach. Animals were sacrificed on day 1, 4, 7 or 14. A 15% decrease in basal cell viabilities was observed after 2 weeks of treatment with the high concentration, i.e. 0.5% sodium hypochlorite. Morphological changes in cells were observed after 7 and 14 days of treatment with the 0.5% solution and 14 days with the 0.1% solution. It was concluded that a 0.1% solution of sodium hypochlorite could be used for long-term maintenance of the wound due to the relatively low toxicity.

Female SENCAR mice (Robinson, 1986) were treated with aqueous solutions of hypochlorous acid (1, 10, 100, 300, 1000 ppm) and sodium hypochlorite (1000 ppm) by whole body exposure (except head) for 10 minutes daily on 4 consecutive days. There was a dose-related response to hypochlorous acid (pH 6.5) treatment, the minimally effective dose being 100 ppm. Skin thickness (interfollicular epidermis) and the number of cells (total and basal) were increased. The sodium hypochlorite solution (pH 8.5) showed similar effects at 1000 ppm (the only concentration tested). The NOAEL was derived at 10 ppm sodium hypochlorite.

In a non-standard study (Wohlrab, Wozniak 1982) for the effect of sodium hypochlorite solutions on skin, 10 male and 10 female guinea-pigs per group were exposed to a 0.125% sodium hypochlorite solution on the dorsal side of their ears. This was done daily for 1, 2, 4 and 8 weeks. There were no treatment related effects on the parameters measured (e.g. number of epidermal cells, area of epidermis, area of papillary layer).

Summary

The active substance covered by this assessment is "active chlorine released from chlorine". Chlorine gas is handled exclusively in closed systems and an exposure to the gas is only accidentally. Due to its gaseous aggregate state, inhalation is the only possible exposure route.

In water, chlorine forms hypochlorous acid (HClO), which is in equilibrium with the hypochlorite ion (ClO^-) characterised by its well-known irritating/corrosive effects, and chlorine (Cl_2). In biological systems, characterised by pH values in the range 6-8, the most abundant species is HClO. At alkaline pH values, ClO^- is predominant, whilst Cl_2 is the main species only below pH 4.

As outlined above, the primary effect of chlorine is driven by the corrosive/irritant properties caused by the local reaction of the hypochlorite ion. Studies on the acute inhalation toxicity potential as well as repeated dose studies (exposure via inhalation) are available on chlorine; missing data of kinetic behaviour, repeated dose, subchronic and chronic studies relevant for the derivation of the reference values can be replaced by data obtained from sodium hypochlorite, by applying the read-across principles. Due to the local mode of action of chlorine, only local reference values are deemed necessary as it is the case for sodium hypochlorite.

Chlorine is not acutely toxic by the oral or dermal route.

Chlorine is classified according to Regulation (EC) No 1272/2008, Annex VI (CLP, harmonized classification) as Acute Tox. (inhal.) 3 ("Toxic if inhaled") and STOT SE 3 ("May cause respiratory irritation"). Based on the assessed data on chlorine, chlorine is proposed for classification as Acute Tox. (inhal.) 2 ("Fatal if inhaled").

Chlorine is classified according to Regulation (EC) No 1272/2008, Annex VI (CLP, harmonized classification) as Eye Irrit. 2 ("Causes serious eye irritation") and Skin Irrit. 2 ("Causes skin irritation").

Chlorine has no potential to be a skin sensitizer.

It is not genotoxic/mutagenic *in vitro* or clastogenic *in vivo* and has no carcinogenic potential. It shows no potential for developmental or reproductive toxicity.

Deduction of reference values for chlorine, hypochlorous acid and chlorate

The mode of action of chlorine was extensively discussed at Technical Meeting (TOX TMI-2012, 19 March 2012) and BPC Working Group level (TOX-WGII-2016, 16 March 2016 and TOX-WGIII-2016, 26 May 2016).

Before WGIII-2016, the eCA presented the statement *"Chlorine-related toxicity is based on local effects (with few secondary systemic effects at high doses)"* detailing that based on the weight of evidence, chlorine acts via a local mode of action (with secondary systemic effects at high doses only). In particular, effects on body and liver weight observed in the 90-day and 104-week studies performed with sodium hypochlorite were discussed in detail and considered as secondary to the local toxicity of sodium hypochlorite.

The BPC WG members finally supported that an assessment for systemic effects should not be performed and only a local risk assessment should be included. In addition, the WG agreed that AEL values should not be derived.

In addition, before WGIII-2016, the eCA presented the statement *"Deduction of reference values for NaOCl, $Ca(OCl)_2$, Cl_2 and HOCl"*, including a proposal for a set of local reference values for chlorine species and routes of exposure relevant for performing a local exposure and

risk assessment.

It should be noted that for chlorine and HClO, all (in-use) concentrations are expressed as available chlorine (avCl; w/w) and not as Cl_2 (v/v) or HClO (w/w). Hence, exposure towards chlorine or HClO should be compared with the relevant AECs for available chlorine and not with the AECs for Cl_2 of HClO itself.

Chlorine: $NOAEC_{dermal}$
Dermal exposure towards chlorine gas is not relevant. However, skin contact with aqueous solutions of chlorine gas may occur. As the common active species are hypochlorite and hypochlorous acid, the $NOAEC_{dermal}$ was thus derived from sodium hypochlorite studies:

During TMI-2012 meeting, a dermal NOAEC of 1% was discussed, however, not formally agreed upon according to the meeting minutes. Although not explicitly stated in the meeting minutes it is assumed that the concentration refers to aqueous solutions of NaOCl containing 1% available chlorine.

Data on human skin clearly indicate an irritating effect at 5% NaOCl and above (Nixon, 1975). Lower values (around 2% NaOCl) for irritating concentration have been reported in dermatitis patients, which represent a specific susceptible population, not suitable for setting limits for the general population (Habets, 1986). In the same study, no reaction was observed at concentrations of 1% and 0.5% NaOCl.
As a conservative approach, it was decided during the TMI-2012 that sodium hypochlorite (and hence active/available chlorine) shows irritant properties at concentration >1%, which was agreed by the WGII-2016 meeting.

$NOAEC_{dermal}$ to be used for risk characterization of Cl_2: **$NOAEC_{dermal}$ = 1% avCl**

Chlorine: $AEC_{inhalation}$
The BPC TOX-WGIII-2016 finally agreed to derive the $AEC_{inhalation}$ on the NOAEC of 0.5 ppm avCl (1.5 mg avCl/m^3) based on the rhesus monkey ([redacted] 1987) and human studies (Rotman 1983; Schins, 2000).

SCOEL has also based the deduction of the STEL for chlorine on these three studies and disregarded the 6-week rat study (Barrow, 1979) and the 104-day rat and mice study (Wolf, 1995).

Since the NOAEC of 0.5 ppm avCl (1.5 mg avCl/m^3) has been derived based on the rhesus monkey and human studies, there is no need to consider an inter-species toxicodynamic and -kinetic assessment factor (AF).

An intra-species toxicokinetic assessment factor is not considered relevant based on the local mode of action of chlorine which is characterized by primary local effects, namely irritation, corrosion and oxidation at the port of entry (skin, eye, upper respiratory or GI tract) without influence of local metabolism (kinetics). However, the WGIII-2016 agreed on an intra-species toxicodynamic AF of 3.2 for precautionary reasons.

The WG members further agreed that the lack of reproductive toxicity studies did not raise additional concern or the need for an extra AF, as chlorine was not considered to have systemic effects.

Based on these considerations, the $AEC_{inhalation}$ for chlorine is derived as follows (inter-species AF (toxicodynamics x -kinetics): 1 x 1, intra-species AF (toxicodynamics x -kinetics): 3.2 x 1, AF for duration: 1, AF for other uncertainties: 1):

$AEC_{inhalation}$ to be used for risk characterization of Cl_2:

$AEC_{inhalation}$ = 1.5 mg avCl/m^3 / 3.2 ≈ 0.5 mg avCl/m^3

Chlorine: $NOAEC_{oral}$
Chlorine is not classified as acutely toxic via the oral route, and as it is a gas, the primary route of exposure is via inhalation. Moreover, ARfD and/or ADI are only relevant for substances with a systemic mode of action. Since local effects are the only relevant effects for

chlorine, deduction of an ARfD and/or ADI is considered to be not relevant. In line with the approach for local dermal effects, an oral NOAEC should be derived instead.

During TMI-2012, deduction of an oral NOAEC has already been discussed and the NTP study as well as the studies of Hasegawa (rat, 1986) and Daniel (rat, 1990 and mouse, 1991) (performed with NaOCl) were proposed as point of departure to derive an oral NOAEC for NaOCl, which applies also to chlorine.

Taking into account the complete data package of repeated dose toxicity and carcinogenicity studies, an oral NOAEC of 1000 ppm (0.1%) available chlorine (avCl) can be derived based on the Hasegawa (1986) study.

$NOAEC_{oral}$ to be used for risk characterization of Cl_2: **$NOAEC_{oral}$ = 0.1% avCl**

Hypochlorous acid: $AEC_{inhalation}$

Hypochlorous acid (HClO) is a gas at room temperature and pressure and one of the three chlorine species at equilibrium in water (i.e. Cl_2, HClO, ClO^- as a function of pH, please also refer to chapter 2.4 "Transformation" of the EU RAR on NaOCl, 2007).

At pH values > 10, the hypochlorite anion (ClO^-) is the predominant species which does not evaporate. The minute fraction of volatile hypochlorous acid (HClO) is considered negligible.

At pH values of about 4-6, hypochlorous acid (HClO) is the predominant species and exposure to HClO vapour is considered relevant.

In the EU RAR on NaOCl (2007), the chlorine species HClO has only been addressed in a qualitative manner and no exposure and risk assessment has been performed for HClO.

There is no repeated dose/subchronic inhalation toxicity study on HClO available since HClO does not exist as such but is only formed in aqueous solutions of NaOCl or chlorine.

In the absence of data, the BPC TOX WGIII-2016 agreed to derive the $AEC_{inhalation}$ for HClO based on chlorine data, namely the NOAEC of 0.5 ppm avCl (1.5 mg avCl/m^3) as derived based on the rhesus monkey ([redacted] 1987, read-across study) and human studies (Rotman 1983, Schins 2000). It is anticipated that the use of data on chlorine gas is likely to be a realistic assessment of the potential effects of HClO gas under real case conditions.

Based on the NOAEC of 0.5 ppm avCl (1.5 mg avCl/m^3) and applying the same consideration as for deriving the $AEC_{inhalation}$ for chlorine gas, the $AEC_{inhalation}$ for HClO is derived as follows (inter-species AF (toxicodynamics x -kinetics): 1 x 1, intra-species AF (toxicodynamics x -kinetics): 3.2 x 1, AF for duration: 1, AF for other uncertainties: 1):

$AEC_{inhalation}$ to be used for risk characterization of HClO:

$AEC_{inhalation}$ (HClO as avCl) = 1.5 mg avCl/m^3 / 3.2 ≈ 0.5 mg avCl/m^3

Chlorate

Due to the high reactivity of chlorine species, residues on surfaces degrade very rapidly (decomposition to physiological chloride). Hence, residue formation is assumed to be negligible for aqueous solutions of chlorine. This conclusion is further supported by the conclusions drawn in the ENV part of the dossier. Finally, no systemic assessment is required for substances such as chlorine which act by a local mode of action only.

The BPC APCP-WGII-2016 concluded that chlorate residues may still be relevant as chlorate is considered a stable metabolite. Chlorate can be formed from hypochlorite in aqueous chlorine solutions during storage. Thus, chlorate may represent a worst-case for chlorine residues.
In the absence of data, the WGIII-2016 agreed on the ADI and ARfD values proposed by the EFSA Panel on Contaminants in the Food Chain (Scientific Opinion on risks for public health related to the presence of chlorate in food. EFSA Journal 2015;13(6):4135,103 pp).

ARfD and ADI to be used for risk characterization of chlorate:

ARfD = 36 µg chlorate/kg bw
ADI = 3 µg chlorate/kg bw

In addition to the EFSA Opinion, the following data sources are available including but not limited to the "Chlorite and Chlorate in Drinking-water" background document of the WHO (2005) in which a TDI (equivalent to ADI) of 30 µg/kg bw and a provisional guideline value of 0.7 mg/litre was derived for chlorate.
The provisional guideline value WHO for drinking water of 0.7 mg chlorate/L is also mentioned in the draft Guidance on Disinfection By-Products (vers. 1, April 2016) which is currently undergoing a PEG process.

Table 2.2.2.1-1: Summary of reference values

Substance	Exposure route	Reference value
Cl_2	Oral	$NOAEC_{oral}$ = 0.1% available chlorine
	Dermal	$NOAEC_{dermal}$ = 1% available chlorine
	Inhalation	AEC_{inhal} = 0.5 mg/m³ available chlorine
HClO	Inhalation	AEC_{inhal} = 0.5 mg/m³ available chlorine
Chlorate	Oral	ARfD = 36 µg chlorate/kg bw ADI = 3 µg chlorate/kg bw

To be noted that the reference values for local risk assessment, i.e., AEC inhalation and NOAEC dermal, have not been intended to protect hyperresponsive and/or sensitised subjects since both values were derived from observations in healthy volunteers, while data in the CAR clearly indicates higher sensitivity in subpopulations.

2.2.1.2 Exposure assessment and risk characterisation

Chlorine is used in professional settings only in PT2. Intended uses are summarised in the table below.

Table 2.2.2.1-1: Intended uses of chlorine in PT2.

	Field of use envisaged	Likely concentration at which chlorine (in aqueous solution, as available chlorine) will be used
MG1/ PT2	Disinfection of sewage/waste water before the waste water plant - professional use	5-40 mg/L
	Disinfection of sewage/waste water after the waste water plant - professional use	5-40 mg/L
	Disinfection of public swimming pools - professional use	3 mg/L (in-use) 50 mg/L (shock dosing)

General considerations on exposure and risk assessment

Primary exposure

Chlorine is a gas at room temperature and normal pressure, and upon contact with water forms hypochlorous acid, which is in equilibrium with the hypochlorite ion (ClO^-). This means that chlorine (Cl_2) itself is no longer available for dermal or oral exposure and in the human exposure scenarios solutions containing hypochlorous acid and hypochlorite ions have to be considered.

The primary mode of action of chlorine and its aqueous solutions is local irritation and oxidation at the site of first contact triggered by direct chemical reactivity without prior metabolism. Chlorine, hypochlorous acid and hypochlorite do not become systemically available upon dermal contact, ingestion or inhalation. Any systemic effects seen in animal studies (at high doses) are considered to be secondary to local irritation/corrosion. Consequently, only a local exposure and risk assessment is performed for all relevant routes of

exposure (i.e. oral, dermal, inhalation) which is considered to also cover the risk resulting from potential systemic effects. For all intended uses within PT2, the Guidance on the BPR, Volume III Human Health – Part B Risk Assessment (vers. 2.0, Oct. 2015) is followed for the local assessment of chlorine gas and the relevant in-use solutions.

Dermal exposure: For the dermal route of exposure, a semi-quantitative (Tier-1) assessment was performed for the relevant chlorine species (as available chlorine). For chlorine gas, dermal exposure is considered not relevant.

Oral exposure: For the oral route of exposure, a semi-quantitative (Tier-1) assessment was performed for chlorine and the relevant chlorine species (as available chlorine).

Inhalation exposure: For the inhalation route of exposure, a quantitative assessment (Tier-1 and Tier-2) was performed. Exposure towards chlorine gas and HClO vapour (as avCl) is conceivable.

At pH values > 10, the hypochlorite anion (ClO^-) is the predominant species and only exposure to aerosols of ClO^- (as avail. chlorine) is considered relevant. The minute fraction of volatile hypochlorous acid (HClO) is considered negligible.

At pH values of about 4-6, hypochlorous acid (HClO) is the predominant species and exposure to vapours of HClO (as avail. chlorine) is considered relevant.

Swimming pool water is expected to have a pH of 6.5 which is set forth e.g. in German norm DIN 19463, Part 1.

Oral, dermal and inhalation absorption: In the absence of clear systemic effects, the BPC TOX-WGIII-2016 (26 May 2016) concluded that oral, dermal and inhalation absorption values are not deemed necessary.

Exposure to chlorine gas

For the intended uses of chlorine gas in PT2, automated dosing systems are designated. Thus, exposure to chlorine gas can occur only during mixing and loading, i.e. during connecting/disconnecting chlorine containing vessels to a dosing system. Safety procedures and the use of appropriate protective equipment limit the exposure to chlorine to accidental events.

Regarding the exposure assessment, no models are available to estimate the exposure during mixing and loading of a gaseous substance. However, measured exposure data of chlorine concentrations in different workplaces of chlor-alkali plants are available. Workers exposure to chlorine in the atmosphere during chlorine production as measured by Euro Chlor, 2001 is given in table A.2.10-4 of Doc. IIIA, Section A2.

As exposure models for mixing and loading of gases are lacking, the measured exposure data was used for HHRA. Taking into account the safety procedures applied (i.e. the application of low-pressure to avoid chlorine emission), the high degree of technical monitoring (i.e. the presence of alarm sensors) as well as the availability of suitable RPE, using the 90th percentile of the above mentioned measurements (i.e. 0.166 ppm/0.498 mg/m³) is considered a reasonable worst-case for the assessment of inhalation exposure during connecting/disconnecting of chlorine vessels.

