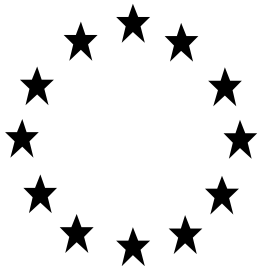
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Active chlorine released from sodium hypochlorite

Product-type 5
(Drinking water)

January 2017

IT

CONTENTS

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 sodium hypochlorite as product-type 5 (Drinking water), 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 sodium hypochlorite (releaser CAS no.: 7681-52-9) was notified as an existing active substance, by the Euro Chlor Sodium Hypochlorite Registration Group at Euro Chlor, hereafter referred to as the applicant, in product-type 5.

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 Sodium Hypochlorite 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 sodium hypochlorite for product-type 5, 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 sodium hypochlorite' ([3]).

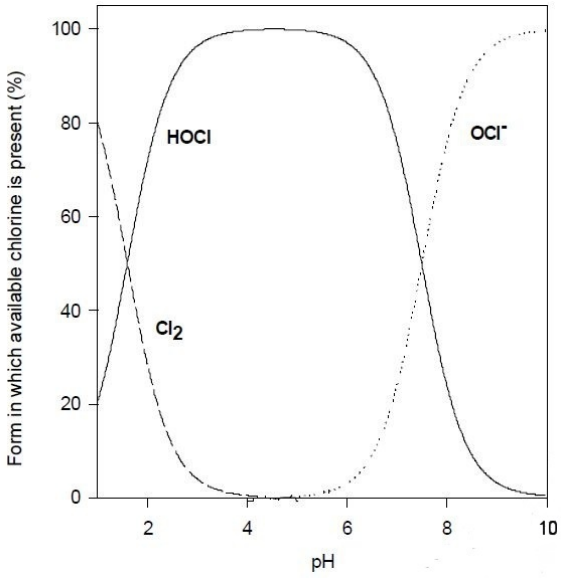
Upon use for MAIN GROUP 1 – Disinfectants (PT5), sodium hypochlorite aqueous solutions release 'active chlorine', *i.e.* efficacious chlorine or available/releasable chlorine that is disinfectant, algaecide, fungicide and microbiocide.

Namely, in water sodium hypochlorite (NaClO) hydrolyzes to hypochlorous acid (HClO) according to:

$NaClO + H_2O \leftrightarrow Na^+ + HClO + OH^-$ ([4])

Furthermore, hypochlorous acid participates in the following equilibrium with chlorine (Cl_2):
$HClO + H_3O^+ + Cl^- \leftrightarrow Cl_2 + 2H_2O$ ([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]) $K_{hydrolysis}(ClO^-) = K_w/K_a$, where $K_a(HClO) = 3.5 \times 10^{-8}$ mol/dm^3 at 20°C (Solvay, International Research Document, 1979)

([5]) $K_{hydrolysis}(Cl_2) = 3.2 \times 10^{-4}$ 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. sodium hypochlorite

Active substance releaser	
CAS-No.	7681-52-9
EINECS-No.	231-668-3
Other No.	017-011-00-1 (Index number)
IUPAC Name	Sodium hypochlorite
CAS name	Hypochlorous acid, sodium salt
Common name, synonyma	Sodium hypochlorite
Molecular formula	ClHO.Na
Structural formula	Na^+ Cl — O^-
Molecular weight	74.44 g/mol
Purity	Aqueous solution with an available (active) chlorine concentration ≤18% w/w ([6]), in compliance with the EN 901:2013
Additives	Sodium hydroxide
Impurities	One relevant impurity is present: sodium chlorate (≤5.4% of the active chlorine) Non-relevant impurities are considered as confidential information and, hence, described in the Annex of Confidential Data

Two manufacturing processes are described in the Euro Chlor dossier and can be found in the Annex of Confidential Data. Due to its instability as a pure salt, sodium hypochlorite is manufactured and handled only as an aqueous solution with a pH value greater than 11 at 20°C. Solutions are kept alkaline in order to decrease the degradation rate of the hypochlorite to chloride and chlorate.

Identification of the biocidal product

The theoretical biocidal products described in the dossier are 14% (w/w) and 5% (w/w) available chlorine-containing solutions. Sodium hypochlorite as manufactured is adjusted with water to the respective concentration of available chlorine.

Biocidal product	
Trade name	Theoretical product 1: Sodium hypochlorite 14% Theoretical product 2: Sodium hypochlorite 5%

([6]) Sodium hypochlorite is determined by a titrimetric method. Results are tipically expressed as available (active) chlorine using by convention the molecular weight of elemental chlorine in calculations, but they can be converted into sodium hypochlorite by applying a conversion factor of **1.05** (MW_{NaOCl} /MW_{Cl2} = 74.44/70.91).

Manufacturer's development code number(s)	None
Active substance released	Active chlorine released from sodium hypochlorite
Physical state of preparation	Liquid
Nature of preparation	SL (soluble concentrate)

Physical-chemical properties of the active substance releaser (sodium hypochlorite)

Due to its instability as a pure salt, sodium hypochlorite is manufactured and handled exclusively as an aqueous solution with a pH value greater than 11 at 20°C.

In compliance with EN 901:2013, sodium hypochlorite aqueous solutions with an active chlorine concentration up to 18% w/w are considered for the purpose of the approval. However, sodium hypochlorite aqueous solutions with an active chlorine concentration up to 25% w/w are manufactured for industrial use.

A sodium hypochlorite aqueous solution with an active chlorine concentration of 24.3% w/w was considered for physical-chemical testing as the highest available concentration. The tested solution is a yellow limpid liquid, with faint chlorinous odour and freezing point of -28.9 ± 0.5 °C; relative density ($D^{21.2}_4$) is 1.300 ± 0.001.