Accordingly, the 90th percentile for maintenance (i.e. 0.160 ppm/0.480 mg/m³), was used for the exposure assessment during maintenance tasks.

Exposure to hydrochloric acid

During BPC TOX-WG-IV-2016, the question was raised whether hydrochloric acid (HCl) should be included in the exposure and risk assessment.

When introduced into water, Cl_2 forms HClO and HCl. Notably, both acids (and HCl in particular, as it is a strong acid) will immediately dissociate into H_3O^+ and Cl^- (HCl) or H_3O^+ and ClO^- (HClO). Neither H_3O^+ nor Cl^- ions are of concern, as both are natural constituents of the human body. Considering dermal exposure, the pH of the pool water may however be of interest. The pH of pool water is ~ 6.5 (near neutral) as set forth for example by the German

norm DIN 19463. At a near neutral pH, H_3O^+ and Cl^- are the predominant species, and thus no further evaluation of HCl formed when introducing chlorine in water is necessary.

In any case, HCl - as chlorine, hypochlorite and HClO - exerts only local effects (classification of HCl as Skin Irrit. 2, 10% ≤ C < 25%) which are considered to be covered by the local exposure and risk assessment for chlorine, hypochlorite and HClO.

The only relevant uses in PT2 are disinfection of public swimming pools and sewage waste water and the same argumentation applies to the disinfection of sewage waste water in PT2, which is also expected to have a pH in the near neutral range.

Based on the argumentation above, the WG agreed that HCl does not need to be included in the exposure and risk assessment.

Secondary exposure

Indirect exposure includes exposure of persons (bystanders/general public) who are present during or following the use of biocidal product.

Secondary exposure of professional or non-professional bystanders/non-users upon dermal contact with aqueous solutions of chlorine is considered to be non-relevant. Due to the high reactivity of chlorine species, residues degrade very rapidly. Decomposition to physiological chloride ions takes place which are not expected to arise any health risk. Furthermore, the applied in-use solutions are of a low concentration.

Hence, residue formation and chronic secondary exposure is assumed to be negligible for aqueous solutions of chlorine.

Therefore, only inhalation exposure after application of chlorine as disinfectant is considered to be relevant for the assessment of secondary exposure.

An exception is the use of chlorine as disinfectant for swimming pool water. For this use, also dermal and oral exposure to chlorine species is considered relevant.

Dietary risk assessment

Due to the high reactivity of chlorine species, residues on surfaces degrade very rapidly (decomposition to physiological sodium and chloride). Hence, residue formation is assumed to be negligible for aqueous solutions of chlorine. This conclusion is further supported by the conclusions drawn in the ENV part of the dossier. Finally, no systemic assessment is required for substances such as chlorine which act by a local mode of action only.

The BPC APCP-WGII-2016 concluded that chlorate residues may still be relevant as chlorate is considered a stable metabolite.

Sodium and calcium chlorate are by-products of the manufacturing process of sodium and calcium hypochlorite and can be formed during storage. In addition, chlorate can be formed from hypochlorite in aqueous solutions of sodium/calcium hypochlorite and chlorine during storage. Thus, chlorate may represent a worst-case for chlorine residues.

Furthermore, the BPC TOX-WGII-2016 agreed that exposure via food should be assessed during active substance approval so this is available at product authorization.

In the BPC TOX-WGIII-2016 it was finally discussed that only chlorate is relevant for the dietary risk assessment.

A preliminary dietary exposure and risk assessment was performed for intended uses in PT5, however, was not considered relevant for PT2.

The relevant reference value for chlorate as agreed during BPC WGIII-2016 is the ADI of 0.003 mg/kg bw (according to EFSA CONTAM Panel, 2015. Scientific Opinion on risks for public health related to the presence of chlorate in food. EFSA Journal 2015; 13:4135).

Primary exposure assessment and risk characterisation - professionals

Taking into account the considerations as outlined above, exposure and risk of professionals handling chlorine gas for disinfection of sewage/waste water and swimming pool water was

assessed and are summarised in Table 2.2.2.1-2.

Disinfection of sewage/waste water before and after the waste water plant

For disinfection of sewage/waste water before and after the waste water plant, exposure to chlorine gas can take place during mixing and loading, i.e. during connecting/disconnecting chlorine containing vessels.

In absence of sound exposure models, measured exposure data of workers during filling operations is used for the human health exposure assessment during mixing and loading of chlorine gas. The 90th percentile of the measured data was 0.498 mg/m³ (0.166 ppm) chlorine species, resulting in 99.6% AEC_{inhal}.

Exposure towards chlorine gas may also occur during maintenance tasks. For maintenance tasks, the 90th percentile value of measured data was 0.480 mg/m³ (0.160 ppm) resulting in 96% AEC_{inhal}.

Dermal and oral contact to chlorine is not considered relevant.

Dermal contact to in-use dilutions of chlorine can occur during maintenance tasks such as repair of dosing pumps. Semi-quantitative assessment results in 0.4% of $NOAEC_{dermal}$. Inhalation exposure towards aerosols containing dissolved chlorine results in 0.01% AEC_{inhal}.

In conclusion, primary exposure during disinfection of sewage/waste water before and after the waste water plant is acceptable without PPE.

Disinfection of public swimming pools - professional use

As outlined above for the disinfection of sewage/waste, exposure to chlorine gas can take place during mixing and loading, i.e. during connecting/disconnecting chlorine containing vessels.

In absence of sound exposure models, measured exposure data of workers during filling operations is used for the human health exposure assessment during mixing and loading of chlorine gas. The 90th percentile of the measured data was 0.498 mg/m³ (0.166 ppm) chlorine species, resulting in 99.6% AEC_{inhal}.

Exposure towards chlorine gas may also occur during maintenance tasks. For maintenance tasks, the 90th percentile value of measured data was 0.480 mg/m³ (0.160 ppm) resulting in 96% AEC_{inhal}.

Dermal and oral contact to chlorine is not considered relevant.

Dermal contact to in-use dilutions of chlorine can occur during maintenance tasks such as repair of dosing pumps. The worst-case situation is contact to the shock dosing concentration of 50 mg avCl/L, which results in 0.5% $NOAEC_{dermal}$ and 0.009% AEC_{inhal} for the exposure towards aerosol.

In conclusion, primary exposure during disinfection of public swimming pools is acceptable without PPE.

Qualitative local assessment

According to the Guidance on BPR, Vol. III B - Risk Assessment (Vers. 2, October 2015), risk characterisation for local effects is not required when the active substance and/or co-formulants in a product are classified for local effects but are present at concentrations that do not trigger classification of the product according to the CLP criteria. The concentration of chlorine in the in-use solution is below the classification trigger of 10% for local irritant effects (skin, eyes), and moreover below the $NOAEC_{dermal}$ of 1% avCl.

Table 2.2.2.1-2: Results of exposure assessment and risk characterisation for the primary exposure of professionals

Intended use	Task	Oral		Dermal		Inhalation		PPE	acceptable yes/no
		Exposure (Cl_2 as avCl)	**%AEC $NOAEC_{oral}$ 0.1% avCl**	**Exposure** (Cl_2 as avCl)	**%AEC $NOAEC_{dermal}$ 1% avCl**	**Exposure** (total as mg avCl/m^3)	**%AEC AEC_{inhal} 0.5 mg/m^3 avCl**		
PT2: Disinfection of sewage/waste water before the waste water plant – professional use	Mixing & loading	n.r.	n.r.	n.r.	n.r.	0.498	99.6%	none	yes
	Application	no exposure	no exposure	no exposure	no exposure	no exposure	no exposure	-	yes
	Post-application (Maintenance: contact to gas)	n.r.	n.r.	n.r.	n.r.	0.480	96%	none	yes
	Post-application (Maintenance: contact to in-use dilution)	n.r.	n.r.	0.004%	0.4%	0.00004	0.01%	none	yes
PT2: Disinfection of sewage/waste water after the waste water plant – professional	Mixing & loading	n.r.	n.r.	n.r.	n.r.	0.498	99.6%	none	yes
	Application	no exposure	no exposure	no exposure	no exposure	no exposure	no exposure	none	yes
	Post-application (Maintenance: contact to gas)	n.r.	n.r.	n.r.	n.r.	0.480	96%	none	yes

use	Post-application (Maintenance: contact to in-use dilution)	n.r.	n.r.	0.004%	0.4	0.00004	0.01%	none	yes
PT2: Disinfection of public swimming pools – professional use	Mixing & loading	n.r.	n.r.	n.r.	n.r.	0.498	99.6%	None	yes
	Application	no exposure	no exposure	no exposure	no exposure	no exposure	no exposure	None	yes
	Post-application (Maintenance: contact to gas)	n.r.	n.r.	n.r.	n.r.	0.480	96%	None	yes
	Post-application (Maintenance: contact to in-use dilution)	n.r.	n.r.	0.0003%	0.03	0.000003	0.001%	None	yes
	Post-application (Maintenance: contact to shock-dosing dilution)	n.r.	n.r.	0.005%	0.5	0.00005	0.009%	None	yes

Indirect exposure assessment and risk characterisation

Due to the high reactivity of chlorine species, residues on surfaces degrade rapidly. Moreover, in-use dilutions are of low concentration. Thus, secondary exposure via dermal route is considered negligible, and only indirect inhalation exposure was assessed. Due to the rapid chemical degradation and the local mode of action, only acute secondary scenarios are considered relevant.

An exception is the exposure during swimming in pools treated with chlorine, where oral, dermal and inhalation exposure was assessed.

Indirect exposure of professionals

Indirect exposure of professionals is summarised in Table 2.2.2.1-1.

Secondary inhalation exposure of professional bystanders during mixing and loading tasks

Professional bystanders may be exposed to chlorine gas when they are present during mixing and loading (i.e. during connecting/disconnecting vessels). This is considered relevant for the mixing and loading step in the following scenarios:

- *Disinfection of sewage/waste water before the waste water plant – professional use*
- *Disinfection of sewage/waste water after the waste water plant – professional use*
- *Disinfection of public swimming pools – professional use*

In absence of sound exposure models, measured exposure data of workers during filling operations is used for the human health exposure assessment during mixing and loading of chlorine gas. The 90th percentile of the measured data was 0.498 mg/m³ (0.166 ppm) chlorine species, resulting in 99.6% AEC_{inhal}.

Secondary inhalation exposure of swim instructors

A swim instructor is exposed via the inhalation route to chlorine species evaporating from the swimming pool surface when water is disinfected with chlorine. This is a relevant scenario for:

- *Disinfection of public swimming pools – professional use.*

Swimming pool water is expected to have a pH of 6.5 which is set forth e.g. in German norm DIN 19463, Part 1. At this pH value, hypochlorous acid (HClO) is the predominant species and exposure to vapours of HClO (as avail. chlorine) is considered relevant. For evaporation estimation, the vapour pressure of HClO was calculated as outlined in the list of endpoints, chapter 3.

Quantitative assessment for inhalation exposure results in 1.5% of the AEC_{inhal}.

Table 2.2.2.1-1: Results of exposure assessment and risk characterisation for the secondary exposure of professionals

Intended use	Task	Oral		Dermal		Inhalation		PPE	Acceptable yes/no
		Exposure (Cl_2 as avCl)	**%AEC NOAEC$_{oral}$ 0.1% avCl**	**Exposure** (Cl_2 as avCl)	**%AEC NOAEC$_{dermal}$ 1% avCl**	**Exposure** (total as mg avCl/m³)	**%AEC AEC$_{inhal}$ 0.5 mg/m³ avCl**		
PT2: Secondary inhalation exposure of professional bystanders during M&L tasks	Mixing & loading	n.r.	n.r.	n.r.	n.r.	0.498	99.6%	none	yes
PT2: Secondary inhalation exposure of swim instructors	Application	n.r.	n.r.	n.r.	n.r.	0.007	1.5%	none	yes

Indirect exposure of the general public

Indirect exposure of the general public is summarised in Table 2.2.2.1-1.

Secondary oral, dermal and inhalation exposure of swimming pool users (baby, child, adult)

Swimmers are exposed to chlorine species during swimming in public and private pools. Exposure occurs via dermal and inhalation route as well as by accidental swallowing of swimming pool water.

- *Disinfection of public swimming pools – professional use*

A semi-quantitative exposure assessment was performed for oral and dermal exposure, while a quantitative exposure assessment was performed for the inhalation route.

Babies exposed during baby swimming represent the worst-case. Exposure assessment results in 0.3% $NOAEC_{oral}$ and 0.03% $NOAEC_{dermal}$. Inhalation exposure to HClO vapour evaporating from the pool water resulted in 1.9% $AEC_{inhal.}$

Table 2.2.2.1-1: Results of exposure assessment and risk characterisation for the secondary exposure of the general public

Intended use	Task	Oral		Dermal		Inhalation		Acceptable yes/no
		Exposure (Cl_2 as avCl)	**%AEC $NOAEC_{oral}$ 0.1% avCl**	**Exposure** (Cl_2 as avCl)	**%AEC $NOAEC_{dermal}$ 1% avCl**	**Exposure** (total as mg avCl/m^3)	**%AEC AEC_{inhal} 0.5 mg/m^3 avCl**	
PT2: Secondary oral, dermal and inhalation exposure of swimming pool users (baby, child, adult)	Application babies	0.0003	0.3%	0.0003	0.03%	0.009	1.9%	yes
	Application Child, adult	0.0003	0.3%	0.0003	0.03%	0.007	1.5%	

Assessment of disinfection-by-products

During the BPC TOX working group (WGII-2016) meeting, the members indicated that it would be useful to perform an assessment on disinfectant by-products (DBPs) in the CAR, but that in the absence of guidance this is not possible. The members recognised that the draft guidance on DBPs is only for swimming pool scenarios in PT2. Finally, the working group concluded that the assessment will be done at product authorisation.

Combined exposure

Combined exposure is not relevant based on the absence of systemic effects after exposure towards chlorine and relevant chlorine species (i.e. hypochlorite). The primary mode of action of chlorine and relevant chlorine species is characterized by local irritation/corrosion and oxidation at the site of first contact; thus effects triggered by chlorine are rather concentration than time-dependent.

For this reason, only the highest exposure level (concentration as % avCl or mg avCl/m^3) is relevant for risk characterization and the addition of exposure levels and the calculation of a combined exposure during the different tasks (e.g. M&L, application and post-application/maintenance) is not relevant.

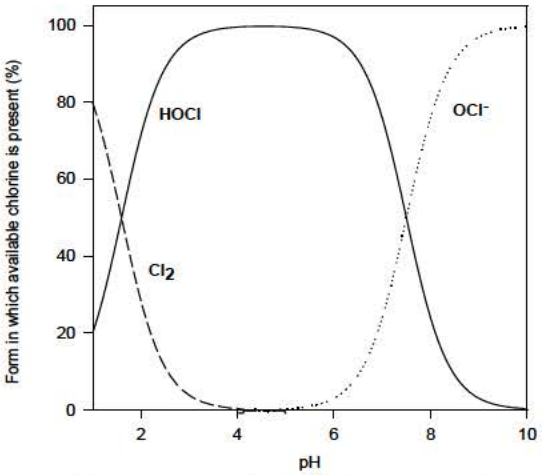
Conclusion

Based on the results obtained in the (semi-)quantitative and qualitative exposure and risk assessments, exposure of professional users in the intended uses within PT2 results in no unacceptable risk.

The same conclusion applies to secondary exposure of professional and non-professional bystanders/non-users.

2.2.2 Environmental Risk Assessment

The active substance released from chlorine in water is active chlorine (please, refer to the beginning of para 2.1.1). The hypochlorite acid (HClO) is in equilibrium with hypochlorite anion (ClO^-) and chlorine. The equilibrium depends on the pH value: chlorine is available below pH 4, in the neutral pH range hypochlorous acid is the predominant species, and at pH values higher than 10, the only species present is the hypochlorite ion, see figure below.



The sum of these species (hypochlorite ion + hypochlorous acid + chlorine) is defined as active chlorine or available chlorine. For the chemical reactivity in aqueous solution with the same active chlorine concentrations and the same pH conditions, it is irrelevant whether active chlorine is generated from either chlorine gas, calcium hypochlorite or sodium hypochlorite. Therefore, all studies investigating hypochlorite aqueous solutions can be used for evaluation and assessment of active chlorine released from any of the three substances.

The following estimated half-lives of hypochlorite were used in the exposure assessment to consider the degradation of hypochlorite based on processes related to the specific uses of the active substance and degradation in the relevant compartments. The DT_{50} values were transferred to an environmental temperature of 12°C using the Arrhenius equation:

$$\mathbf{DT_{50}\ (X°C) = DT_{50}\ (t)\ e^{(0.08\ (T-X))}}$$

Table 2.2.2: Estimated half-lives of hypochlorite in the environment

Compartment	**DT_{50} of hypochlorite measured in tests**	**DT_{50} of hypochlorite transferred to an environmental temperature of 12°C** (by Arrhenius)	**Reference**
Sewer system Due to similar high content of organic substance, also transferable to the aeration tank of the STP	20 sec (*)	**56 sec**	Vandepitte and Schowanek (1997), Doc. IIIA, Sec. A7.1.2
Surface water/ Sediment	20 min (*)	**56 min**	Worst case assumption, based on the kinetic model of Vandepitte and Schowanek (1997),

Compartment	DT_{50} of hypochlorite measured in tests	DT_{50} of hypochlorite transferred to an environmental temperature of **12°C** (by Arrhenius)	Reference
			Doc. IIIA, Sec. A7.1.2, assuming slower degradation due to lower content of Corg in surface water and sediment when compared to raw sewer
Soil	20 sec (*)	**56 sec**	Worst case assumption, based on the kinetic model of Vandepitte and Schowanek (1997), Doc. IIIA, Sec. A7.1.2, assuming slower degradation due to lower content of Corg in soil when compared to raw sewer
Air	114.6 days	--	Görg, J, Glöckner, T (2007), Doc. IIIA, Sec. A7.3.1

* No temperature was indicated; a temperature of 25°C was assumed as worst case

2.2.2.1. Hazard identification and effects assessment

Short and long term toxicity data from literature are available for fish, invertebrates, algae and micro-organisms. Only flow-through tests or static test with a reliable analytical monitoring of the test concentration over the test duration should be used for the effects assessment and as a basis for the environmental risk assessments. Most tests with a static test design result in by a factor of 100 – 500 higher end-points (NOEC, LC_{50}) than studies performed according to a flow-through design. Due to the very fast hypochlorite decay, the static test system is not exposed during the complete test duration to the same hypochlorite concentration. When data from literature were considered not valid or incomplete for the risk assessment, new toxicity laboratory studies were performed and included in the CAR.
The evaluation and comparison of toxicity data is complicated by the complexity of the active chlorine chemistry in water and by the different analytical methods used in the tests performed for the monitoring of the test item concentration in the test medium. TRC (total residual chlorine) is a measurement of both free and combined chlorine (such as chloramines). It is difficult to separate the contribution to toxicity of the FAC (free available chlorine) such as $HClO/ClO^-$ from that of the combined chlorine species. In addition, the relative amounts of the different chlorine species vary from test to test, depending on test duration, pH and other medium related effects such as ammonium level and others. For those studies where the percentage of FAC (free available chlorine) from TRC (total residual chlorine) was measured, the toxicity endpoints were expressed also as FAC/L. In the tests with chlorinated seawater, test-item concentrations were expressed as TRO (total residual oxidant) or CPO (chlorine produced oxidants), which include, in addition to free and combined chlorine, also other oxidative species, such as bromine species.

Aquatic compartment

Acute toxicity studies were submitted for three aquatic trophic levels. Acute toxicity studies are available in freshwater and seawater fish and invertebrates, freshwater algae, microorganisms. In short term tests, fish, invertebrates and algae show a similar sensitivity: 48h LC_{50} = 32 μg TRO/L, 48h EC_{50} = 35 μg active Cl/L and ErC_{50} = 36.5 μg available chlorine/L, respectively.
For molluscs and fish, long-term toxicity studies have also been performed. Molluscs (15d NOEC = 7 μg TRO/L) were shown to be more sensitive than fish fry (28d NOEC (fry survival) = 40 μg CPO/L). A multispecies microcosm study performed in a periphytic community was submitted too and the endpoint considered for the risk assessment is the 7d NOEC (toxicity to algae) = 2.1 μg FAC/L.
NOEC values were defined for each trophic level: fish, invertebrates (molluscs) and algae. From the available NOEC dataset, the lowest endpoint is derived from algae with a NOEC = 2.1 μg FAC/L, which was selected as reference value for the risk assessment.
For the deduction of the aquatic PNEC an Assessment Factor (AF) of 50 is used. This is justified because, according to the TGD on Risk Assessment, an AF of 50 can be used when two long-term NOECs from fresh- or saltwater species representing two trophic levels and one long-term NOEC from an additional marine taxonomic group (molluscs) are available.
After WGII2016 an Ad hoc follow-up was launched: comments from FR, NL and DE were received. NL pointed out that differences in water characteristics will influence the chemical equilibria. The presence of bromide in seawater will lead to a shift towards bromine species instead of chlorine, and HBrO will be formed. It is noted that in the EU RAR on hypochlorite, the datasets for freshwater and marine species have been kept separately, but in the CAR for fish a comparison between freshwater and marine tests is not possible due to lack of reliable data. For now, the lack of data makes a proper comparison of data impossible. Therefore it is considered appropriate to keep the AF of 50 as proposed by the eCA. If, at product authorisation additional information is provided it could become possible to lower the assessment factor.
In addition comments from the applicant were received. The applicant still holds the opinion that an AF of 10 is justified since a complete data set for acute and chronic effects covering species from three trophic levels are available. The acute as well as the chronic data demonstrate that there is no species sensitivity against the active substances. According to the BPR guidance (Guidance on the BPR: Volume IV, Part B; Version 1.0 April 2015) "pooling of available marine and freshwater ecotoxicity data for derivation of the freshwater PNEC is possible as long as the species sensitivity between freshwater and marine organisms is within a factor of 10". This requirement is fulfilled and data on freshwater or marine fish, crustacea and algae can be used interchangeably for evaluation of the risks to either compartment.

$PNEC_{aquatic}$ = 2.1 μg FAC/L : 50 = **0.042 μg FAC/L**

Sediment

The **$PNEC_{sediment}$** was calculated to be **0.045 μg FAC/kg ww** on the basis of the $PNEC_{aquatic}$, using the equilibrium partitioning method according to the TGD.

Microbial activity in STP

The lowest available EC_{50} and NOEC value for micro-organisms in the activated sludge is 77.1 mg available chlorine/L and 41.1 mg available chlorine/L, respectively. The WGII2016 agreed that the $PNEC_{STP}$ should be derived in accordance to previous agreements (TAB entry ENV-4) and that an AF 10 to the NOEC (or EC_{10}) should be applied. An assessment factor of 10 was applied to the NOEC value (lowest available endpoint), resulting in a **$PNEC_{STP}$** of **4.11 mg available chlorine/L**. The fate of HClO and ClO^- in the environment, in the sewer and during sewage treatment is modelled by Vandepitte and Schowanek and is estimated to drop down to "zero" within a few minutes after release into the sewer.

Atmosphere

At environmental pH values (6.5-8.5) half of the active chlorine is in the un-dissociated form of hypochlorous acid and half is dissociated to the hypochlorite anion. Only the hypochlorous acid fraction is volatile. The measured Henry's Law constant for hypochlorous acid of 0.11 Pa m^3 mol^{-1} indicates that concentration in air is very low. Consequently, air is not an environmental compartment of concern.

Terrestrial compartment

The risk assessment for the terrestrial compartment was performed on the basis of the $PNEC_{aquatic}$ using the equilibrium partitioning method. The **$PNEC_{soil}$** was calculated to be **0.015 µg FAC/kg ww** on the basis of the $PNEC_{aquatic}$, using the equilibrium partitioning method according to the TGD. At the WGII2016 it was agreed that in accordance with the BPR guidance (Guidance on the BPR: Volume IV, Part A; Version 1.1 November 2014) toxicity tests on terrestrial organisms are not required for the uses assessed in the active substance dossier since there is no direct exposure to soil.
Soil is only being exposed to hypochlorite via the STP pathway by the application of sewage sludge or by the application of slurry/manure from PT3 uses. The active chlorine is highly reactive and reacts rapidly with organic matter in the sewer systems, STP and also during storage of slurry/manure. The fast degradation in these systems results in PEC_{soil} values which are very low indicating that the emission to soil can be regarded to be negligible (see Doc IIB).
However, it was decided at the WGII2016 meeting that PEC/PNEC values for the soil compartment should be provided in the CAR and the $PNEC_{soil}$ value should be calculated by using the equilibrium partitioning method (EPM) based on the $PNEC_{aquat\ c}$ value according to the Guidance on the BPR (Volume IV, Part B; Version 1.0 April 2015). The calculation is based on a theoretical Koc value of 13.22 L/kg. The $PNEC_{soil}$ for the risk assessment for the terrestrial compartment was calculated to be 0.015 µg FAC/kg ww.
The WGII2016 acknowledged that the use of a theoretical Koc value is not the most appropriate value for inorganic substances for the equilibrium partitioning calculation since for inorganic substances Kd values would be more appropriate.
Nevertheless, for the assessed uses it is justified to use the theoretical Koc values for the calculation of the $PNEC_{soil}$ value since there is no direct release to soil and there is a high degradation rate of the substance in the preceding compartments (e.g. sewer system, STP) which results in a very low emission to soil. Furthermore, measured Kd values are not available and by considering the low PEC_{soil} values further data would not have an impact on the general outcome of the environmental exposure and risk assessment.

2.2.2.2. Exposure assessment and risk characterisation

Emission and exposure resulting from all stages of the life-cycle of active chlorine released from chlorine have to be assessed in the exposure and risk assessments. The calculated PEC values, according to the ESD PT2, are reported in the tables below.

Aquatic compartment (incl. sediment)

Surface water

In Doc. IIA, Chapter 4, a PNEC of 0.042 µg/L (i.e. 42 x 10^{-5} mg/L) was derived from a long-term toxicity study in algae (most sensitive species). The risk assessment for surface water was calculated on the basis of this PNEC and the product type specific PEC for surface water as calculated in the exposure assessment (see Doc. IIB, Chapter 3.3.3.2).
An overview on the results of the aquatic risk assessment for active chlorine released from chlorine is provided in Table 2.2.2.2-01 and Table 2.2.2.2-02.

Table 2.2.2.2-01: Overview on the calculated PEC/PNEC for the aquatic compartment not taking into account degradation in sewer system

Exposure scenario	$PNEC_{sw}$ = 4.2 x 10^{-5} mg/L	
	PEC_{sw} [mg/L]	$PEC/PNEC_{sw}$
PT2		
PT2a - Disinfection of sewage/ waste water in the primary settler of the STP (pre-chlorination)	9.97 x 10^{-40}	2.37 x 10^{-35}
PT2b - Disinfection of sewage/ waste water in the effluent stream of the STP (post-chlorination)	2.76	**65696**
PT2c - Disinfection of public swimming pools - acute situation (shock disinfection) - chronic situation	 0.249 3.78 x 10^{-04}	 **5940** **9.0**

n.a. = not applicable

The above results show that for three relevant application of active chlorine released from chlorine in PT2, the requirements for acceptable risk according to the TGD on Risk Assessment are not met when no degradation in sewer system has been considered for PT2b (post-chlorination), PT2c (Disinfection of public swimming pools – acute situation) and PT2c (Disinfection of public swimming pools – chronic situation).

Table 2.2.2.2-02: Overview on the calculated PEC/PNEC for the aquatic compartment considering degradation in sewer system

Exposure scenario	$PNEC_{sw}$ = 4.2 x 10^{-5} mg/L	
	PEC_{sw} [mg/L]	$PEC/PNEC_{sw}$
PT2		
PT2a - Disinfection of sewage/ waste water in the primary settler of the STP (pre-chlorination)	n.a.	n.a.
PT2b - Disinfection of sewage/ waste water in the effluent stream of the STP (post-chlorination)	n.a.	n.a.
PT2c - Disinfection of public swimming pools		
- acute situation (shock disinfection)	1.11 x 10^{-20}	2.64 x 10^{-16}
- chronic situation	1.68 x 10^{-23}	4.00 x 10^{-19}

n.a. = not applicable

The above results show that, for relevant applications of active chlorine released from chlorine in PT2a and PT2c, the requirements for acceptable risk according to the TGD on Risk Assessment are met when the degradation in sewer system has been considered: the PEC/PNEC values are below the trigger value of 1. Since for PT2b (Disinfection of sewage/waste water in the effluent stream of the STP (post-chlorination)) no degradation in the sewer system can be taken into account, the unacceptable risk for the surface water persists. In the PEC calculation the DT_{50} value for surface water of 56 min was used for the residence time of 30 min (see Doc. IIB). This is a worst case approach since normally the residence time is more than 30 min, technical systems (e.g. labyrinths and longer release pipe) should exist which allow a longer residence time or a faster reduction of the active substance in the effluent of the STP. Furthermore, this disinfection process is only required if a high load with e.g. *E. coli* occurs. Therefore, it could be expected that organic material is still available which would result in a lower DT_{50} value than 56 min. At the product authorisation phase adequate risk mitigation methods should be provided to demonstrate a safe use.

Freshwater sediment

In Doc. IIA, Chapter 4, a PNEC of 0.045 µg/kg wwt (i.e. 4.5 x 10^{-5} mg/kg wwt) for freshwater sediment was derived on the basis of the $PNEC_{aquat\ c}$, using the equilibrium partitioning method according to the TGD.
The risk assessment for freshwater sediment was based on this PNEC and the product type specific PEC for sediment as calculated in the exposure assessment (see Doc. IIB, Chapter

3.3.3.2).
Since both PEC and PNEC were calculated using the equilibrium partitioning method as described in the TGD, the PEC/PNEC in sediment is equal to the PEC/PNEC in surface water.
An overview on the results of the freshwater sediment risk assessment for active chlorine released from chlorine is provided in Table 2.2.2.2-03 and Table 2.2.2.2-04.

Table 2.2.2.2-03: Overview on the calculated PEC/PNEC for the sediment compartment not taking into account degradation in sewer system

Exposure scenario	**$PNEC_{sed}$ = 4.5 x 10^{-5} mg/kg**	
	PEC_{sed} [mg/kg]	**$PEC/PNEC_{sed}$**
PT2		
PT2a - Disinfection of sewage/ waste water in the primary settler of the STP (pre-chlorination)	1.1 x 10^{-39}	2.4 x 10^{-35}
PT2b - Disinfection of sewage/ waste water in the effluent stream of the STP (post-chlorination)	2.95	**65581**
PT2c - Disinfection of public swimming pools - acute situation (shock disinfection) - chronic situation	 0.27 4.04 x 10^{-04}	 **5930** **9.0**

n.a. = not applicable

The above results show that for three relevant application of active chlorine released from chlorine in PT2, the requirements for acceptable risk according to the TGD on Risk Assessment are not met when no degradation in sewer system has been considered for PT2b (post-chlorination), PT2c (Disinfection of public swimming pools – acute situation) and PT2c (Disinfection of public swimming pools – chronic situation).

Table 2.2.2.2-04: Overview on the calculated PEC/PNEC for the aquatic compartment considering degradation in sewer system

Exposure scenario	**$PNEC_{sed}$ = 4.5 x 10^{-5} mg/kg**	
	PEC_{sed}[mg/kg]	**$PEC/PNEC_{sed}$**
PT2		
PT2a - Disinfection of sewage/ waste water in the primary settler of the STP (pre-chlorination)	n.a.	n.a.
PT2b - Disinfection of sewage/ waste water in the effluent stream of the STP (post-chlorination)	n.a.	n.a.
PT2c - Disinfection of public swimming pools - acute situation (shock disinfection) - chronic situation	 1.19 x 10^{-20} 1.80 x 10^{-23}	 2.64 x 10^{-16} 4.00 x 10^{-19}

n.a. = not applicable

The above results show that for all relevant applications of active chlorine released from chlorine in PT2 the requirements for acceptable risk according to the TGD on Risk Assessment are met when the degradation in sewer system has been considered: the PEC/PNEC values are below the trigger value of 1. Since for PT2b (Disinfection of sewage/ waste water in the effluent stream of the STP (post-chlorination)) no degradation in the sewer system can be taken into account, the unacceptable risk for the sediment persists. See argumentation provided in chapter 2.1.1 (surface water).

Sewage treatment plant

PEC for STP as calculated in the exposure assessment (see Doc. IIB, Chapter 3.3.3.1).
An overview on the results of the risk assessment for active chlorine released from chlorine in the STP is provided in Table 2.2.2.2-05 and Table 2.2.2.2-06.

Table 2.2.2.2-05: Overview on the calculated PEC/PNEC for sewage treatment plant (STP)

Exposure Scenario	$PNEC_{STP}$ = 4.11 mg/L	
	PEC_{STP} [mg/L]	$PEC/PNEC_{STP}$
PT2		
PT2a - Disinfection of sewage/ waste water in the primary settler of the STP (pre-chlorination)	9.97×10^{-39}	2.43×10^{-39}
PT2b - Disinfection of sewage/ waste water in the effluent stream of the STP (post-chlorination)	n.a.	n.a.
PT2c - Disinfection of public swimming pools: - acute situation (shock disinfection) - chronic situation	 2.49 3.78×10^{-3}	 0.61 9.20×10^{-4}

n.a. = not applicable

The above results show that for all relevant applications of active chlorine released from chlorine in PT2, the requirements for acceptable risk according to the TGD on Risk Assessment are met when no degradation in sewer system has been considered.