The vapour pressure of sodium hypochlorite solutions is reported by EN 901:2013 to be approximately 2.5 kPa at 20°C, due to water ([7]). At pH >11 the hypochlorite anion is the predominant species, whereas none of the volatile species at equilibrium (hypochlorous acid and chlorine) are virtually present. As an ionic species, the hypochlorite anion has high water solubility and is unlikely to evaporate to the gaseous phase. Thus, it can be assumed that the hypochlorite anion has a negligible vapour pressure. No Henry's law constant is derived, either. However, for the purpose of risk assessment only, the Henry's law constant of hypochlorous acid is also reported in the LoEPs as determined experimentally by Blatchley et al. (1992) ([8]) by the air stripping method, being hypochlorous acid the only volatile chlorine species present at the equilibrium at in-use pH values under PT5.

The CRC Handbook of Chemistry and Physics ([9]) indicates for sodium hypochlorite a solubility in water of 26 g/100 g H_2O at 0°C, whereas a solubility of 79.9 g/100 g H_2O at 25°C is given by the Perry's Chemical Engineers' Handbook ([10]). The latter value is not from a peer-reviewed handbook and will not be included in the LoEPs. The high solubility in water of sodium hypochlorite is confirmed by a calculation provided by the applicant using WSKOW v1.41, though the result (1 kg/L at 25°C) is out of the validation domain of the model and therefore will not be included in the LoEPs, either.

Sodium hypochlorite is not used in organic solvents due to its nature as a strong oxidiser.

Sodium hypochlorite hydrolyzes in water according to:
$NaClO + H_2O \leftrightarrow Na^+ + HClO + OH^-$
$K_{hydrolysis}(NaClO) = K_w/K_a$, where $K_a(HClO)$ is 3.5×10^{-8} mol/dm^3 at 20°C ([11]).

In water sodium hypochlorite degrades to chlorate and chloride. The degradation rate is a function of the active chlorine concentration and of temperature. For a sodium hypochlorite

([7]) The vapour pressure of pure water, as given in different handbooks, is 2.34 kPa at 20°C.
([8]) 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.
([9]) Internet Version 2005, David R. Lide, ed., <http://www.hbcpnetbase.com>, CRC Press, Boca Raton, FL, 2005.
([10]) 7th Ed., Robert H. Perry, Don W. Green, James O'Hara Maloney, eds., McGraw-Hill, New York, 1997. Not peer-reviewed.
(9) Solvay, International Research Document, 1979.

aqueous solution with an active chlorine concentration of 10% w/w, the half-life is reported to be 800 days at 15 °C; 220 days at 25 °C; 3.5 days at 60 °C; 0.079 days at 100 °C. Whereas, for an active chlorine concentration of 5% w/w, the half-life is reported to be 5000 days at 15 °C; 790 days at 25 °C; 13.5 days at 60 °C; 0.25 days at 100 °C.

The surface tension of the tested solution (sodium hypochlorite aqueous solution with an active chlorine concentration of 24.3% w/w) is 82.4 ± 0.8 mN/m at 20.2-20.3 °C. Dynamic viscosity is 6.2-6.6 mPa s at 20 ± 0.2 °C; 4.0 mPa s at 40 ± 0.2 °C. A flash-point higher than 110 °C is considered. At 110 °C, the test item boiled and overflowed from the cup just after the presentation of flame; then the test stopped. Furthermore, sodium hypochlorite solutions are not known to spontaneously ignite when exposed to air or to emit flammable gases.

Harmonized classification was approved by EU for 'sodium hypochlorite, solution … % Cl active', which was inserted into Annex VI of CLP under Index number 017-011-00-1. No classification for physical hazards applies. Nevertheless, no evidence was provided by the applicant as regards either oxidizing and explosive properties of sodium hypochlorite aqueous solutions. New tests according to the UN Recommendation on the Transport of Dangerous Goods, Manual of Tests and Criteria need to be provided (at the maximum available concentration of sodium hypochlorite in water), at the latest six months before the date of approval.

Common metals should never be used for the storage and handling of sodium hypochlorite aqueous solutions. Suitable materials are listed in the embedded file below:

Packaging materials for NaClO.docx

Analytical methods for detection and identification

Sodium hypochlorite as manufactured (aqueous solutions)

An analytical method is available for the determination of sodium hypochlorite in sodium hypochlorite aqueous solutions 1% w/w. Upon appropriate dilution, the method is applicable also to higher sodium hypochlorite concentrations. 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 NaClO (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 NaClO (corresponding to 0.48% w/w as active chlorine) is proposed.

Apart from sodium chlorate, which is a relevant impurity, impurities of sodium hypochlorite are regarded as confidential information. Therefore, information on the analytical methods for their identification/quantification can be found in the Annex of Confidential Data.
The analytical methods available in the original dossier lacked validation data. The WGII2016 conclusion was that fully-validated analytical methods (in compliance with Guidance on the BPR Volume I: Identity / physico-chemical properties / analytical methodology – Part A: Information Requirements) are required for the identification/quantification of impurities in

sodium hypochlorite and should be provided to the eCA-IT six months before the date of approval.

Formulation analysis
In principle, the same analytical method described above will apply.

Residues analysis
The active substance is "active chlorine released from sodium hypochlorite", 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 the hypochlorite anion is present at pH >10).
At the in-use pH values in PT5, chlorine is virtually non-present at the equilibrium, whereas the predominant species are the hypochlorous acid and the hypochlorite anion or (at higher pH values) the hypochlorite anion only.

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 PT5, spray applications are not envisaged.

At the in-use pH values under PT5, exposure to gaseous chlorine is not expected, but through accidental events (chlorine can be formed and released when the active chlorine equilibrium is shifted to low pHs by strong acids, e.g. by mixing hypochlorite-based solutions with acidic cleaning agents).
In case of an accidental release of chlorine, two analytical methods ([12],[13]) for the monitoring of chlorine in workplace air are available in the CAR, 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. 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, hypochlorous acid/hypochlorite anion 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 the validation is not in accordance with the Additional

[12] 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
[13] 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

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.

Analytical method for residues in surface water

Residue definition: $HClO/ClO^-$

Not required. Environmental exposure is expected *via* the facility drain into the STP, but rapid degradation occurs with organic matter therein. Rapid degradation occurs also with the organic matter in surface water ($DT50_{surface\ water}$ = 56 min at environmental temperature).