Table 2.2.2.2-06: Overview on the calculated PEC/PNEC for sewage treatment plant (STP) considering degradation in sewer system

Exposure Scenario	$PNEC_{STP}$ = 4.11 mg/L	
	PEC_{STP} [mg/L]	$PEC/PNEC_{STP}$
PT2		
PT2a - Disinfection of sewage/ waste water in the primary settler of the STP (pre-chlorination)	n.a.	n.a.
PT2b - Disinfection of sewage/ waste water in the effluent stream of the STP (post-chlorination)	n.a.	n.a.
PT2c - Disinfection of public swimming pools: - acute situation (shock disinfection) - chronic situation	 1.11×10^{-19} 1.68×10^{-22}	 2.70×10^{-20} 4.09×10^{-23}

n.a. = not applicable

The above results show that for all relevant applications of active chlorine released from chlorine in PT2 the requirements for acceptable risk according to the TGD on Risk Assessment are met when the degradation in sewer system has been considered: the PEC/PNEC values are below the trigger value of 1.

Atmosphere

Hypochlorite might enter the atmosphere due to volatilisation from the sewage treatment plant.
The exposure assessment showed that the emission to air via these pathways is negligible. The highest annual average PEC in air after use of active chlorine released from chlorine in PT2 was calculated to be 2.77×10^{-25} mg/m³ for PT2c – Disinfection of public swimming pools (acute situation).
In addition, it was outlined in Doc. IIA, chapter 4.1.2, that the adsorption of hypochlorite to aerosol particles, the volatilisation from water into air and the adsorption of hypochlorite onto soil are very low. Thus, hypochlorite will remain in the aqueous phase and degrade very rapidly.

Terrestrial compartment

In Doc. IIA, Chapter 4, a PNEC of 0.015 µg/kg wwt (i.e. 1.5×10^{-5} mg/kg wwt) in soil was derived on the basis of the $PNEC_{aquatic}$, using the equilibrium partitioning method according to the TGD.
The risk assessment for soil was based on this PNEC and the product type specific PEC for soil as calculated in the exposure assessment (see Doc. IIB, Chapter 3.3.3.4).
An overview on the results of the soil risk assessment for active chlorine released from chlorine

is provided in Table 2.2.2.2-07a.
Table 2.2.2.2-07a: Overview on the calculated PEC/PNEC for the soil compartment without considering degradation

Exposure scenario	$PNEC_{soil}$ = 1.5 x 10^{-5} mg/kg	
	PEC_{soil} [mg/kg]	$PEC/PNEC_{soil}$
PT2		
PT2a - Disinfection of sewage/ waste water in the primary settler of the STP (pre-chlorination)	1.28 x 10^{-44}	8.51 x 10^{-40}
PT2b - Disinfection of sewage/ waste water in the effluent stream of the STP (post-chlorination)	n.a.	n.a.
PT2c - Disinfection of public swimming pools:		
- acute situation (shock disinfection)	3.20 x 10^{-6}	0.21
- chronic situation	4.84 x 10^{-9}	3.23 x 10^{-4}

n.a. = not applicable

Table 2.2.2.2-07b: Overview on the calculated PEC/PNEC for the soil compartment taking into account degradation

Exposure scenario	$PNEC_{soil}$ = 1.5 x 10^{-5} mg/kg	
	PEC_{soil} [mg/kg]	$PEC/PNEC_{soil}$
PT2		
PT2a - Disinfection of sewage/ waste water in the primary settler of the STP (pre-chlorination)	n.a.	n.a.
PT2b - Disinfection of sewage/ waste water in the effluent stream of the STP (post-chlorination)	n.a.	n.a.
PT2c - Disinfection of public swimming pools:		
- acute situation (shock disinfection)	1.42 x 10^{-25}	9.47 x 10^{-21}
- chronic situation	2.15 x 10^{-28}	1.44 x 10^{-23}

n.a. = not applicable

The above results show that for all relevant applications of active chlorine released from chlorine in PT2 the requirements for acceptable risk are met according to the TGD on Risk Assessment: the PEC/PNEC values are below the trigger value of 1.

Groundwater

The active chlorine concentration in the pore water of agricultural soil (after application of sewage sludge to agricultural land) is taken as an indication of potential groundwater levels. According to the TGD, this is a worst-case assumption, because degradation in soil, transformation and dilution in deeper soil layers are not taken into account. Under real life conditions, it is very unlikely that any hypochlorite will reach the groundwater because active chlorine rapidly degrades in sewage sludge and soil.
An overview on the results of the groundwater risk assessment for active chlorine is provided in Tables 2.2.2.2.-08a and 2.2.2.2-08b.

Table 2.2.2.2-08a: Overview on the calculated PEC/Limit value for groundwater not taking degradation into account

Exposure scenario	Limit value= 0.1 µg/L	
	PEC_{gw} [µg/L]	PEC/Limit value
PT2		
PT2a - Disinfection of sewage/ waste water in the primary settler of the STP (pre-chlorination)	<< 0.1	<< 1
PT2b - Disinfection of sewage/ waste water in the effluent stream of the STP (post-chlorination)	n.a.	n.a.

Exposure scenario	Limit value= 0.1 µg/L	
	PEC_{gw} [µg/L]	PEC/Limit value
PT2e - Disinfection of public swimming pools:		
- acute situation (shock disinfection)	3.9×10^{-3}	0.039
- chronic situation	5.9×10^{-6}	5.9×10^{-5}

Table 2.2.2.2-08b: Overview on the calculated PEC/Limit value for groundwater taking degradation into account

Exposure scenario	Limit value= 0.1 µg/L	
	PEC_{gw} [µg/L]	PEC/Limit value
PT2		
PT2a - Disinfection of sewage/ waste water in the primary settler of the STP (pre-chlorination)	n.a.	n.a.
PT2b - Disinfection of sewage/ waste water in the effluent stream of the STP (post-chlorination)	n.a.	n.a.
PT2e - Disinfection of public swimming pools:		
- acute situation (shock disinfection)	<< 0.1	<< 1
- chronic situation	<< 0.1	<< 1

The above results show that for all relevant applications of active chlorine in PT2 the requirements for acceptable risk are met according to the TGD on Risk Assessment: all PEC/Limit values are below the trigger value of 1.

Assessment of disinfection-by-products

Due to the absence of guidance on disinfectant by-products (DBPs) an assessment of DBPs is not possible. The draft guidance on DBPs is only for swimming pool scenarios in PT2. Finally, the working group (BPC TOX-WGII-2016 meeting) concluded that the assessment will be done at product authorisation.

Aggregate risk assessment

Biocidal active substances are used in various applications and are often contained in many different products. The exposure assessment of single uses may therefore underestimate the actual concentrations of the active substance to be found in the environment.
Article 19(2) of the new Biocidal Products Regulation (BPR, 528/2012 EU) states that "the evaluation [...] shall take into account the following factors: [...] (d) cumulative effects, (e) synergistic effects." This is further elaborated in Annex VI (common principles for the evaluation of biocidal products) which states that the risks associated with the relevant individual components of the biocidal product shall be assessed, taking into account any cumulative and synergistic effects.
This refers to the environmental risk assessment of an active substance contained in different products of the same Product Type (PT) or of different PTs. Sodium hypochlorite, calcium hypochlorite and chlorine were notified as active chlorine releasers in PTs 1 to 5, in PTs 2 to 5, and in PTs 2 and 5, respectively. The main entry pathways into the environment are equal for all applications mentioned above (via STP), thus a combination of exposures to active chlorine released from sodium hypochlorite, active chlorine released from calcium hypochlorite and active chlorine released from chlorine for all affected environmental compartments is both possible and realistic.

Aggregate risk assessment for surface water considering all PTs

	Σ PEC/PNEC sw [mg/L]
PT 1	1.3×10^{-18}
PT 2	2.3×10^{-15}
PT 3	2.3×10^{-17}
PT 4	1.9×10^{-17}
PT 5	2.0×10^{-17}
Σ PEC/PNEC$_{sw}$ PT 2, 5 = 2.4 10^{-15} mg/L	

Aggregate risk assessment for sediment considering all PTs

	Σ PEC/PNEC sed [mg/kg]
PT 1	1.3×10^{-18}
PT 2	2.3×10^{-15}
PT 3	2.3×10^{-17}
PT 4	1.9×10^{-17}
PT 5	2.0×10^{-17}
Σ PEC/PNEC$_{sed}$ PT 2, 5 = 2.4 10^{-15} mg/kg	

Aggregate risk assessment for STP considering all PTs

	Σ PEC/PNEC STP [mg/L]
PT 1	1.3×10^{-22}
PT 2	2.4×10^{-19}
PT 3	2.3×10^{-21}
PT 4	1.9×10^{-21}
PT 5	2.0×10^{-21}
Σ PEC/PNEC$_{STP}$ PT 2, 5 = 2.5 10^{-19} mg/L	

Aggregate risk assessment for soil considering all PTs

	Σ PEC/PNEC soil [mg/kg]
PT 1	4.6×10^{-23}
PT 2	8.4×10^{-20}
PT 3	8.1×10^{-22}
PT 4	6.7×10^{-22}
PT 5	7.2×10^{-22}
Σ PEC/PNEC$_{soil}$ PT 2, 5 = 8.6 10^{-20} mg/kg	

Aggregate risk assessment for STP considering all PTs

	Σ PEC/PNEC STP [mg/L]
PT 1	7.1×10^{-23}
PT 2	5.8×10^{-19}
PT 3	7.2×10^{-21}
PT 4	2.5×10^{-21}
PT 5	2.0×10^{-21}
Σ PEC/PNEC$_{STP}$ PT 1-5 = 5.9 10^{-19} mg/L	

Aggregate risk assessment for soil considering all PTs

	Σ PEC/PNEC soil [mg/kg]
PT 1	4.6×10^{-23}
PT 2	2.0×10^{-19}
PT 3	1.1×10^{-21}
PT 4	6.7×10^{-22}
PT 5	7.2×10^{-22}
Σ PEC/PNEC$_{soil}$ PT 1-5 = 2.0 10^{-19} mg/kg	

The aggregate risk assessment is acceptable for all PTs in all environmental compartments.

2.2.2.3. Fate and distribution in the environment

Release and environmental degradation - Chlorine releases to the environmental compartments (atmosphere and water) are of natural and anthropogenic origin.
In the atmosphere, molecular chlorine is converted to atomic chlorine by photolysis during daylight. In the atmosphere, chlorine degrades during daylight, with a half-life of 2-4 hours. Chlorine is removed from the atmosphere by wet and dry deposition processes and washout by rain.
In water, at environmentally-relevant pH values, chlorine is converted to hypochlorous acid and hypochlorite anion. The fate of HClO and ClO^- in the environment, in the sewer and during sewage treatment is calculated to be "zero" after the first minutes in the sewer (see below). No chlorine gas will be released from aqueous emissions, as the pH of the waste stream is regulated to ensure that all chlorine is converted to hypochlorite.

Distribution - The adsorption of chlorine to aerosol particles, the volatilisation from water into air and the adsorption of chlorine onto soil are very low. Thus, chlorine (as hypochlorite/hypochlorous acid) remains in the aqueous phase, where it degrades very rapidly to chloride.
Accumulation - Chlorine does not bioaccumulate or bioconcentrate due to its high water solubility and high reactivity.
The concentration of hypochlorite in the environment is modelled by Vandepitte and Schowanek and is estimated to drop down to "zero" within the first minutes after release in the sewer.

The fate and behaviour of active chlorine (as hypochlorite/hypochlorous acid) in the environment is described in detail in Doc. IIA, 4.1. Active chlorine is highly reactive: it reacts rapidly with organic matter in the sewer, STP, surface water and soil. Where organic and nitrogenous materials are present, it acts as a highly reactive oxidizing agent. It reacts rapidly with organic matter and most (≈ 99%) of the active chlorine is converted to inorganic chloride (Jolley and Carpenter, 1975).
Hypochlorite anion is very strong oxidizing agent. Rapid decomposition of hypochlorite in contact with organic matter (in sewage or in activated sludge) is described for example in study: Vandepitte V. and Schowanek D. Oxidation is probably the predominant chemical reaction occurring in chlorine's disinfection processes. Furthermore, circumstances influencing the reactivity of hypochlorite are time, temperature, pH and the availability of amount and type of organic matter. The content of organic matter in soil is lower than in sewage or activated sludge, but it is enough high to ensure complete decomposition in relative short time. The Vandepit and Schowanek kinetic model is also applicable to the soil (TMI 12). Contamination of soils due to direct application of chlorinated water will not be of permanent origin. The high content of organic matter in a soil will allow a quick (order of seconds) reduction of HClO, too. Hypochlorite reacts rapidly in soil with soil organics. The ultimate fate in soil is a reduction to chloride.
The kinetic model of Vandepitte and Schowanek (Doc. IIIA, Section A7.1.2) shows that hypochlorite is eliminated during transport in the sewer within the first minutes. The abundance of reaction partners allows a very quick reaction. The $HClO/ClO^-$ (expressed as FAC) concentration estimated at the end of the sewer, drops below 1×10^{-32} µg/L. The drop in FAC is parallel to a sharp increase of the chloramine concentration, which can be explained by the high availability of ammonia in the sewer. Chloramine further reacts like an oxidant during additional transport in the sewer, the STP and the river. The extensive degradation of chloramine in the activated sludge can be explained by the presence of reduced organic material. Chloramine is estimated to fall below 5×10^{-10} µg/L in the river.
At environmental pH values (6.5-8.5), half of the active chlorine is present in the undissociated form of hypochlorous acid and half is dissociated to the hypochlorite anion. Only the hypochlorous acid fraction is volatile, but the amount of hypochlorous acid that could volatilise from water into air is expected to be very low. The calculated half-life (Atkinson calculation) for hypochlorous acid in the atmosphere is 114.6 days (2750 hours), but there are indications that

the half-life is shorter, i.e. only a few hours (see Doc IIIA, section A7.3.2/02).

2.2.2.4. PBT and POP assessment

PBT assessment

P criterion: Half-life > 40 d in freshwater (> 60 d in marine water) or > 120 d in freshwater sediment (> 180 d in marine sediment) or > 120 d in soil.

Active chlorine reacts rapidly in soil and in the sewer with organic matter.
The photolysis half-life of aqueous chlorine in clear sky, summer noon sunlit (47°N) water of pH 8 is 12 min when measured at the surface. It increases with decreasing pH due to the decreasing ratio of ClO^-/HClO to 37 min at pH 7 and to 60 min at pH 5.
Therefore, the P criterion is not fulfilled.

B criterion: measured BCF >2000. If measured BCF values are not available, a substance is considered to potentially fulfil the B criterion if log K_{ow} exceeds a value of 4.5.

Active chlorine is inorganic (Kow is not required) and degrades rapidly in the environment, so no bioaccumulation is expected. Therefore, the B criterion is not fulfilled.

T criterion: Long term NOEC or EC_{10} < 0.01 mg/L for marine or freshwater organisms or CMR, or other evidence of chronic toxicity.

As regards the human health, active chlorine is not CMR. There is no evidence for chronic toxicity, either.
Regarding the toxicity to aquatic organisms, algae is the most sensitive species (periphytic community) for which a NOEC of 0.0021 mg FAC/L has been derived from a microcosm study.
Therefore, the T criterion is fulfilled.

Conclusion for the risk characterisation: active chlorine does not meet the PBT criteria.

POP assessment

Not applicable to inorganic substances, such as active chlorine released from chlorine.

2.2.3 Assessment of endocrine disruptor properties

Based on the available experimental results (read-across from active chlorine released from sodium hypochlorite), there is no indication that active chlorine released from chlorine affects the endocrine system. Structural characteristics and SAR do not hint to possible effects of active chlorine released from chlorine as endocrine disruptor.

2.3 Overall conclusions

The outcome of the assessment for active chlorine released from chlorine in product-type 2 is specified in the BPC opinion following discussions at the BPC-18 meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA website.

2.4 Requirement for further information related to the reference biocidal product

At product authorization, physical-chemical data (e.g., density, acidity) on the specific chlorine product to be authorized are necessary. In particular, a long-term storage stability study needs to be provided in support of the shelf-life claim. Also the effect of temperature, the effect of light, the effect of humidity and the reactivity towards the container material need to be addressed.

2.5 List of endpoints

The most important endpoints, as identified during the evaluation process, are listed in Appendix I.