Analytical method for residues in body fluids and tissues

Residue definition: $HClO/ClO^-$

Not required. Hypochlorous acid/ hypochlorite anion 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

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

Under PT5, fully-validated analytical methods for residues of both active chlorine ($HClO/ClO^-$) and the relevant metabolite chlorate (ClO_3^-) are requested for monitoring purposes in various matrices and for the estimation of human and animal exposure. Nevertheless, active chlorine degrades rapidly in contact with food matrices, hence the request for analytical methods for their residues in food/feeding stuff cannot be met, but for chlorate only. Methods should be submitted at the latest six months before the active substance approval.

2.1.2. Intended Uses and Efficacy

Sodium hypochlorite, as active chlorine releaser, has strong bactericidal, fungicidal, sporicidal and virucidal activity. It has also been reported to inactivates prions (Block 5th edition, Ch. 33 page 659 – S. Prusiner *et al*. Decontamination procedures). However, as for mycobacteria, such activity has not been supported by targeted tests for the purpose of this dossier.

Field of use envisaged
The use assessed belongs to the product-type 5:

- Drinking water disinfection

The "organism to be protected" is man. The aim of the treatment is to control spreading of infectious diseases (0.5 mg/L active chlorine).

Professional use only is envisaged.

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 hypochlorite are unspecific.

For bacteria it is shown that inactivation of spores need more drastic conditions than inactivation of viable forms. Biofilms consisting of bacteria are characterized by a high resistance against active chlorine and other biocides. Mycobacteria and fungi are more difficult to inactivate by active chlorine in comparison with bacteria. For viruses a wide range of inactivation conditions can be found. Prions can be inactivated by applying high concentrations and longer treatment times. In general higher temperatures and lower pH increase the efficiency of inactivation.

Efficacy studies from literature have been reported in Doc. IIIA using numerous different organisms, concentrations and test conditions. At low concentrations, active chlorine is still able to maintain the concentration of pathogens below a critical level. In this 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 in which the disinfectant activity was correctly demonstrated using Eau de Javel 12°Cl (about 3.6 % available chlorine) and a product containing 2.74% available chlorine as product tests. Concentration of available chlorine showing bactericidal, fungicidal, sporicidal and virucidal action ranged between 3.6 and 3600 mg/L, depending on the organisms tested, conditions of the tests, etc. (studies IIIB 05.10.01 to 05.10.12). 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.

Acceptable studies from the literature have been provided that support the efficacy of the a.s. also at much lower concentrations, specifically those indicated for PT2 and PT5 applications.

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

Current classification

Sodium hypochlorite is listed on Annex VI, Table 3.1 of Regulation (EC) 1272/2008 (CLP Regulation, Index No 017-011-00-1).with the following classification and labelling:

Harmonized classification of "sodium hypochlorite, solution ...% Cl" active according to Annex VI, Table 3.1 of Regulation (EC) 1272/2008 (CLP)

Classification	
Hazard Class and Category	Skin Corr. 1B Aquatic Acute 1
Hazard Statement Codes	H314: Causes severe skin burns and eye damage. H400: Very toxic to aquatic life.
Suppl. Hazard Statement Code	EUH031: Contact with acids liberates toxic gas.
Labelling	
GHS Pictogram	GHS05, GHS09
Signal Word (Code)	Danger (Dgr)
Hazard Statement	H314: Causes severe skin burns and eye damage. H400: Very toxic to aquatic life.
Suppl. Hazard Statement Code	EUH031: Contact with acids liberates toxic gas.
Specific concentration limits	EUH031: C ≥ 5 %
As precautionary statements are not included in Annex VI of Regulation EC 1272/2008, no proposal is made.	

Proposed classification

Based on the results from toxicity and ecotoxicity studies performed for sodium hypochlorite solution according to Regulation EC 1272/2008 (CLP):

Proposed classification of "sodium hypochlorite, solution ...% Cl active"

Classification	
Hazard Class and Category	Skin Corr. 1B Aquatic Acute 1 Aquatic Chronic 1
Hazard Statement Codes	H314: Causes severe skin burns and eye damage. H400: Very toxic to aquatic life. H410: Very toxic to aquatic life with long-lasting effects.
Suppl. Hazard Statement Code	EUH031: Contact with acids liberates toxic gas.
Labelling	
GHS Pictogram	GHS05, GHS09
Signal Word (Code)	Danger (Dgr)
Hazard Statement	H314: Causes severe skin burns and eye damage. H400: Very toxic to aquatic life. H410: Very toxic to aquatic life with long-lasting effects.

Suppl. Hazard Statement Code	EUH031: Contact with acids liberates toxic gas.
Specific concentration limits, M factor	EUH031: C ≥ 5 % M=10 (H400) M=1 (H410)
As precautionary statements are not included in Annex VI of Regulation EC 1272/2008, no proposal is made.	

In June 2016, RAC decided to change the harmonized classification (acc. to Annex VI to CLP) with respect to the aquatic endpoints:

- for Aquatic Acute 1 (H400), an M-factor of 10 was assigned;
- classification as Aquatic Chronic 1 (H410) with M-factor of 1 was added.

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 sodium hypochlorite".

In water, sodium hypochlorite dissociates into the sodium cation (Na^+) and hypochlorite anion (ClO^-), which is characterised by its well-known irritating/corrosive effects. Further, hypochlorite is in equilibrium with hypochlorous acid (HClO) and chlorine (Cl_2). The remaining sodium cation is a physiologically-essential element and required in the intermediary metabolism. Hence, it cannot be regarded as a typical xenobiotic when entering the body.

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 sodium hypochlorite are not available, reference is made to the respective Euro Chlor data obtained with chlorine. 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 sodium hypochlorite and potential systemic effects are secondary to its direct irritating reactivity.

Absorption, distribution, metabolism and excretion

Oral administration of sodium hypochlorite
Two studies on the absorption, distribution, metabolism and excretion were conducted with [^{36}Cl]-radio-labelled test substance in rats (Abdel-Rahman, 1982). These studies suggest that after exposure via oral route, HClO 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%.

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 and inhalation administration
No data on ADME are available for dermal and inhalation exposure for the active chlorine releaser sodium hypochlorite.

Regarding dermal exposure, 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 sodium 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.

For consistency, the WG members also considered that the inhalation absorption values are not relevant due to the lack of systemic effects.