Appendix I: List of endpoints

Chapter 1: Identity, Physical and Chemical Properties, Classification and Labelling

Active substance (ISO Name)	Active chlorine released from chlorine When added to water upon use, chlorine releases active chlorine, which consists of chlorine (Cl_2), hypochlorous acid (HClO) and hypochlorite anion (ClO^-) in equilibrium. The predominant species will depend on pH value (chlorine is available only at pH < 4, hypochlorous acid is predominant in the range 4 to 5.5, whereas only hypochlorite anion is present at pH >10)
Product-type	2

Identity of the releaser, i.e. chlorine

Chemical name (IUPAC)	Chlorine
Chemical name (CA)	Chlorine
CAS No	7782-50-5
EC No	231-959-5
Other substance No.	017-001-00-7 (Index number)
Minimum purity of the active substance as manufactured (g/kg or g/l)	995 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	None
Molecular formula	Cl2
Molecular mass	70.906 g/mol
Structural formula	Cl — Cl

Physical and chemical properties of the releaser, i.e. chlorine

Freezing point (state purity)	-101.03 °C at ambient pressure
Boiling point (state purity)	-34.03 °C at ambient pressure
Thermal stability / Temperature of decomposition	Chlorine is known to be stable at room temperature and ambient pressure. Thermal dissociation into chlorine atoms occurs only at elevated temperatures (at 1000 K the degree of atomization is reported to be 0.019%)
Appearance (state purity)	Greenish-yellow gas at room temperature and ambient pressure, with a characteristic stringent odour

Relative density (state purity)	3.169 g/dm^3 at 0 °C and 1 atm 1.411 kg/dm^3 at 20 °C for compressed liquid chlorine (pressure: 10 kg/cm^2)
Surface tension (state temperature and concentration of the test solution)	18.2 mN/m at 20 °C (calculated for liquid chlorine)
Vapour pressure (in Pa, state temperature)	6.780 x 10^5 Pa at 20 °C (estimation) 7.788 x 10^5 Pa at 25 °C (estimation)
Henry's law constant (Pa m^3 mol $^{-1}$)	6.5 x 10^3 Pa m^3 mol^{-1} at 20 °C (calculated) For the purpose of risk assessment only, a HLC of 0.11 Pa m^3 mol^{-1} at 20 °C is considered for hypochlorous acid, which is the only volatile chlorine species present at the equilibrium at in-use pH values under PT2
Solubility in water (g/l or mg/l, state temperature)	9.78 g/l (at 10 °C) 7.41 g/l (at 20 °C) 5.91 g/l (at 30 °C)
Solubility in organic solvents (in g/l or mg/l, state temperature)	Tetrachloromethane: 159 g/kg (at 10 °C) 114 g/kg (at 20 °C) 91 g/kg (at 30 °C) Benzene: 290 g/kg (at 10 °C) 218 g/kg (at 20 °C) 157 g/kg (at 30 °C) Acetic acid: 121 g/kg (at 15 °C)
Stability in organic solvents used in biocidal products including relevant breakdown products	Not relevant. Chlorine is not used in organic solvents
Partition coefficient (log P_{OW}) (state temperature)	Not required for inorganic substances
Dissociation constant	In water, chlorine hydrolyses: $Cl_2 + H_2O \leftrightarrow HClO + H^+Cl^-$ $K_{hydrolysis}(Cl_2)$ = 3.2 x 10^{-4} mol/dm^3 at 20°C Further, the hypochlorous acid (HClO) partially dissociates: $HClO + H_2O \leftrightarrow ClO^- + H_3O^+$ $K_a(HClO)$ = 3.5 x 10^{-8} mol/dm^3 at 20°C
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	ε_o^{max} = 70 at 333 nm (estimated at 0 K)
Flammability or flash point	Chlorine is known to be a non-flammable gas Flash-point: not applicable to gases
Explosive properties	Not applicable to gases

Oxidising properties	New test on oxidising gases according to the UN Recommendation on the Transport of Dangerous Goods, Manual of Tests and Criteria needs to be provided, at the latest six months before the date of approval
Auto-ignition or relative self ignition temperature	Auto-ignition temperature: testing is not required for gases having no flammable range

Classification and proposed labelling of the releaser, i.e. chlorine

	Harmonized classification of chlorine according to Annex VI, Table 3.1 of Regulation (EC) 1272/2008 (CLP) with ATP01corr
with regard to physical hazards	Danger GHS03, GHS04 H270: May cause or intensify fire; oxidiser
with regard to human health hazards	Danger GHS06 H331: Toxic if inhaled H319: Causes serious eye irritation H335: May cause respiratory irritation H315: Causes skin irritation
with regard to environmental hazards	GHS09 H400: Very toxic to aquatic life
	M factor=100

Chapter 2: Methods of Analysis

Analytical methods for the active substance and the releaser, i.e. chlorine

Active substance and releaser (principle of method)	Active chlorine (a.s.): Iodometric titration LOQ = 0.5% w/w as sodium hypochlorite (corresponding to 0.48% w/w as active chlorine) Chlorine (releaser): ISO 2120, 1972, Liquid chlorine for industrial use - Determination of the content of chlorine by volume in the vaporized product
Impurities in the releaser (principle of method)	ISO 2120 for residual non-condensable gases
	Molecular absorption spectrometry
	Titration method
	Cold vapour atomic absorption spectrometry
	Gravimetric method

Analytical methods for residues

Soil (principle of method and LOQ)	Not required. Active chlorine ($HClO/ClO^-$) reacts rapidly with organic matter
Air (principle of method and LOQ)	Determination of gaseous chlorine in workplace air (in the range 0.3-7.0 mg chlorine/m^3) by: - sampling in sulphamic acid solution and trapping of chlorine as chloramines; - spectrometric determination of the chloramines as tri-iodide at 288 nm (a) or with DPD reagent at 510 nm (b) a) OSHA Method «Chlorine in Work place Atmosphere» 05.01.83; Smith & Cochran Spectrophotometric determination of Free Chlorine in Air using Sulphamic acid/Tri-iodide procedure - Anal Chem 1986 Vol 58 pp 1591-1592 b) OSHA Method «Chlorine in Work place Atmosphere» 05.01.83; NIOSH free chlorine in air 01.01.75; ISO 7392/2 Water quality – Determination of free and total chlorine Part 2 Colorimetric method using DPD for routine control purposes 15.10.85
Water (principle of method and LOQ)	Drinking water: fully-validated analytical methods need to be provided for monitoring purposes for both the active chlorine ($HClO/ClO^-$) and the relevant metabolite chlorate (ClO_3^-), at the latest six months before the date of approval Surface water: Not required. Active chlorine ($HClO/ClO^-$) reacts rapidly with organic matter

Body fluids and tissues (principle of method and LOQ)	Not required. Active chlorine ($HClO/ClO^-$) reacts rapidly with organic matter In case of accidental release of gaseous chlorine, analytical methods available for the monitoring of chlorine in workplace air are meaningful for monitoring human exposure (see "Air" above).
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Not required under PT2
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required under PT2

Chapter 3: Impact on Human Health

In water, chlorine forms hypochlorous acid (HClO), which is in equilibrium with the hypochlorite ion (ClO^-) characterised by its well-known irritating/corrosive effects, and chlorine (Cl_2). In biological systems, characterised by pH values in the range 6-8, the most abundant species is HClO. At alkaline pH values, ClO^- is predominant, whilst Cl_2 is the main species only below pH 4.
Since in aqueous solutions, sodium hypochlorite (NaOCl) and chlorine share the same anion (ClO^-) and, thus, release the very same active substance (i.e. active chlorine, thought to consist of hypochlorite, hypochlorous acid and chlorine in equilibrium), read-across is possible for all the toxicological end-points.

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	BPC TOX-WGIII-2016 agreed that human health effects are primarily due to the local mode of action of chlorine gas (and related chlorine species) and potential systemic effects are secondary to its direct irritating reactivity. Moreover, chorine is a gas, and thus not available for oral absorption Consequently, oral absorption of chlorine is not relevant
Rate and extent of dermal absorption*:	BPC TOX-WGIII-2016 agreed that human health effects are primarily due to the local mode of action of chlorine gas (and related chlorine species) and potential systemic effects are secondary to its direct irritating reactivity. Moreover, chorine is a gas, and thus not available for dermal absorption Consequently, dermal absorption of chlorine is not relevant
Distribution:	BPC TOX-WGIII-2016 agreed that human health effects are primarily due to the local mode of action of chlorine gas (and related chlorine species) and potential systemic effects are secondary to its direct irritating reactivity In water, different chlorine species are available. The final metabolite in physiological systems is most likely the chloride ion, which is a physiologically essential metabolite
Potential for accumulation:	BPC TOX-WGIII-2016 agreed that human health effects are primarily due to the local mode of action of chlorine gas (and related chlorine species) and potential systemic effects are secondary to its direct irritating reactivity Due to the high reactivity of chlorine species, no potential for accumulation is expected

Rate and extent of excretion:	After exposure towards [^{36}Cl]-hypochlorous acid, no radioactivity was detected in expired air throughout the 96 h study Excretion mainly through urine as chloride (36.43% + 5.67 of the administered dose after 96 h) Excretion through faeces 96 h after exposure (14.8% + 3.7 of the administered dose after 96 h) The total recovery was slightly higher than 50% The final metabolites in physiological systems are chloride ions, which are physiologically essential metabolites
Toxicologically significant metabolite(s)	None

* the dermal absorption value is applicable for the active substance and might not be usable in product authorization

Acute toxicity

Rat LD_{50} oral	Read-across to sodium hypochlorite: LD_{50}>2000 mg avCl/kg bw No classification for acute toxicity (oral) warranted
Rat LD_{50} dermal	Read-across to sodium hypochlorite: LD_{50}>2000 mg avCl/kg bw No classification for acute toxicity (dermal) warranted
Rat LC_{50} inhalation	$LC_{50(1h)}$=1321 mg/m³ (448 ppmV based on a mole volume of 24.055 L/mol at 20°C) Regulation (EC) 1272/2008 (CLP) requires conversion of existing inhalation toxicity data which have been generated using a 1-hour testing exposure to 4-hour exposures. As chlorine exerts only local effects at the side of first contact, such conversion is not considered necessary Based on this study, chlorine warrants classification as Acute Tox. (inhal.) 2, H330, even if no time extrapolation is performed Harmonised classification according to Annex VI, Regulation (EC) 1272/2008: Acute Tox. (inhal.) 3, H331

Skin corrosion/irritation	No studies are available for chlorine; Read-across to sodium hypochlorite: With sodium hypochlorite solutions ≥5% avCl skin irritating properties were shown Harmonised classification according to Annex VI, Regulation (EC) 1272/2008: Skin Irrit. 2, H315

Eye irritation	No studies are available for chlorine; Read-across to sodium hypochlorite: With sodium hypochlorite solutions ≥5% avCl, eye irritation properties were shown Harmonised classification according to Annex VI, Regulation (EC) 1272/2008: Eye irrit. 2, H319
Respiratory tract irritation	Harmonised classification according to Annex VI, Regulation (EC) 1272/2008: STOT SE 3, H335
Skin sensitisation (test method used and result)	No sensitisation studies are available for chlorine; Read-across to sodium hypochlorite: Three skin sensitisation studies in guinea pigs (Buehler test) with sodium hypochlorite showed no sensitising properties No classification for skin sensitisation warranted
Respiratory sensitisation (test method used and result)	As there are no indications for skin sensitising potential of chlorine, no potential for respiratory sensitisation is expected

Repeated dose toxicity

Short term

Species / target / critical effect	Rats (oral, inhalation)/local irritation at site of first contact, no systemic effects
Relevant oral NOAEC / LOAEC	No oral repeated dose studies are available for chlorine; Read-across to sodium hypochlorite: LOAEC: not detected NOAEC: >7500 ppm avCl
Relevant dermal NOAEC / LOAEC	No dermal repeated dose studies are available for chlorine Human data is available for sodium hypochlorite (see below)
Relevant inhalation NOAEC / LOAEC	LOAEC: 3.0 ppm equivalent to 9.0 mg/m^3 NOAEC: 1.0 ppm equivalent to 3.0 mg/m^3

Subchronic

Species/ target / critical effect	Rats, mice and monkeys (oral, inhalation)/local irritation at site of first contact, no systemic effects
Relevant oral NOAEC / LOAEC	No oral repeated dose studies are available for chlorine; Read-across to sodium hypochlorite: LOAEC: 0.2% avCl NOAEC: between 0.02% avCl (highest dose tested) and 0.1% avCl
Relevant dermal NOAEC / LOAEC	No dermal repeated dose studies are available for chlorine Human data is available for sodium hypochlorite (see below)
Relevant inhalation NOAEC / LOAEC	LOAEC: 2.3 ppm avCl (6.9 mg/m³ avCl) NOAEC: 0.5 ppm avCl (1.5 mg/m³ avCl)

Long term

Species/ target / critical effect	Rats and mice (oral, inhalation)/local irritation at site of first contact, no systemic effects
Relevant oral NOAEC / LOAEC	No oral repeated dose studies are available for chlorine; Read-across to sodium hypochlorite: LOAEC: 0.2% avCl NOAEC: between 0.0275% avCl (highest dose tested) and 0.1% avCl
Relevant dermal NOAEC / LOAEC	No dermal repeated dose studies are available for chlorine Human data is available for sodium hypochlorite (see below)
Relevant inhalation NOAEC / LOAEC	LOAEC: 0.4 ppm avCl (1.2 mg/m³) NOAEC: <0.4 ppm avCl (<1.2 mg/m³)

Genotoxicity	No genotoxicity studies are available for chlorine; Read-across to sodium hypochlorite: Hypochlorite solutions show sporadic equivocal/positive results in *in vitro* assays (three Ames tests, cytogenetic assay in mammalian cells) which is due to the ability to generate reactive oxygen species and to induce DNA damage Standard *in vivo* studies (two micronucleus tests, bone marrow aberration assay, DNA damage in renal tissue) were negative. A

	non-standard germ cell assay was equivocal. The biological relevance of any result from an *in vivo* study is questionable in view of uncertainty of the availability of the test substance at the target organ Weight of evidence indicates no concern of mutagenic/genotoxic potential *in vivo*

Carcinogenicity

Species/type of tumour	Rat and mouse (oral, inhalation); there were no treatment related increases in non-neoplastic lesions or tumour incidence
Relevant NOAEC/LOAEC	Studies performed with chlorine (inhalation route): LOAEC: 0.4 ppm avCl (1.2 mg/m³) NOAEC: <0.4 ppm avCl (<1.2 mg/m³) Studies performed with sodium hypochlorite (oral route): LOAEC: 0.2% avCl NOAEC: between 0.0275% avCl (highest dose tested) and 0.1% avCl

Reproductive toxicity

Developmental toxicity

Species/ Developmental target / critical effect	No reproductive toxicity studies are available for chlorine Read-across to sodium hypochlorite: No indication of prenatal developmental toxicity, however test concentration too low
Relevant maternal NOAEC	NOAEC: >100 mg/L avCl
Relevant developmental NOAEC	NOAEC: ≥100 mg/L avCl

Fertility

Species/critical effect	No indication for influence on fertility, however test concentration too low
Relevant parental NOAEL	NOAEL: ≥5 mg/kg/bw/d
Relevant offspring NOAEL	NOAEL: ≥5 mg/kg/bw/d
Relevant fertility NOAEL	NOAEL: ≥5 mg/kg/bw/d

Neurotoxicity

Species/ target/critical effect	No neurotoxicity studies available; studies are waived due to lack of evidence of a neurotoxic effect from other acute, subacute, subchronic and chronic studies

Developmental Neurotoxicity

Species/ target/critical effect	No developmental neurotoxicity studies available; studies are waived as the structure of chlorine is not related to known neurotoxic substances

Immunotoxicity

Species/ target/critical effect	No immunotoxicity studies available

Developmental Immunotoxicity

Species/ target/critical effect	No developmental immunotoxicity studies available

Other toxicological studies

Read-across to sodium hypochlorite:

Tissue toxicity of sodium hypochlorite solutions in female guinea pigs after dermal exposure towards 0.1 or 0.5% sodium hypochlorite solution: 15% decrease in basal cell viabilities after 2 weeks of treatment at 0.5%, morphological changes in cells after 7 and 14 days of treatment at 0.5% and 14 days at 0.1%. It was concluded that a 0.1% solution of sodium hypochlorite could be used for long-term maintenance of the wound due to the relatively low toxicity

Whole body exposure of mice (except head) with aqueous solutions of hypochlorous acid (1, 10, 100, 300, 1000 ppm) and sodium hypochlorite (1000 ppm) for 10 minutes daily on 4 consecutive days: dose-related response to hypochlorous acid (pH 6.5) treatment, the minimally effective dose being 100 ppm, skin thickness (interfollicular epidermis) and the number of cells (total and basal) increased, sodium hypochlorite solution (pH 8.5) showed similar effects at 1000 ppm. NOAEL at 10 ppm sodium hypochlorite

Effect of sodium hypochlorite solutions on skin of guinea-pigs at 0.125% daily for 1, 2, 4 and 8 weeks: no treatment related effects on the parameters measured (e.g. number of epidermal cells, area of epidermis, area of papillary layer)

Medical/human data

A huge set of human data on "hypochlorite bleaches" and chlorine gas is available:

Oral exposure towards hypochlorite solutions

Accidental human data reported for ingestion and parenteral route; recovery is expected rapid and without any permanent health consequences

No indications of chronic toxicity in humans following exposure to sodium hypochlorite reported in the literature

Some studies reported small relative risks for colon and bladder cancer incidence for population consuming chlorinated drinking water for long periods of time, however, studies refer to DBPs, are equivocal or insufficient to establish a causal relationship, are of poor quality, incomplete and prone to confounding factors

Dermal exposure towards hypochlorite solutions

Patch test on intact human skin: solutions ≥5% avCl irritant

Patch test on human skin in dermatitis patients: weak to moderate irritation with 2% NaOCl; no irritation with 1% NaOCl

Accidental spillage of hypochlorite bleach into the eyes expected to cause slight, temporary discomfort, which subsides within a short period of time or after rinsing with water

Dermatological case studies (poorly reported and not fully conclusive) indicate a few isolated cases of allergic contact sensitization

Inhalation of chlorine gas

Human volunteer repeated dose study: sensory irritation and a transient impairment in lung function at 1.0 ppm corresponding to 3.0 mg/m^3 chlorine (LOAEC), only trivial changes of lung function parameters at 0.5 ppm corresponding to 1.5 mg/m^3 chlorine (NOAEC)