Acute Toxicity

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).

In the acute **inhalation** toxicity study (Anonymous, 1970), inactivity and lacrimation were evident at the dose of 10.5 mg avCl/L (1 h exposure). No deaths occurred (LC_0 >10.5 mg avCl/L). Thus, the LC_{50} was determined to be greater than 10.5 mg avCl/L.

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 4 for dusts and mists according to Annex I, notes to Table 1.1, paragraph c). However, in the case of sodium hypochlorite 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. >10.5 mg avCl/L.

Conclusion on acute toxicity
Based on the results of the studies performed with sodium hypochlorite solutions, sodium hypochlorite does not warrant classification for acute oral, dermal and inhalation toxicity.
Sodium hypochlorite is not legally classified with respect to acute oral, dermal and inhalation toxicity according to Regulation (EC) No 1272/2008 (CLP).

Irritation and Corrosivity

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 harmonized classification of "sodium hypochlorite, solution …% Cl active" is Skin Corr. 1B, H314.
Data on animal skin clearly indicate an irritating effect at 5% avCl and above. Animal studies showed eye irritation potential of sodium hypochlorite solutions. In addition to the available studies, the EU-RAR (2007), DAR (2009) and the REACh dossier provide a variety of animal and human studies which investigated the skin and eye irritation potential of hypochlorite

bleaches at different concentrations.

These results may support the former Specific Concentration Limits (SCL) obtained for sodium hypochlorite under Council Directive 67/548/EEC (DSD):

Concentration NaOCl (as avCl)	Classification (DSD)
Concentration ≥ 25%	C; corrosive; R34
10% ≤ Concentration < 25%	C ; corrosive; R34
5% ≤ Concentration < 10%	Xi; irritant; R36/38

However, these SCLs have not been transferred to Annex VI, Table 3.1 or 3.2 of Regulation (EC) 1272/2008 (CLP Regulation, Index No 017-011-00-1) and only Skin Corrosion 1B was assigned to "sodium hypochlorite, solution …% Cl active". For the purpose of classifying sodium hypochlorite mixtures/dilutions, it is generally assumed that the harmonized classification as Skin Corrosion 1B applies to a hypothetical 100% pure substance. Consequently, the generic concentration limits of the CLP triggering classification of the mixture as corrosive/irritant to the skin/eye apply to NaOCl mixtures.

In addition, sodium hypochlorite aerosols may be irritant to the respiratory tract. According to the Guidance on the Application of the CLP Criteria (Version 4.1, 2015, Chapter 3.8.2.5), a classification for corrosivity is considered to implicitly cover the potential to cause respiratory tract irritation. Consequently, no additional classification is required.

Sensitisation

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

Conclusion on skin sensitisation
On the basis of the data available it can be considered that sodium hypochlorite is not a skin sensitizer.
Sodium hypochlorite aerosols are not expected to be sensitizer to the respiratory tract.

Sodium hypochlorite is not legally classified with respect to skin or respiratory tract sensitisation according to Regulation (EC) No 1272/2008 (CLP).

Repeated dose toxicity

Oral administration of 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 hypochlorite decomposes rapidly after "port of entry" contact, only sodium or 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 sodium hypochlorite

No repeated dermal toxicity studies on the active chlorine releaser sodium hypochlorite are available. The conduction of a dermal repeated dose toxicity study is considered to be not necessary for the following reasons:

1) Due to its oxidative and corrosive nature sodium hypochlorite will cause skin destructions. These effects are considered to be of local nature due to the reaction of the substance with the surrounding tissue. Systemic toxicity would therefore occur only secondary to locally irritating effects. In the available studies there are no indications for any other mechanism of toxicity.
2) The irritant effect of sodium hypochlorite is caused by its oxidative property and basic nature of hypochlorite and its solutions, which create a high-pH environment on exposed body tissues. According to OECD 404 no tests should be performed with substances having a pH of 11.5 or higher which is the case for 5% and 14% concentrated sodium hypochlorite solutions. 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 is not required for animal welfare reasons. In addition, some human data exist (see in the following) from which it is possible to derive a NOAEC.

Administration of sodium hypochlorite via inhalation

There is no repeated dose inhalation toxicity study on sodium hypochlorite available. An inhalation study is considered to be not necessary due to the following reasons:

1) Due to the intrinsic properties of the test substance and to its high reactivity the mechanism of action of sodium hypochlorite is restricted to primary local effects like irritation, corrosion and oxidation after contact with surrounding tissue which are shown by the acute dermal irritation and eye irritation study.
2) Systemic toxicity after inhalation exposure towards sodium hypochlorite would therefore occur only secondary to locally irritating effects mainly caused by the local oxidation and basic nature of hypochlorite and its solutions. The remaining sodium and chloride ions are physiologically essential elements and are required in the intermediary metabolism and can therefore not be regarded as typical xenobiotics when entering the body. In the available studies there are no indications for any other mechanism of toxicity.

For the evaluation of local effects of repeated inhalation exposure to sodium hypochlorite aerosols, the EU-RAR (2007) proposed to use data from chlorine gas. The NOAEC for repeated exposure was derived at 0.5 ppm available chlorine (1.5 mg/m^3) based on human studies.

Given the similar chemical reactivity based on the same active principle (i.e. the reactions of the hypochlorite ion), use of chlorine data is also justified for evaluating local effects of sodium hypochlorite after inhalation exposure. Therefore, relevant studies performed with chlorine gas are summarized in the following.

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. The NOAEC of <0.4 ppm (<1.2 mg/m³) 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 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. corrosion/irritation at first site of contact). NOAECs in the range of <0.4 ppm to 1.0 ppm (<1.2 mg/m³ to 3.0 mg/m^3) were derived from the rat and mice studies, whereas a NOAEC 0.5 ppm (1.5 mg/m³) was derived from the monkey study.

Genotoxicity

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, no genotoxic potential of sodium hypochlorite is expected.

Carcinogenicity

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.

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

Reproductive toxicity

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.

Based on the available data, no prenatal developmental toxicity potential of sodium hypochlorite is expected.

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).

Based on the available data, no reproductive toxicity potential of sodium hypochlorite is expected.

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, no prenatal developmental and reproductive toxicity potential of sodium hypochlorite is expected.

Neurotoxicity

Special neurotoxicity studies were not performed with the active chlorine releaser sodium hypochlorite. There is no evidence of a neurotoxic effect from other acute, subacute, subchronic and chronic studies with 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

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 related to exposure

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 sodium hypochlorite".

In water, sodium hypochlorite dissociates into the sodium cation (Na^+) and hypochlorite anion ($ClO^–$), which is characterised by its well-known irritating/corrosive effects. Further, hypochlorite is in equilibrium with hypochlorous acid (HClO) and chlorine (Cl_2). The remaining sodium cation is a physiologically-essential element and required in the intermediary metabolism. Hence, it cannot be regarded as a typical xenobiotic when entering the body.

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.

As outlined above, the primary effect of sodium hypochlorite is driven by the corrosive/irritant properties caused by the local reaction of the hypochlorite ion. Studies on the acute toxicity, irritation and sensitization potential as well as repeated dose toxicity, reproductive/prenatal developmental toxicity, genotoxicity and carcinogenicity are available on sodium hypochlorite; missing data for inhalation exposure in chronic studies relevant for the derivation of the reference values can be replaced by data obtained from chlorine, by applying the read-across principles.

On the basis of acute toxicity data, sodium hypochlorite is not toxic via the oral, dermal or inhalation route.

Concerning the dermal route, sodium hypochlorite has to be classified as corrosive (Skin Corr. 1B, "Causes severe skin burns and eye damage"; H314) according to Annex VI, Regulation (EC) No 1272/2008 (CLP; harmonized classification).

Sodium hypochlorite 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 NaOCl, HClO and chlorate

The mode of action of NaOCl 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, sodium hypochlorite 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 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 NaOCl or HClO, all (in-use) concentrations are expressed as available chlorine (avCl; w/w) and not as NaOCl (w/w) or HClO (w/w). Hence, exposure towards NaOCl or HClO should be compared with the relevant AECs for available chlorine and not with the AECs for NaOCl of HClO itself.

NaOCl: $NOAEC_{dermal}$

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% and above (Nixon, 1975). Lower values (around 2%) 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 chlorine) shows irritant properties at concentration >1%, which was agreed by the WGII-2016 meeting.

$NOAEC_{dermal}$ to be used for risk characterization of NaOCl:

$NOAEC_{dermal}$ = 1% avCl

NaOCl: $AEC_{inhalation}$

The BPC TOX WGIII-2016 finally agreed to derive the $AEC_{inhalation}$ for NaOCl 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) 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).

It is anticipated that the use of data on chlorine gas is likely to be a conservative assessment of the potential effects of NaOCl aerosol as under real case conditions only a low proportion of the product is in the respirable range. This is in line with the conclusions of the EU RAR on NaOCl (2007, p. 217f).

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 NaOCl 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 NaOCl was not considered to have systemic effects.

Based on these considerations, the $AEC_{inhalat\ on}$ for NaOCl 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 NaOCl:

$AEC_{inhalation}$ (NaOCl as avCl) = 1.5 mg avCl/m³ / 3.2 ≈ 0.5 mg avCl/m³

NaOCl: $NOAEC_{oral}$

Sodium hypochlorite is not classified as acutely toxic by the oral route. 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 NaOCl, 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) were proposed as point of departure to derive an oral NOAEC.

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 NaOCl:

$NOAEC_{oral}$ = 0.1% avCl

HClO: $AEC_{inhalation}$

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 HOCl 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.

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/m³) as derived based on the rhesus monkey ([redacted] 1987) 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.

It should be noted that in this CAR on NaOCl, all (in-use) concentrations are expressed as available chlorine (avCl; w/w) and not as NaOCl (w/w) or HClO (w/w). Hence, HClO concentrations should also be expressed as available chlorine and exposure towards HClO be compared with the $AEC_{inhalat\ on}$ for (available) chlorine (and not with an $AEC_{inhalat\ on}$ for HClO).

Based on the NOAEC of 0.5 ppm avCl (1.5 mg avCl/m³) and applying the same consideration as for deriving the $AEC_{inhalation}$ for NaOCl, 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/m³ / 3.2 ≈ 0.5 mg avCl/m³

Chlorate

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 NaOCl. 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 NaOCl 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 chlorate is a by-product of the manufacturing process and can be formed during storage. Thus, chlorate may represent a worst-case for NaOCl 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 2.2.1.1-1: Summary of reference values

Substance	Exposure route	Reference value
NaOCl	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
	Oral	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

Sodium hypochlorite is used in professional settings in PT5. Intended uses are summarised in the table below.

Table 2.2.1.2-1: Intended uses of sodium hypochlorite in PT5

MG1/PT5	Field of use envisaged	Likely concentration at which sodium hypochlorite (calculated as available chlorine) will be used
	Drinking water disinfection (large scale chlorination) – professional use	0.5 mg/L

General considerations on exposure and risk assessment

Primary exposure

The primary mode of action of NaOCl is characterised by local irritation/corrosion and oxidation at the site of first contact triggered by direct chemical reactivity without prior metabolism. NaOCl does 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 was 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 PT5, the Guidance on the BPR, Volume III Human Health – Part B Risk Assessment (vers. 2.0, Oct. 2015) was followed for the local assessment of theoretical product 1 (NaOCl 14% w/w avCl).

Dermal exposure: For the dermal route of exposure, a semi-quantitative (Tier-1) assessment, and if required (i.e. in case the dermal NOAEC is exceeded in Tier-1), a qualitative (Tier-2) assessment was performed.

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

Inhalation exposure: For the inhalation route of exposure, a quantitative assessment (Tier-1 and Tier-2) is performed. Exposure towards aerosol (NaOCl as avCl) and vapour (HClO as avCl) is conceivable. Additionally, a qualitative assessment was performed for secondary exposure scenarios in case the quantitative assessment led formally to an unacceptable use.

According to Doc. IIIB, Section B3, a 5.4% NaOCl (as avCl) product has a pH of 12.5. The respective 1% (in-use) solution (corresponding to 0.05% avCl) has a pH of 10.3. Hence, both theoretical products (5% and 14%) and their relevant in-use dilutions are expected to have a pH > 10.