Human volunteer repeated dose study: No significant effects in respiratory function nasal lavage fluid parameters at 0.5 ppm corresponding to 1.5 mg/m^3 chlorine (NOAEC)

Several reports on accidental exposure to chlorine are available. Depending on chlorine concentrations signs of toxicity: dyspnea and coughing, irritation of the throat and eyes, headache, temporary changes in lung function, cytopathological features and tracheobronchial congestions

Summary

	Value	Study	Safety factor
*ADI (chlorate)	3 µg chlorate/kg bw	based on the TDI for perchlorate (derived from human observations) according to EFSA CONTAM Panel (EFSA Journal 2015;13(6):4135)	-
*ARfD (chlorate)	36 µg chlorate/kg bw	based on human 12-wks repeated dose oral (drinking water) clinical study according to EFSA CONTAM Panel (EFSA Journal 2015;13(6):4135	-
$NOAEC_{oral}$	0.1% avCl	rat 90-d subchronic repeated dose oral	1

		(drinking water) study rat 104-wks chronic repeated dose oral (drinking water) study	
$NOAEC_{dermal}$	1% avCl	human (dermatitis patients) 48 h-patch test study	1
$NOAEC_{inhalation}$ (chlorine)	0.5 ppm avCl (1.5 mg avCl/m³)	monkey 52-wks subchronic repeated dose inhalation study human volunteer single dose inhalation study (4-8 h) human volunteer repeated dose inhalation study (3 d, 6 h/d)	3.2 (intra-species toxicodynamic factor)
$AEC_{inhalation}$ (chlorine)	$AEC_{inhalation}$ (chlorine) = 0.5 mg avCl/m³		
$AEC_{inhalation}$ (HClO)	No repeated dose inhalation toxicity study on HClO is available since HClO does not exist as such but is only formed in aqueous solutions of chlorine. In the absence of data, the BPC TOX-WGIII-2016 agreed to derive an $AEC_{inhalation}$ based on chlorine data (please see above) $AEC_{inhalation}$ (HClO) = 0.5 mg avCl/m³		

***ADI and ARfD are not relevant for PT2**

MRLs

Relevant commodities	Not relevant for substances such as chlorine which act by a local mode of action only For chlorate (relevant stable metabolite), no MRL was set

Reference value for groundwater

According to BPR Annex VI, point 68	0.1 µg/L

Dermal absorption

Study (*in vitro/vivo*), species tested	Dermal absorption is considered as not relevant because chlorine-related toxicity is based on local effects only (with secondary systemic effects at high doses) In the absence of clear systemic effects, the BPC TOX-WGIII-2016 concluded that dermal absorption values are not deemed necessary
Formulation (formulation type and including concentration(s) tested, vehicle)	-
Dermal absorption values used in risk assessment	-

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	Very rapid degradation (~ 300 s) in the presence of organic matter
pH 5	
pH 9	
Other pH: *[indicate the value]*	
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	The photolysis half-life of aqueous chlorine in clear sky, summer noon sunlit (47°N) water of pH 8 is 12 min (ClO^-) when measured at the surface. It increases with decreasing pH due to the decreasing ratio of ClO^-/HClO to 37 min at pH 7 and to 60 min at pH 5
Readily biodegradable (yes/no)	Not applicable to inorganic substances
Inherent biodegradable (yes/no)	Not applicable to inorganic substances
Biodegradation in freshwater	Not applicable to inorganic substances
Biodegradation in seawater	Not applicable to inorganic substances
Non-extractable residues	Not relevant
Distribution in water / sediment systems (active substance)	No distribution in the sediment is expected
Distribution in water / sediment systems (metabolites)	Not relevant

Route and rate of degradation in soil

Mineralization (aerobic)	Not relevant, active chlorine degrades to chloride
Laboratory studies (range or median, with number of measurements, with regression coefficient)	Not relevant due to very rapid degradation
DT_{50lab} (20°C, aerobic):	
DT_{90lab} (20°C, aerobic):	
DT_{50lab} (10°C, aerobic):	
DT_{50lab} (20°C, anaerobic):	
degradation in the saturated zone:	
Field studies (state location, range or median with number of measurements)	Not relevant, see above
DT_{50f}:	
DT_{90f}:	
Anaerobic degradation	Not relevant, see above
Soil photolysis	Not relevant, see above

Non-extractable residues	Not relevant, active chlorine degrades to chloride
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	Not relevant, active chlorine degrades to chloride
Soil accumulation and plateau concentration	Not relevant, see above

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	Not relevant, active chlorine degrades to chloride

Fate and behaviour in air

Direct photolysis in air	2–4 hours (during day light) main reaction product is atomic chlorine which could react with saturated and unsaturated hydrocarbons and ozone Tropospherical DT_{50} for hypochlorous acid is estimated to be 114.6 days (24-hr day), corresponding to 2750 hours
Quantum yield of direct photolysis	No data available
Photo-oxidative degradation in air	Latitude: ..... Season: ..... DT_{50} .....
Volatilization	As the concentration of chlorine gas in water is low at environmentally relevant pH, the amount of chlorine that could volatilise from water into air is expected to be very low

Reference value for groundwater

According to BPR Annex VI, point 68	0.1 µg/L

Monitoring data, if available

Soil (indicate location and type of study)	No data available
Surface water (indicate location and type of study)	No data available
Ground water (indicate location and type of study)	No data available
Air (indicate location and type of study)	No data available

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group)

Species	Time-scale	Endpoint	Toxicity[1, 2]
Fish			
Coho salmon (*Oncorhynchus kisutch)* Sea water	Not reported	Mortality	LC_{50}(96 hours) = 0.032 mg TRO/L (mm)
Tidewater Silverside fry (*Menidia peninsulae*) Sea water	28 days	Mortality	LOEC (28 days) = 0.210 mg CPO/L (mm) NOEC (28 days)= 0.040 mg CPO/L (mm)
Invertebrates			
Ceriodaphnia dubia Fresh water	48 hours	Immobilisation	EC_{50}(48 hours) = 0.035 active Cl/L (nc)
Crassostrea virginica (Molluscs) Oysters, Sea water	15 -19 days	Mortality and growth	NOEC (15 days) = 0.007 mg TRO/L (shell deposition) (mm)
Algae			
Periphytic community Fresh water	7 days	Inhibition concentration	IC_{80} (7 days) = 0.358 mg FAC/L (mm) IC_{50} (7 days) = 0.023 mg FAC/L (mm) NOEC (7 days) = 0.0021 mg FAC/L (mm)
Pseudokirchneriella subcapitata Freshwater	72 hours	Inhibition of cell growth	E_rC_{50} = 0.0365 mg available chlorine/L (ic) E_bC_{50} = 0.0183 mg available chlorine/L (ic)
Microorganisms			
Activated sludge	3 hours	Respiration inhibition	EC_{50} = 77.1 mg available chlorine/L (nc)

[1]TRC= total residual chlorine, TRO= total residual oxidant, FAC= free available chlorine, CPO= chlorine produced oxidant

[2]mm= mean measured concentration, nc=nominal concentration, ic= initial measured concentrations

Effects on earthworms or other soil non-target organisms

Acute toxicity to ……..	Not necessary due to the very rapid degradation in soil
Reproductive toxicity to ……	Not necessary due to the very rapid degradation in soil

Effects on soil micro-organisms

Nitrogen mineralization	Not applicable
Carbon mineralization	Not applicable

Effects on terrestrial vertebrates

Acute toxicity to mammals	No data available and no data required
Acute toxicity to birds	No data available and no data required
Dietary toxicity to birds	No data available and no data required
Reproductive toxicity to birds	No data available and no data required

Effects on honeybees

Acute oral toxicity	No data available and no data required
Acute contact toxicity	No data available and no data required

Effects on other beneficial arthropods

Acute oral toxicity	No data available and no data required
Acute contact toxicity	No data available and no data required
Acute toxicity to ……..	No data available and no data required

Bioconcentration

Bioconcentration factor (BCF)	Not applicable (inorganic substance, very rapid degradation in the environment)
Depuration time (DT_{50})	Not applicable: no test performed
Depuration time (DT_{90})	Uptake into the organism of fish can be excluded, due to the instantaneous degradation of active chlorine in contact with organic material
Level of metabolites (%) in organisms accounting for > 10 % of residues	Not applicable

Chapter 6: Other End Points

None.

Appendix II: List of Intended Uses

Object and/or situation	Product Name	Organisms controlled	Formulation		Application			Applied amount per treatment			Remarks
			Type	Conc. of a.s.	method kind	number min max	interval between applications (min)	g a.s./L min max	water L/m^2 min max	g a.s./m^2 min max	
Disinfection of sewage / waste water before receiving the waste water plant (pre-chlorination), after the waste water plant (professional use)	Chlorine	Bacteria, fungi, viruses, spores	gas	99.5% w/w	Dissolution in water	--	--	5-40 mg/L	--	--	
Disinfection of swimming pools, public pools (continuous flow) (professional use)	Chlorine	Bacteria, fungi, viruses, spores	gas	99.5% w/w	Dissolution in water	--	Continuously	3 mg/L	--	--	
Disinfection of swimming pools, public pools (shock disinfection) (professional use)	Chlorine	Bacteria, fungi, viruses, spores	gas	99.5% w/w	Dissolution in water	--	--	50 mg/L	--	--	

Appendix III: List of studies

Data protection is claimed by the applicant in accordance with Article 60 of Regulation (EU) No 528/2012.

Section No/ Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
III-A 2.10.1/02 Cl2	Anonymous	2001	Reference document on best available techniques in the chlor-alkali manufacturing industry Source: EC Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 121-001	No	N.R.
III-A 3.1.1/01 Cl2	Gest	2002	Physical, thermodynamic and selected chemical properties of chlorine - chapter 1 - basic properties Source: Euro Chlor Publication, Gest 91/168, Chapter 1, 1st Edition, September 2002 Report No.: GEST 91/168, Chapter 1 Not GLP; (published) Doc. No.: 112-001	No	Euro Chlor
III-A 3.1.3/01 Cl2	Gest	2002	Physical, thermodynamic and selected chemical properties of chlorine - chapter 4 - density and specific volume Source: Euro Chlor Publication, Gest 91/168, Chapter 4, 1st Edition, September 2002 Report No.: GEST 91/168, Chapter 4 Not GLP; (published) Doc. No.: 113-001	No	Euro Chlor
III-A 3.2.1/01 (ALL)	Holzwart G, Balmer RG, Soni L	1984	The fate of chlorine and chloramines in cooling towers Source: Water Res. Vol. 18, No. 11, (1984), pp. 1421-1427 Report No.: Not applicable Not GLP; (published) Doc. No.: 792-002	No	N.R.

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III-A 3.2/01 Cl2	Gest	2002	Physical, thermodynamic and selected chemical properties of chlorine - chapter 6 - thermodynamic properties Source: Euro Chlor Publication, Gest 91/168, Chapter 6, 1st Edition, September 2002 Report No.: GEST 91/168, Chapter 6 Not GLP; (published) Doc. No.: 115-001	No	Euro Chlor
III-A 3.4/01 Cl2	Gest	2002	Physical, thermodynamic and selected chemical properties of chlorine - chapter 2 - optical properties Source: Euro Chlor Publication, Gest 91/168, Chapter 2, 1st Edition, September 2002 Report No.: GEST 91/168, Chapter 2 Not GLP; (published) Doc. No.: 117-001	No	Euro Chlor
III-A 3.4/02 Cl2	Anonymous	2007	Nist data - chlorine Source: NIST, Online databases, Chlorine, June 2007 http://webbook.nist.gov/cgi/cbook.cgi Report No.: Not indicated Not GLP; (published) Doc. No.: 117-002	No	N.R.
III-A 3.5/01 Cl2	Gest	2002	Physical, thermodynamic and selected chemical properties of chlorine - chapter 7 - physico-chemical properties Source: Euro Chlor Publication, Gest 91/168, Chapter 7, 1st Edition, September 2002 Report No.: GEST 91/168, Chapter 7 Not GLP; (published) Doc. No.: 114-001	No	Euro Chlor

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III-A 3.6/01 NaOCl + CaOCl	Pinto G & Rohrig B	2003	Use of chloroisocyanuarates for disinfection of water source: JChemEd.chem.wisc.edu, January 2003, 80, 1, 41-44 Report No.: Not applicable Not GLP; (published) Doc. No.: 192-003	No	N.R.
III-A 3.9/01 (ALL)	Anonymous	2007	Log kow calculation hypochlorus acid Source: Not indicated Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 114-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 3.9/02 Cl2	Anonymous	2007	Log kow calculation chlorine Source: Not indicated Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 114-003	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 3.13/01 (ALL)	Ferron N	2007	Surface tension on the sodium hypochlorite 5% Source: Defitrates Report No.: 07-905015-012 GLP; (unpublished) Doc. No.: 116-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 3.14/01 Cl2	Gest	2002	Physical, thermodynamic and selected chemical properties of chlorine - chapter 5 - mechanical properties Source: Euro Chlor Publication, Gest 91/168, Chapter 5, 1st Edition, September 2002	No	Euro Chlor

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			Report No.: GEST 91/168, Chapter 5 Not GLP; (published) Doc. No.: 116-001		
III-A 3.17/01 Cl2	Gest	2004	Materials of construction for use in contact with chlorine Source: Euro Chlor Publication, Gest 79/82, 8th Edition, June 2004 Report No.: GEST 79/82 Not GLP; (published) Doc. No.: 162-001	No	Euro Chlor
III-A 4.1.1/01 Cl2	Anonymous	1972	Liquid chlorine for industrial use - determination of the content of chlorine by volume in the vaporized product Source: International Organization for Standardization Report No.: ISO 2120-1972 (E) Not GLP; (published) Doc. No.: 411-001	No	Euro Chlor
III-A 4.1/02 Cl2	Anonymous	1994	Methods for the analysis of liquid chlorine - analytical 9 Source: Euro Chlor Publication, Analytical 9, 1st Edition, December 1994 Report No.: Anal 9, 1st Edition Not GLP; (published) Doc. No.: 412-001	No	Euro Chlor
III-A 4.2b (ALL)	Anonymous	1988	Determination of chlorine in workplace air - analytical 8 Source: Euro Chlor Publication, Analytical 8, 1st Edition, 1988 Report No.: Anal 8, 1st Edition Not GLP; (published) Doc. No.: 436-001	No	Euro Chlor
III-A 4.2c (ALL)	Anonymous	2000	Water quality - determination of free Chlorine and total chlorine - part 1 - titimetric method using n,n-diethyl-	No	N.R.

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			1,4phenylenediamine Source: Deutsche Norm, April 2000, DIN EN ISO 7393-1 Report No.: Not indicated Not GLP; (published) Doc. No.: 435-001		
III-A 5.3.1/01 (ALL)	Gutiérrez CB et al.	1995	Efficacy of a variety of disinfectants against actinobacillus pleuropneumoniae serotype 1 Source: Am J Vet Res, 1995, 56 (8), 1025-1029 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-044	No	N.R.
III-A 5.3.1/02 (ALL)	Babb JR, Bradley CR, Ayliffe GA	1980	Sporicidal activity of glutaraldehydes and hypochlorites and other factors influencing their selection for the treatment of medical equipment Source: Journal of Hospital Infection, 1980, 1, 63-75 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-014	No	N.R.
III-A 5.3.1/03 (ALL)	Bloomfield SF & Uso EE	1985	The antibacterial properties of sodium hypochlorite and sodium dichloroisocyanurate as hospital disinfectants Source: Journal of Hospital Infection, 1985, 6, 20-30 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-023	No	N.R.
III-A 5.3.1/04 (ALL)	Bloomfield SF & Arthur M	1992	Interaction of bacillus subtilis spores with sodium hypochlorite, sodium dichloroisocyanuruate and chloramine-t Source: Journal of Applied Bacteriology, 1992, 72, 166-172 Report No.: Not applicable Not GLP; (published)	No	N.R.

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			Doc. No.: 392-022		
III-A 5.3.1/05 (ALL)	Best M et al.	1994	Feasibility of a combined carrier test for desinfectants - studies with a mixture of five types of microorganisms Source: AJIC AM J Infect Control, 1994, 22, 152-162 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-018	No	N.R.
III-A 5.3.1/06 (ALL)	Sagripanti J-L, Bonifacino A	1996	Comparative sporicidal effects of liquid chemical agents Source: Applied and Environmental Microbiology, 1996, 62 (2), 545-551 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-059	No	N.R.
III-A 5.3.1/07 (ALL)	Grönholm L et al.	1999	Screening of antimicrobial activities of disinfectants and cleaning agents against foodborne spoilage microbes Source: Z Lebensm. Unters Forsch A, 1999, 289-298 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-041	No	N.R.
III-A 5.3.1/08 (ALL)	Wirtanen G, Martilla-Sandholm T	1982	Removal of foodborne biofilms - comparison of surface ans suspension tests. Part i Source: Lebensm. Wiss. U. Technol, 1992, 25, 43-49 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-066	No	N.R.
III-A 5.3.1/09 (ALL)	Blaser MJ et al.	1986	Inactivation of campylobacter jejuni by chlorine and monochloramine Source: Applied and Environmental Microbiology, 1986, 51 (2), 307-311 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-019	No	N.R.

Section No/ Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
III-A 5.3.1/10 (ALL)	Orth R & Mrozek H	1989	Is the control of listeria, campylobacter and yersinia a disinfection problem Source: Fleischwirtsch. 1989, 69 (10), 1575-1578 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-052	No	N.R.
III-A 5.3.1/11 (ALL)	Berman D, Rice EW, Hoff JC	1988	Inactivation of particle-associated coliforms by chlorine and monochloramine Source: Applied and Environmental Microbiology, 1988, 54 (2), 507-512 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-016	No	N.R.
III-A 5.3.1/12 (ALL)	Bloomfield, SF et al.	1993	Comparative testing of disinfectants using proposed european surface test methods Source: Letters in Applied Microbiology, 1993, 17, 119-125 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-021	No	N.R.
III-A 5.3.1/13 (ALL)	Maris P	1992	Biofilms and disinfection - development of a microorganism carrier-surface method Source: Science des Aliments, 1992, 12, 721-728 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-050	No	N.R.
III-A 5.3.1/14 (ALL)	Parnes CA	1997	Efficacy of sodium hypochlorite bleach and "alternative" products Source: Environmental Health 1997, 14-19 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-053	No	N.R.
III-A 5.3.1/15	Jones MV, Wood MA,	1992	Comparative sensitivity of vibrio cholerae 01 el tor and	No	N.R.

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(ALL)	Herd TM		escherichia coli to disinfectants Source: Letters in Applied Microbiology, 1992, 14, 51-53 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-045		
III-A 5.3.1/16 (ALL)	Kempter J	1986	Clorox vol ii, epa registration no. 5813-1, your amendment application dated february 1, 1985 Source: Not applicable Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 962-003	No	Euro Chlor
III-A 5.3.1/17 (ALL)	Kuchta JM et al.	1985	Enhanced chlorine resistance of tap water-adapted legionella pneumophila as compared with agar medium-passaged strains Source: Applied and Environmental Microbiology, 1985, 50 (1), 21-26 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-047	No	N.R.
III-A 5.3.1/18 (ALL)	Muraca P Stout JE & Yu VL	1987	Comparative assessment of chlorine, heat, ozone, and uv light for killing legionella pneumophila within a model plumbing system Source: Applied and Environmental Microbiology, 1987, 52 (2), 447-453 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-051	No	N.R.
III-A 5.3.1/19 (ALL)	Lopes JA	1986	Evaluation of dairy and food plant sanitizers against - salmonella typhimurium and listeria monocytogenes Source: Not indicated Report No.: Not applicable Not GLP; (published) Doc. No.: 392-049	No	N.R.
III-A	El-Kest SE &	1988	Inactivation of listeria	No	N.R.

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5.3.1/20 (ALL)	Marth E H		monocytogenes by chlorine Source: Journal of Food Protection, 1988, 51, 520-524 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-038		
III-A 5.3.1/21 (ALL)	EPA-List-December	2006	List b - epa registered tuberculocide products effective against mycobactererium tuberculosis Source: Environmental Protection Acency, USA Report No.: Not indicated Not GLP; (unpublished) Doc. No.: 962-002	No	Euro Chlor
III-A 5.3.1/22 (ALL)	Rutala WA et al.	1991	Inactivation of mycobacterium tuberculosis and mycobacterium bovis by 14 hospital disinfectants Source: The American Journal of Medicine, 1991, 91, (38), 267-271 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-057	No	N.R.
III-A 5.3.1/23 (ALL)	Best M et al.	1990	Efficacies of selected disinfectants against mycobacterium tuberculosis Source: Journal of Clinical Microbiology, 1990, 28 (10), 2234-2239 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-017	No	N.R.
III-A 5.3.1/24 (ALL)	Anderson R L et al.	1990	Effect of disinfectants on pseudomonads colonized on the interior surface of pvc pipes Source: AJPH, 1990, 80 (1), 17-21 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-013	No	N.R.
III-A	Tanner RS	1989	Comparative testing and	No	N.R.

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5.3.1/25 (ALL)			evaluation of hard-surface disinfectants Source: Journal of Industrial Microbiology, 1989, 4, 145-154 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-065		
III-A 5.3.1/26 (ALL)	Peter J & Spicher G	1998	Model tests for the efficacy of disinfectants on surfaces iv. Communication - dependence of test results on the amount of contamination and the kind of active substance Source: Zent. Bl. Hyg. Umweltmed. 1998, 201, 311-323 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-054	No	N.R.
III-A 5.3.1/27 (ALL)	Bungaard-Nielsen K, Nielsen V	1995	Fungicidal effect of 15 disinfectants against 25 fungal contaminants commonly found in bread and cheese manufacturing Source: Journal of Food Protection, 1995, 59 (3), 268-275 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-029	No	N.R.
III-A 5.3.1/28 (ALL)	Shaheen EA Ikawa JY	1996	Public health benefits of bleach - a critical review Source: The Clorox Company, 1996, 23-71 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-063	No	N.R.
III-A 5.3.1/29 (ALL)	Sattar SA et al.	1989	Chemical disinfection of non-porous inanimate surfaces experimentally contaminated with four human pathogenic viruses Source: Epidem. Inf., 1989, 102, 492-505 Report No.: Not applicable	No	N.R.

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			Not GLP; (published) Doc. No.: 392-060		
III-A 5.3.1/30 (ALL)	Brown P et al.	1982	Chemical disinfection of creutzfeldt-jakob disease virus Source: The new England Journal of Medicine, 1982, 306 (21), 1297-1282 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-027	No	N.R.
III-A 5.3.1/31 (ALL)	Centers for Disease Control	2006	Interim guidance about ebola virus infection for airline flight crews, cargo and cleaning personnel, and personnel interacting with arriving passengers Source: CDS, 2006, 1-4 Report No.: Not applicable Not GLP; (published) Doc. No.: 992-002	No	N.R.
III-A 5.3.1/32 (ALL)	Grabow WOK et al.	1983	Inactivation of hepatitis a virus and indicator organisms in water by free chlorine residuals Source: Applied and Environmental Microbiology, 1993, 46 (3), 619-624 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-040	No	N.R.
III-A 5.3.1/33 (ALL)	Bond WW et al.	1983	Inactivation of hepatitis b virus by intermediate-to-high-level disinfectant chemicals Source: Journal of Clinical Microbiology, 1983, 18 (3), 535-538 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-024	No	N.R.
III-A 5.3.1/34 (ALL)	Prince HN, Prince DL, Prince RN	1991	Principles of viral control and transmission Source: Disinfactants and Antiseptics. B. by Type of Microorganisms, Chapter 25, 1991, 25, 411-444	No	N.R.

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			Report No.: Not applicable Not GLP; (published) Doc. No.: 392-056		
III-A 5.3.1/35 (ALL)	Prince HN, Prince DL, Prince RN	1990	Inactivation of human immunodeficiency virus type 1 and herpes simplex virus type 2 by commercial hospital disinfectants Source: Chemical Times & Trends, 1990, 14-16, 54, Report No.: Not applicable Not GLP; (published) Doc. No.: 392-055	No	N.R.
III-A 5.3.1/36 (ALL)	Grouse L	1985	HTLV-III transmission Source: JAMA, 1985, 254 (15), 2130-2131 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-042	No	N.R.
III-A 5.3.1/37 (ALL)	Gustafson PR & Andres N	1986	Precautions for health care workers of aids patients Source: Supplied by the British Library-The world´s knowledge, 1986, 82, 28-31 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-043	No	N.R.
III-A 5.3.1/38 (ALL)	Centers for Disease Control	1987	Recommendations for prevention of HIV transmission in health-care settings Source: MMWR, Supplements, 1987, 36, 1-11 Report No.: Not applicable Not GLP; (published) Doc. No.: 391-001	No	N.R.
III-A 5.3.1/39 (ALL)	Sattar SA, Springthorpe VS	1991	Survival and disinfectant inactivation of the human immonudeficiency virus - a critical review Source: Reviews of Infectious Diseases, 1991 (May-June), 13, 430-447 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-061	No	N.R.

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III-A 5.3.1/40 (ALL)	Brown TT	1981	Laboratory evaluation of selected disinfectants as virucidal agents against porcine parvovirus, pseudorabies virus, and transmissible gastroenteritis virus Source: Am J Vet Res, 1981, 42 (6), 1033-1036 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-028	No	N.R.
III-A 5.3.1/41 (ALL)	Lloyd-Evans N, Springthorpe S, Sattar SA	1986	Chemical disinfection of human rotavirus-contaminated inanimate surfaces Source: J. Hyg. Camb, 1986, 91, 163-173 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-048	No	N.R.
III-A 5.7.1/01	Saby S, Leroy P, Block J-C	1999	Escherichia Coli resistance to chlorine and glutathione synthesis in response to oxygenation and starvation Source: Applied and Environmental Microbiology, Dec. 1999, 65, 12, 5600-5603 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-068	No	N.R.
III-A 5.7.1/02	Bloomfield S	2008	Submission to scenihr - february 2008 - assessment of the antibiotic resistance effects of biocides Source: www.ifh-homehygiene.org Report No.: Not applicable Not GLP; (published) Doc. No.: 392-069	No	N.R.
III-A 5.7.2/01	Beumer R et al.	2003	Biocide usage and antimicrobial resistance in home settings: an update - a review by the international scientific forum on home hygiene (IFH)	No	N.R.

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			Source: International Scientific Forum on Home Hygiene (IFH), October 2003 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-070		
III-A 6.1.1/01 Ca(OCl)2	[redacted]	1975	Acute oral ld 50 in rats using calcium hypochlorite [redacted] Not GLP; (unpublished) Doc. No.: 521-004	Yes	Euro Chlor
III-A 6.1.1/01 NaOCl	BioFax	1970	Bio - fax - sodium hypochlorite Source: Industrial Bio-Test Laboratories Inc. Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 581-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 6.1.2/01 NaOCl	BioFax	1970	Bio - fax - sodium hypochlorite Source: Industrial Bio-Test Laboratories Inc. Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 581-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 6.1.3/01 Ca(OCL)2	[redacted]	1998	An acute inhalation toxicity study of calcium hypochlorite in rats [redacted] Not GLP; (unpublished) Doc. No.: 523-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 6.1.3/01 Cl2	[redacted]	1987	Acute inhalation toxicity of chlorine in rats and mice [redacted]	Yes (Data on existing a.s.	Euro Chlor

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			[redacted] GLP; (unpublished) Doc. No.: 523-001	submitted for the first time for entry into Annex I)	
III-A 6.1.3/01 NaOCl	BioFax	1970	Bio - fax - sodium hypochlorite Source: Industrial Bio-Test Laboratories Inc. Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 581-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 6.1.4/01 (ALL)	Pashley EL et al.	1985	Cytotoxic effects of naoci on vital tissue efecto citotoxico del naoci en el tejido vital Source: Journal of Endodontists Vol. 11, No. 12, December 1985, pp. 525-528 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-090	No	N.R.
III-A 6.1.4/02 (ALL)	Carter RO& Griffin JF	1965	Experimental bases for the realistic assessment of safety of tropical agents Source: Toxicology and Applied Pharmacology, 7, (1965), pp. 60-73 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-013	No	N.R.
III-A 6.1.4/03 (ALL)	Nixon GA, Tyson CA, Wertz WC	1975	Interspecies comparisons of skin irritancy Source: Toxicology and Applied Pharmacology 31, (1975) pp. 481-490 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-035	No	N.R.
III-A 6.1.5/01 NaOCl	[redacted]	1982	Ecm bts 730 e2050.01 delayed contact hypersensivity in guinea pigs [redacted]	Yes (Data on existing a.s.	Euro Chlor

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			[redacted] Not GLP; (unpublished) Doc. No.: 567-001	submitted for the first time for entry into Annex I)	
III-A 6.1.5/01 Ca(OCl)2	[redacted]	2000	Delayed contact dermal sensitization test - buehler method [redacted] GLP; (unpublished) Doc. No.: 567-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 6.1.5/02 NaOCl	[redacted]	1985	Guinea pig sensitiation testing by ritz, h.l. and buchler, E.V. on E-2707.01 [redacted] Not GLP; (unpublished) Doc. No.: 567-003	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 6.1.5/03 NaOCl	[redacted]	1985	Guinea pig sensitiation testing by ritz, h.l. and buchler, E.V. on E-2707.01 [redacted] Not GLP; (unpublished) Doc. No.: 567-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 6.2/01 Cl2	Nodelman V, Ultman JS	1999	Longitudinal distribution of chlorine absorption in human airways - comparison of nasal and oral quiet breathing Source: The American Physiological Society, (1999), pp. 1984-1993 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-173	No	N.R.

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III-A 6.2/01 NaOCl	Abdel - Rahman MS, Couri D, Bull RJ	1982	Metabolism and pharmacokinetics of alternate drinking water disinfectants Source: Environmental Health Perspectives o. 46, (1982), pp. 19-23 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-065	No	N.R.
III-A 6.2/02 Cl2	Scully FE et al.	1990	Identification of organic n-chloamines in vitro in stomach fluid from the rat after chlorination Source: Chem. Res. Toxicol, 3, (1990), pp. 301-306 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-137	No	N.R.
III-A 6.2/02 NaOCl	Abdel - Rahman MS, Waldron DM, Bull RJ	1983	A comparative kinetics study of monochloramine and hypochchlorous acid in rat Source: Journal of Applied Toxicology, Vol. 3, No. 4, (1983), pp. 175-179 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-071	No	N.R.
III-A 6.3.1/01 (ALL)	BioFax	1970	Bio - fax - sodium hypochlorite Source: Industrial Bio-Test Laboratories Inc. Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 581-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 6.3.3/01 Cl2	Barrows CS et al.	1979	An inhalation toxicity study of chlorine in fischer 344 rats following 30 days of exposure Source: Toxicology and Applied Pharmacology 49, (1979), pp. 77-88 Report No.: Not applicable Not GLP; (published)	No	N.R.

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			Doc. No.: 592-052		
III-A 6.4.1/01 (ALL)	Hasegawa R et al.	1986	Carcinogenicity study of sodium hypochlorite in f344 rats Source: Fd. Chem. Toxic. Vol. 24, No. 12 (1986), pp. 1295-1302 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-096	No	N.R.
III-A 6.4.1/02 (ALL)	Daniel FB et al.	1990	Comparative subchronic toxicity studies of three disinfectants Source: Resarch und Technology, Journal AWWA, October 1990,pp. 61-69 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-139	No	N.R.
III-A 6.4.1/03 (ALL)	Daniel FB et al.	1991	Comparative subchronic toxicity of chlorine and monochloramine in the B6C3F1 mouse Source: Research and Technology Journal AWWA, November 1991, pp. 68-75 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-144	No	N.R.
III-A 6.4.3/01 Cl2	[redacted] et al.	1987	One-year inhalation toxicity study of chlorine in rhesus monkeys (macaca mulatta) [redacted] Not GLP; (unpublished) Doc. No.: 592-113	No	N.R.
III-A 6.5/01 Cl2	Wolf DC et al.	1995	Chlorine gas induces nasal lesions but does not cause cancer in mice or rats Source: Chemical Industry Institute of Toxicology (CIT), Vol. 15, No. 3, pp. 1-12 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-159	No	N.R.
III-A 6.5/01	Hasegawa R et al.	1986	Carcinogenicity study of sodium hypochlorite in f344	No	N.R.

Section No/ Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
NaOCl			rats Source: Fd. Chem. Toxic. Vol. 24, No. 12 (1986), pp. 1295-1302 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-096		
III-A 6.5/02 (ALL)	NTP-TR	1992	Toxicology and carcinogenesis studies of chlorinated water (cas nos. 7782-50-5 and 7681-52-9) and chloraminated water (cas no. 10599-90-3) Source: National Toxicology Program, Technical report Series, No. 392, March 1992 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-147	No	N.R.
III-A 6.5/03 (ALL)	Wolf DC et al.	1995	Two-year inhalation exposure of female and male b6c3f1 mice and f344 rats to chlorine gas induces lesions confined to the nose Source: Fundamental and Applied Toxicology 24, (1995), pp. 111-131 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-158	No	N.R.
III-A 6.6.1/01 (ALL)	Ishidate M et al.	1994	Primary mutagenicity screening of food additives currently used in japan Source: Fd. Chem. Toxic, Vol. 22, No. 8 (1984), pp. 623-636 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-154	No	N.R.
III-A 6.6.1/02 (ALL)	Kawachi T et al.	1980	Results of recent studies on the relevance of varios short-term screening tests in japan Source: Applied Methods in Oncology, Bd. 3, 1980, pp. 253-267 Report No.: Not applicable	No	N.R.