At pH values > 10, the hypochlorite anion (ClO^-) is the predominant species and only exposure to aerosols of NaOCl (as avCl) 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 avCl) is considered relevant.

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.

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 treated surfaces is considered to be non-relevant. Due to the high reactivity of chlorine species such as NaOCl, residues on surfaces degrade very rapidly. Decomposition to

physiological sodium and chloride ions takes place which are not expected to arise any health risk. Furthermore, the applied in-use solutions are of a low concentration and/or are further diluted during the water-rinse procedure which takes normally place. Hence, residue formation and chronic secondary exposure is assumed to be negligible for aqueous solutions of NaOCl.

Therefore, with the exception of the drinking water consumption and showering scenario, only inhalation exposure after application of NaOCl solutions is considered to be relevant for the assessment of secondary exposure.

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 NaOCl. 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 NaOCl 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 chlorate is a by-product of the manufacturing process and can be formed during storage. Thus, chlorate may represent a worst-case for NaOCl 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 authorisation.

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

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).

Risk mitigation measures and personal protective equipment

As described above, a (semi-)quantitative local risk assessment was performed for the dermal route of exposure. In case this (semi-)quantitative risk assessment leads to an unacceptable use, a qualitative assessment was performed in addition (according to Guidance on the BPR, Volume III, Part B, Vers. 2.0, October 2015).

For professional users, risk mitigation measures (RMM) and personal protective equipment (PPE) were considered (in line with the guidance).

Primary exposure assessment and risk characterisation – professionals

Taking into account the considerations as outlined above, exposure and risk of professionals handling sodium hypochlorite for disinfection of drinking water were assessed and are summarised in Table 2.2.1.2-2.

Drinking water disinfection (large scale chlorination) – professional use

Dermal and inhalation exposure of the worker occurs during mixing & loading, i.e. when containers are connected or disconnected to the automated pumping system or when the hypochlorite solution is pumped into the circuit. Exposure via the dermal route results in 1400% $NOAEC_{dermal.}$ Thus, a qualitative local risk assessment was performed for the dermal route of exposure (please refer to the section "Qualitative local risk assessment for dermal route of exposure" below). Inhalation exposure towards aerosols results in 61.6% of the AEC_{inhal} when considering RPE10.

The hypochlorite solution is then automatically dosed into the system, thus no exposure to operator/worker is expected during the application process.

The post-application phase comprises several tasks. Empty containers are screwed down, stored and finally disposed of. As only minor amounts remain in the containers, exposure to

sodium hypochlorite from empty containers is negligible, and thus considered not relevant.

Dermal and inhalation exposure can occur during maintenance of the pumping system (contact to concentrated product) and during maintenance of the circuit system (contact to in-use dilution). For the maintenance of the pumping system, exposure via the dermal route results in 1400% of the $NOAEC_{dermal}$. Thus, a qualitative local risk assessment was performed for the dermal route of exposure (please refer to the section "Qualitative local risk assessment for dermal route of exposure" below). Inhalation exposure results in 26.3% of the AEC_{inhal}.

For the maintenance of the circuit system, exposure via the dermal route results in 0.005% of the $NOAEC_{dermal}$ and 0.0001% AEC_{inhal}, respectively.

In conclusion, primary exposure during human drinking water disinfection is acceptable without PPE for tasks with exposure to the in-use dilution (i.e. maintenance of the circuit system), and with PPE/RPE for tasks with exposure to the concentrated product (i.e. mixing and loading, maintenance of pumping system).

Qualitative local risk assessment for dermal route of exposure

A (semi-)quantitative local risk assessment was performed for the dermal route of exposure.

For the following scenarios this (semi-)quantitative risk assessment led to an unacceptable use:

- *Drinking water disinfection (large scale chlorination) – professional use: M/L phase, contact to concentrate during maintenance*

Therefore, a qualitative assessment was performed in addition according to Guidance on the BPR, Volume III, Part B, Vers. 2.0, October 2015 (Table 2.2.1.2-3).

According to the Guidance on BPR, 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 NaOCl in the in-use dilution is below the classification trigger for local irritant effects (1% for skin and eyes), and moreover below the $NOAEC_{dermal}$ of 1% avCl.

In conclusion, when considering the application of risk mitigation measures (RMM) and personal protective equipment (PPE/RPE) as described, the mixing and loading for the intended use is acceptable.

Table 2.2.1.2-2: Results of exposure assessment and risk characterisation for the primary exposure of professionals.

Intended use	Task	Oral		Dermal		Inhalation		PPE	Acceptable yes/no
		Exposure (NaOCl as avCl)	**%AEC NOAEC$_{oral}$ 0.1% avCl**	**Exposure** (NaOCl as avCl)	**%AEC NOAEC$_{dermal}$ 1% avCl**	**Exposure** (total as mg avCl/m^3)	**%AEC NOAEC$_{inhal}$ 0.5 mg/m^3 avCl**		
PT5: Drinking water disinfection (large scale chlorination) – professional use	Mixing & loading	n.r.	n.r.	14%	1400%	3.08 (no RPE) 0.31 (RPE 10)	616% (no RPE) 61.6% (RPE 10)	gloves, goggles, protective clothing, closed footwear RPE10	yes (with PPE)
	Application	no exposure	n.r.	no exposure	n.r.	no exposure	n.r.	-	yes
	Post-application (Handling of empty containers)	n.r.	n.r.	negligible	n.r.	negligible	n.r.	-	yes
	Post-application (Maintenance of circuit system)	n.r.	n.r.	0.00005	0.005%	0.0000005	0.0001%	none	yes
	Post-application (Maintenance of pumping system)	n.r.	n.r.	14%	1400%	0.132	26.3%	gloves, goggles, protective clothing, closed footwear	yes (with PPE)

Table 2.2.1.2-3: Qualitative local risk assessment for the professional use in PT5 – mixing and loading/post-application of theoretical product 1 (14% avCl)