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			Not GLP; (published) Doc. No.: 592-054		
III-A 6.6.1/03 (ALL)	Le Curieux F, Marzin D, Erb F	1993	Comparison of three short-term assays - results on seven chemicals - potential contribution to the control of water genotoxicity Source: Mutation Research, Vol. 319, 1993, pp. 223-236 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-153	No	N.R.
III-A 6.6.2/01 (ALL)	Ishidate M et al.	1994	Primary mutagenicity screening of food additives currently used in japan Source: Fd. Chem. Toxic, Vol. 22, No. 8 (1984), pp. 623-636 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-154	No	N.R.
III-A 6.6.2/02 (ALL)	Matsuoka A, Hayashi M, Ishidate M	1979	Chromosomal aberration tests on 29 chemicals combined with s9 mix in vitro Source: Mutation Resarch, 66 (1979), pp. 277-290 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-051	No	N.R.
III-A 6.6.2/03 (ALL)	Sasaki M et al.	1980	Cytogenetic effects of 60 chemicals on cultured human and chinese hamster cells Source: La Kromosomo II-20, 31.12.1980, pp. 574-584 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-057	No	N.R.
III-A 6.6.4/01 (ALL)	Hayashi M et al.	1988	Micronucleus tests in mice on 39 food additives and eight miscellaneous chemicals Source: Fd. Chem. Toxic, Vol. 26, No. 6, (1988), pp. 487-500 Report No.: Not applicable	No	N.R.

Section No/ Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
			Not GLP; (published) Doc. No.: 592-114		
III-A 6.6.4/02 (ALL)	Meier JR et al.	1985	Evaluation of chemicals used for drinking water disinfection for production of chromosomal damage and sperm-head abnormalities in mice Source: Environmental Mutagenesis 7, (1985), pp. 201-211 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-091	No	N.R.
III-A 6.6.5/01 (ALL)	Kasai Y et al.	1987	Oral administration of the renal carcinogen, potassium bromate, specifically produces 8-hydroxydeoxyguanosine in rat TARGET ORGAN DANN Source: Carcinogenesis Vol. 8, No. 12, (1987), pp. 1959-1961 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-106	No	N.R.
III-A 6.6.6/01 (ALL)	Meier JR et al.	1985	Evaluation of chemicals used for drinking water disinfection for production of chromosomal damage and sperm-head abnormalities in mice Source: Environmental Mutagenesis 7, (1985), pp. 201-211 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-091	No	N.R.
III-A 6.7/01 (ALL)	Soffritti M et al.	1997	Results of long-term carcinogenicity studies of chlorine in rats Source: Annals New York Academy of Sciences, pp. 189-208 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-003	No	N.R.

Section No/ Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
III-A 6.7/02 (ALL)	Kurokawa Y et al.	1986	Long-term in vivo carcinogenicity tests of potassium bromate, sodium hypochloite and sodium chlorite conducted in japan Source: Environmental Health Perspectives Vol. 69, (1986), pp. 221-235 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-099	No	N.R.
III-A 6.8.1/01 (ALL)	Abdel - Rahman MS, Berardi MR Bull RJ	1982	Effect of chlorine and monochloramine in drinking water on the developing rat fetus Source: Journal of Applied Toxicology, Vol. 2, No. 3, (1982), pp. 156-159 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-064	No	N.R.
III-A 6.8.2/01 (ALL)	Carlton BD et al.	1986	Reproductive effects of alternative disinfectants Source: Environmental Health, Vol. 69, (1986), pp. 237-241 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-097	No	N.R.
III-A 6.8.2/02 (ALL)	Druckrey H	1968	Chloriertes trinkwasser, toxizitäts-prüfungen an ratten über sieben generationen Source: Fd. Cosmet. Toxicol. Vol. 6, pp. 147-154 (1968), pp. 147-154 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-016	No	N.R.
III-A 6.8.2/03 (ALL)	Les EP	1968	Effects of acidified chlorinated water on reproduction in c3h/hej and C57BL/6J mice Source: Laboratory Animal Care, Vol. 18, No. 2, pp. 210-213 Report No.: Not applicable	No	N.R.

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			Not GLP; (published) Doc. No.: 592-017		
III-A 6.12.2/01 Cl2	Mrvos R et al.	1991	Home exposures to chlorine/chloramine gas - a review of 216 cases Source: Vet. Hum Toxicol 33 (4), August 1991, page 1 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-146	No	N.R.
III-A 6.12.2/01 NaOCl	Becker GL	1974	The sequelae of accidentally injecting sodium hypochlorite beyond the root apex Source: Oral Surg, Oral Med, Oral Pathol. 38, (1974), pp. 633-638 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-030	No	N.R.
III-A 6.12.2/02 Cl2	Charan NB et al.	1985	Effects of accidental chlorine inhalation on pulmonary function Source: The Western Journal of Medicine Clinical Investigation, September 1985, 143, 3, 333-336 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-207	No	N.R.
III-A 6.12.2/02 NaOCl	Dedhia NM et al.	1989	Long-term increase in peritoneal membrane transport rates following incidental intraperitoneal sodium hypochlorite infusion Source: The Journal of Artificial Organs, Vol. 12, No. 11, (1989), pp. 711-714 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-134	No	N.R.
III-A 6.12.2/03 Cl2	Agabiti N et al.	2001	Short term respiratory effects of acute exposure to chlorine due to a swimming pool accident Source: Occup Environ Med 58, (2001), pp. 399-404	No	N.R.

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			Report No.: Not applicable Not GLP; (published) Doc. No.: 592-178		
III-A 6.12.2/03 NaOCl	Grant WM	1974	Toxicology of the eye Source: Charles C Thomas Publishers, (1974), pp. 222-259, 571-573, 852 and 932-934 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-031	No	N.R.
III-A 6.12.2/04 Cl2	Shroff CP	1988	Respiratory cytopathology in chlorine gas toxicity - a study in 28 subjects Source: Diagnostic Cytopathology, March 1988, 4, 1, 28-32 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-208	No	N.R.
III-A 6.12.2/04 NaOCl	Bibra	1990	Toxicity profile - sodium hypochlorite Source: Bibra Toxicology International, 1990, pp. 1-11 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-135	No	N.R.
III-A 6.12.2/05 Cl2	Weil H et al.	1969	Late evaluation of pulmonary function after acute exposure to chlorine gas Source: American Review of Respiratory Disease, 1969, 99, 374-379 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-209	No	N.R.
III-A 6.12.2/06 Cl2	Habets JM W et al.	1986	Sensitization to sodium hypochlorite causing hand dermatitis Contact Dermatitis 15, Vol. 1986, pp. 140-142 Report No.: na Not GLP, published Doc. No.: 592-101	No	N.R.
III-A 6.12.2/07	Rotman HH et al.	1983	Effects of low concentrations of chlorine on pulmonary	No	N.R.

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Cl2			function in humans American Physiological Society, (1983), pp. 1120-1124 Report No.: na Not GLP, published Doc. No.: 592-077		
III-A 6.12.2/08 Cl2	Schins RPF et al.	2000	Nasal inflammatory and respiratory parameters in human volunteers during and after repeated exposure to chlorine ERS Journal 16, (2000), pp. 626-632 Report No.: na Not GLP, published Doc. No.: 592-174	No	N.R.
III-A 6.12.3/01 NaOCl	Coskey RJ	1974	Onycholysis from sodium hypochlorite Source: Arch Dermatol, Vol. 109, Januar 1974, page 96 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-033	No	N.R.
III-A 6.12.3/02 NaOCl	Maddy KT	1990	Illnes injuries and death from pesticide exposure in california 1949-1988 Source: Reviews of Environmental Contamination and Toxicology, Vol. 114, (1990), pp. 57-124 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-141	No	N.R.
III-A 6.12.5/01 NaOCl	Pike DG et al.	1963	A re-evaluation of the dangers of clorox ingestion Source: The Joournal of Pediatrics Volume 63, Number 2, (1963), pp. 303-305 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-011	No	N.R.
III-A 6.12.5/02 NaOCl	Tanyel FC, Büyükpamukcu N,	1988	Chlorine bleach ingestion in children - a review of 80 cases	No	N.R.

Section No/ Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
	Hicsönmez, A		Source: Inc. Türkish Journal of Pediatrics 30, (1988), pp. 105-106 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-119		
III-A 6.12.5/03 NaOCl	Strange DC et al.	1951	Corrosive injury of the stomach Source: A.M.A. Archives of Surgery 62, (1951) pp. 350-357 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-009	No	N.R.
III-A 6.12.5/04 NaOCl	Mühlendahl KE, Oberdisse U, Krienke EG	1978	Local injuries by accidental ingestion of corrosive substances by children Source: Arch. Toxicol. 39, (1978), pp. 299-314 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-050	No	N.R.
III-A 6.12.5/05 NaOCl	Ward MJ, Routledge PA	1988	Hypernatraemia hypechloraemic acidosis bleach ingestion Source: Human Toxicol 7, (1988), pp. 37-38 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-118	No	N.R.
III-A 6.12.6/01 NaOCl	Eun HC, Lee AY, Lee YS	1984	Sodium hypochlorite dermatitis Source: Cont. Derm. 11, (1984), page 45 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-081	No	N.R.
III-A 6.12.6/02 NaOCl	Nixon GA, Tyson CA, Wertz WC	1975	Interspecies comparisons of skin irritancy Source: Toxicology and Applied Pharmacology 31, (1975) pp. 481-490 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-035	No	N.R.
III-A 6.12.6/03	Hostynek JJ et al.	1990	Irritation factors of sodium hypochlorite solutions in	No	N.R.

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NaOCl			human skin Source: Contact Dermatitis 1990, pp. 316-324 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-136		
III-A 6.16/01 NaOCl	Cotter JL et al.	1985	Chemical parameters, antimicrobial activities, and tissue toxicity of 0.1 and 0.5% sodium hypochchlorite solutions Source: Antimicrobial Agents and Chemotherapy,Vol. 28, No.1, Juily 1985, pp. 118-122 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-095	No	N.R.
III-A 6.16/02 NaOCl	Robinson M et al.	1986	Epidermal hyperplasia in mouse skin following treatment with alternative drinking water disinfectants Source: Environmental Health Perspectives Vol. 69, (1986), pp. 293-300 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-100	No	N.R.
III-A 6.16/03 NaOCl	Wohlrab W Wozniak KD	1982	Untersuchungen zu wirkung von natriumhypochlorit als modellsubstanz auf die haut und verschiedene zellsysteme Source: Dermatosen 30, Nr. 3, (1982), pp. 79-83 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-068	No	N.R.
III-A 7.1.2/01 (ALL)	Vandepitte V, Schowanek D	1997	Sodiumhypochlorite - kinetic model on the long term hypochlorite decay in the environment - a specific model for use in the hoci risk assessment Source: Not indicated Report No.: Not indicated Not GLP; (unpublished)	Yes (Data on existing a.s. submitted for the first time for entry into	Euro Chlor

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			Doc. No.: 989-003	Annex I)	
III-A 7.3.1/01 NaOCl + Ca(OCl)2	Görg J, Glöckner T	2007	Estimation of the atmospheric residence time of sodium hypochlorite using the atkinson method Source: Scientific Consulting Company, Wendelsheim, Germany Report No.: 832-005 Not GLP; (unpublished) Doc. No.: 743-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 7.4.1.1/01 (ALL)	Heath J	1977	Toxicity of intermittent chlorination to freshwater fish - influence of temperature and chlorine from Source: Hydrobiologia Vol. 56, 1, (1977), pp. 39-47 Report No.: Not applicable Not GLP; (published) Doc. No.: 892-012	No	N.R.
III-A 7.4.1.1/02 (ALL)	Bellanca MA, Bailey DS	1977	Effects of chlorinated effluents on aquatic ecosystem in the lower james river Source: Journal WPCF, April 1977, pp. 639-645 Report No.: Not applicable Not GLP; (published) Doc. No.: 892-020	No	N.R.
III-A 7.4.1.1/03 (ALL)	Thatcher TO	1978	The relative sensitivity of pacific northwest fishes and invertebrates to chlorination sea water Source: Not indicated Report No.: Not applicable Not GLP; (published) Doc. No.: 892-023	No	N.R.
III-A 7.4.1.1/1b (ALL)	Heath AG	1978	Influence of chlorine from and ambient temperature on the toxicity of intermittent chlorination to freshwater fish Source: Environmental Effects in Freshwater Systems, (1978), pp. 123-133	No	N.R.

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			Report No.: Not applicable Not GLP; (published) Doc. No.: 892-022		
III-A 7.4.1.2/02 (ALL)	Roberts jr. MH, Gleeson RA	1978	Acute toxicity of bromochlorinated seawater to selected estuarine species with a comparison to chlorinated seawater toxicity Source: Marine Environ. Res., 1978, 1, 19-29 Report No.: Not applicable Not GLP; (published) Doc. No.: 892-068	No	N.R.
III-A 7.4.1.2/03 (ALL)	Gallagher, S.P. et al.	2009	Sodium hypochloride: a 48-hour flow-through acute toxicity test with the cladoceran (*Daphnia magna*) Source: Wildlife International Ltd, Easton, Maryland, USA Report N.: 676A-101; 2009-03-26 GLP: yes; (unpublished) Doc. No. 822-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 7.4.1.2/04 (ALL)	Gallagher, S.P. et al.	2011	Sodium hypochloride: a 48-hour flow-through acute toxicity test with the cladoceran (*Ceriodaphnia dubia)* *So*urce: Wildlife International Ltd, Easton, Maryland, USA Report N.: 676A-102; 2011-07-15 GLP: yes; (unpublished) Doc. No. 822-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 7.4.1.3/01 (ALL)	Cairns J, Niederlehner BR, Pratt JR	1990	Evaluation of joint toxicity of chlorine and ammonia to aquatic communities Source: Aquatic Toxicology, 16, (1990), pp. 87-100 Report No.: Not applicable Not GLP; (published) Doc. No.: 892-051	No	N.R.
III-A 7.4.1.3/03 (ALL)	Liedtke, A	2013	Toxicity to *Pseudokirchneriella subcapitata* in a 72-hour Algal Growth Inhibition Test Source: Harlan Laboratories	Yes (Data on existing a.s. submitted	Euro Chlor

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			Ltd, Zelgliweg, Switzerland; Report No.: D62230; 18.07.2013 GLP: yes; (unpublished). Doc No. 823-001	for the first time for entry into Annex I)	
III-A 7.4.1.4/02 (ALL)	Eisner, G	2013	Toxicity to Activated Sludge in a Respiration Inhibition Test Source: Harlan Laboratories Ltd, Zelgliweg, Switzerland Report No.: D62252; 24.06.2013 GLP: yes; (unpublished) Doc No. 842-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 7.4.3.2/01 (ALL)	Goodman LR et al.	1983	Early life-stage toxicity test with tidewater silversides (menidia peninsulae) and chlorine-produced oxidants Source: Environmental Toxicology and Chemistry, Vol. 2, (1983), pp. 337-342 Report No.: Not applicable Not GLP; (published) Doc. No.: 892-036	No	N.R.
III-A 7.4.3.4/01 (ALL)	Liden LH, Burton DT	1980	Effects of chlorobrominated and chlorinated cooling waters on estuarine organisms Source: Journal WPCF, Vol. 52, No. 1, (1980), pp. 173-182 Report No.: Not applicable Not GLP; (published) Doc. No.: 892-032	No	N.R.
(Doc II-A section 4.1/01 Cl2)	Keene WC	N.I.	The natural chemistry of inorganic chlorine in the lower atmosphere: a potential source for organochlorine compounds Source: The Natural Chemistry of Chlorine in the Environment, 2, 5-6 Report No.: Not applicable Not GLP; (published) Doc. No.: 792-018	No	N.R.
III-B	Gest	2002	Physical, thermodynamic	No	Euro

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3.1.1/01 Cl2			and selected chemical properties of chlorine - chapter 1 - basic properties Source: Euro Chlor Publication, Gest 91/168, Chapter 1, 1st Edition, September 2002 Report No.: GEST 91/168, Chapter 1 Not GLP; (published) Doc. No.: 112-001		Chlor
III-B 3.6/01 Cl2	Gest	2002	Physical, thermodynamic and selected chemical properties of chlorine - chapter 4 - density and specific volume Source: Euro Chlor Publication, Gest 91/168, Chapter 4, 1st Edition, September 2002 Report No.: GEST 91/168, Chapter 4 Not GLP; (published) Doc. No.: 113-001	No	Euro Chlor
III-B 3.7.2/01 Cl2	Gest	2004	Materials of construction for use in contact with chlorine Source: Euro Chlor Publication, Gest 79/82, 8th Edition, June 2004 Report No.: GEST 79/82 Not GLP; (published) Doc. No.: 162-001	No	Euro Chlor
III-B 3.7/01 Cl2	Chimocaoggi	1991	Technical sheet - chlorine CAS-NO: 7782-50-5 Source: Chimica oggi, April 1991 Report No.: Not applicable Not GLP; (published) Doc. No.: 031-002	No	Euro Chlor
III-B 3.10/01 (ALL)	Ferron, N.	2007	Surface tension on the sodium hypochlorite 5% Source: Defitrates Report No.: 07-905015-012 GLP; (unpublished) Doc. No.: 116-002	Yes (Data on existing a.s. submitted for the first time for entry	Euro Chlor

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				into Annex I)	
III-B 3.11/01 Cl2	Gest	2002	Physical, thermodynamic and selected chemical properties of chlorine - chapter 5 - mechanical properties Source: Euro Chlor Publication, Gest 91/168, Chapter 5, 1st Edition, September 2002 Report No.: GEST 91/168, Chapter 5 Not GLP; (published) Doc. No.: 116-001	No	Euro Chlor