Hazard			Exposure							Risk
Hazard Category	**Effects in terms of C&L**	**Additional relevant hazard information**	**PT**	**Who is exposed?**	**Tasks, uses, processes**	**Potential exposure route**	**Frequency and duration of potential exposure**	**Potential degree of exposure**	**Relevant RMM&PPE**	**Conclusion on risk**
High	Skin Corr 1B (H314)	-	5	Industrial and professional users	M&L Connecting containers containing theoretical product 1 to automated dosing system (14% avCl) Post-application - Maintenance Repair of broken dosing system/pump; contact to concentrate (14% avCl)	Skin Eye	M&L few minutes per day Post-application - Maintenance as required	14% avCl (splashes, hand to eye transfer)	**RMM** Labelling • Labelling according to CLP Formulation • Product formulation which reduces splashes Trained personnel • Trained workers • Containment as appropriate • Good standard of general ventilation • Regular cleaning of equipment and work area • Avoidance of contact with contaminated tools and objects **PPE** Hand protection: Suitable chemical resistant safety gloves (EN 374).	**Acceptable** + Engineering controls; + Low frequency; + Short duration; + Professionals using PPE; + Professionals following instructions for use; + Good standard of personal hygiene.

									<u>Eye protection:</u> Safety goggles (EN 166) <u>Body protection:</u> Protective clothing and closed footwear. Body protection must be chosen based on level of activity and exposure.	

Indirect exposure assessment and risk characterisation

Due to the high reactivity of chlorine species such as hypochlorite, 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 is assessed. Due to the rapid chemical degradation and the local mode of action, only acute secondary scenarios are considered relevant.

Indirect exposure of professionals

Indirect exposure of professionals is summarised in **Error! Reference source not found.**.

Secondary inhalation exposure of professional bystanders during mixing and loading

Secondary inhalation exposure of professional bystanders during mixing and loading is considered relevant for the following use:

- *Drinking water disinfection (large scale chlorination)*

Quantitative assessment for inhalation exposure of professional bystanders during mixing & loading tasks results in 616% of the AEC_{inhal}. Thus, a qualitative local risk assessment was performed for the inhalation route of exposure (please refer to the section "Qualitative local risk assessment for inhalation route of exposure" below).

Table 2.2.1.2-4: Results of exposure assessment and risk characterisation for the secondary exposure of professionals

Intended use	Task	Oral		Dermal		Inhalation		PPE	Acceptable yes/no
		Exposure (NaOCl as avCl)	%AEC $NOAEC_{oral}$ 0.1% avCl	Exposure (NaOCl as avCl)	%AEC $NOAEC_{dermal}$ 1% avCl	Exposure (total as mg avCl/m^3)	%AEC AEC_{inhal} 0.5 mg/m^3 avCl		
PT5: Secondary inhalation exposure of professional bystanders during M&L tasks	Mixing & loading	n.r.	n.r.	n.r.	n.r.	3.08	616%	see qualitative local risk assessment	yes (with PPE)

Qualitative local risk assessment for inhalation route of exposure

A quantitative local risk assessment was performed for the inhalation route of exposure.

For the following scenario this quantitative risk assessment led to an unacceptable risk:

- *Drinking water disinfection (large scale chlorination) – professional use: bystander during M/L phase*

Therefore, a qualitative assessment was performed in addition according to Guidance on the BPR, Volume III, Part B, Vers. 2.0, October 2015 (Table 2.2.1.2-35).

According to the Guidance on BPR, 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 NaOCl in the in-use dilution is below the classification trigger for local irritant effects (1% for skin and eyes), and moreover below the $NOAEC_{dermal}$ of 1% avCl.

The intended use for sodium hypochlorite is in the professional/industrial setting only. Thus, the application of PPE/RPE for bystanders during mixing and loading is considered acceptable.

In conclusion, when considering the application of risk mitigation measures (RMM) and personal protective equipment (PPE/RPE) as described, the exposure of bystanders during mixing and loading for the intended use is acceptable.

Table 2.2.1.2-5: Qualitative local risk assessment for professional bystanders during M&L tasks (14% avCl)

Hazard			Exposure							Risk
Hazard Category	**Effects in terms of C&L**	**Additional relevant hazard information**	**PT**	**Who is exposed?**	**Tasks, uses, processes**	**Potential exposure route**	**Frequency and duration of potential exposure**	**Potential degree of exposure**	**Relevant RMM&PPE**	**Conclusion on risk**
High	Skin Corr 1B (H314)	-	5	Industrial and professional users	M&L Connecting containers containing theoretical product 1 to automated dosing system (14% avCl)	Inhalation	M&L few minutes per day	3.08 mg avCl /m³ (NaOCl aerosol, as avCl)	**RMM** Labelling • Labelling according to CLP Formulation • Product formulation which reduces splashes Trained personnel • Trained workers • Containment as appropriate • Good standard of general ventilation • Regular cleaning of equipment and work area • Avoidance of contact with contaminated tools and objects **PPE** Hand protection: Suitable chemical resistant	**Acceptable** + Engineering controls; + Low frequency; + Short duration; + Professional bystander is expected to use the same set of PPE as professional user; + Professionals following instructions for use; + Good standard of personal hygiene.

									safety gloves (EN 374). Eye protection: Safety goggles (EN 166) Body protection: Protective clothing and closed footwear. Body protection must be chosen based on level of activity and exposure. Respiratory protection: The professional bystander needs to observe the same set of PPE as the worker: i.e. (half) mask with at least 90% protection (RPE 10).	

Indirect exposure of the general public

Indirect exposure of the general public is summarised in Table 2.2.1.2-6.

Secondary oral, dermal and inhalation exposure of the general public during showering with chlorinated water

The general public is exposed to chlorine species during showering with chlorinated drinking water; this is considered relevant for the following use:

- *Disinfection of drinking water (large scale chlorination) – 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.

As chlorinated drinking water has a near neutral pH (between 6.5 and 9.5 according to Council Directive 98/83/EC). At this pH value, hypochlorous acid (HClO) is the predominant species and exposure to vapours of HClO (as avCl) is considered relevant.

Additionally, exposure to aerosols of NaOCl (as avCl) was estimated to account for splashes during showering. For evaporation estimation, the vapour pressure of HOCl was calculated as outlined in the LoEP, Chapter 3.

Semi-quantitative assessment for oral and dermal exposure of the general public results in 0.05% of the $NOAEC_{oral}$ and 0.005% of the $NOAEC_{dermal}$, respectively. Quantitative assessment for inhalation exposure results in 0.5% of the AEC_{inhal}.

Secondary oral exposure of the general public by consumption of chlorinated drinking water

The general public is exposed to chlorine species by consumption of chlorinated drinking water; this is considered relevant for the following use:

- *Disinfection of drinking water (large scale chlorination) – professional use*

A semi-quantitative exposure assessment was performed for oral exposure of the general public which results in 0.05% of the $NOAEC_{oral}$.

Table 2.2.1.2-6: 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 (NaOCl as avCl)	**%AEC NOAEC$_{oral}$ 0.1% avCl**	**Exposure** (NaOCl as avCl)	**%AEC NOAEC$_{dermal}$ 1% avCl**	**Exposure** (total as mg avCl/m^3)	**%AEC NOAEC$_{inhal}$ 0.5 mg/m^3 avCl**	
PT5: Secondary oral, dermal and inhalation exposure of the general public during showering with chlorinated water	Application	0.00005%	0.05%	0.00005%	0.005%	0.0025	0.5%	yes
PT5: Secondary oral exposure of the general public by consumption of chlorinated drinking water	Application	0.00005%	0.05%	n.r.	n.r.	n.r.	n.r.	yes

Livestock exposure assessment

It has to be noted that the "Guidance on Estimating Livestock Exposure to Active Substances used in Biocidal Products" of Dec. 2010 is currently under revision by ARTFood and should normally not be used. Moreover, ARTFood noted in their project plan of Feb. 2014 that it will be closely linked to the EMA "Guideline on risk characterization and assessment of maximum residue limits (MRL) for biocides" (2015). However, the practical implementation remains still unclear (see Annex reported below).

To be noted that the assessment was based on the concentration of chlorate according to the sodium hypochlorite specification, but the potential generation of chlorate during or post application was not considered.

Dietary risk assessment

Currently, no agreed and published guidance is available for the estimation of dietary risk from transfer of biocidal active substances into food in professional settings. Thus, no dietary risk assessment can be provided at this stage for the intended uses of the active chlorine releaser NaOCl in PT5 (see Annex reported below).

Assessment of disinfection-by-products

During the BPC TOX-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 sodium hypochlorite. The primary mode of action of NaOCl is characterised by local irritation/corrosion and oxidation at the site of first contact; thus effects triggered by NaOCl 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 characterisation 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.

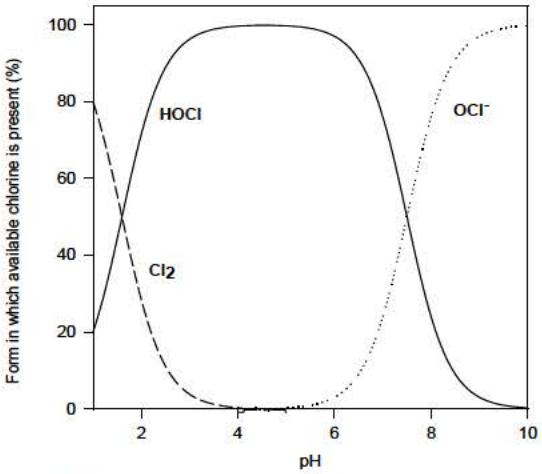
Conclusion

Based on the results obtained in the (semi-)quantitative and qualitative exposure and risk assessments, exposure of professional users in the intended uses within PT5 results in no unacceptable risk.

The same conclusion applies to secondary exposure of professional bystanders/non-users and the general public potentially exposed via food.

2.2.2. Environmental Risk Assessment

The active substance released from sodium hypochlorite 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. No. 989-003 Doc. IIIA, Section A7.1.2
Surface water/ Sediment	20 min (*)	**56 min**	Worst case assumption, based on the kinetic model of

Compartment	DT_{50} of hypochlorite measured in tests	DT_{50} of hypochlorite transferred to an environmental temperature of **12°C** (by Arrhenius)	Reference
			Vandepitte and Schowanek (1997), 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, Section 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 sodium hypochlorite have to be assessed in the exposure and risk assessments. The calculated PEC values, according to the ESD 5, and the corresponding PEC/PNEC ratios are reported in the tables below.

Aquatic compartment (incl. sediment)

Surface water

An overview on the results of the surface water risk assessment for active chlorine released from sodium hypochlorite is provided in Table 2.2.2.2-01.

Table 2.2.2.2-01: Calculated PEC/PNEC for the aquatic compartment

Exposure scenario	$PNEC_{sw}$ = 4.2 x 10^{-5} mg/L	
	PEC_{sw} [mg/L]	$PEC/PNEC_{sw}$
PT5		
PT5 – Drinking water disinfection (large scale chlorination)	2.80 x 10^{-22}	6.67 x 10^{-18}

The above results show that for the application of chlorine released from sodium hypochlorite in PT5 the requirements for acceptable risk are met according to the TGD on Risk Assessment: the PEC/PNEC value is below the trigger value of 1.

Freshwater sediment

An overview on the results of the freshwater sediment risk assessment for active chlorine released from sodium hypochlorite is provided in Table 2.2.2.2-02.

Table 2.2.2.2-02: Calculated PEC/PNEC for the sediment compartment

Exposure scenario	$PNEC_{sed}$ = 4.5 x 10^{-5} mg/kg_{wwt}	
	PEC_{sed} [mg/kg]	$PEC/PNEC_{sed}$
PT5		
PT5 – Drinking water disinfection (large scale chlorination)	3.00 x 10^{-22}	6.66 x 10^{-18}

The above results show that for the application of chlorine released from sodium hypochlorite in PT5 the requirements for acceptable risk according to the TGD on Risk Assessment are met: the PEC/PNEC value is below the trigger value of 1.

Sewage treatment plant

An overview on the results of the STP risk assessment for active chlorine released from sodium hypochlorite is provided in Table 2.2.2.2-03.

Table 2.2.2.2-03: Calculated PEC/PNEC for sewage treatment plant (STP)

Exposure Scenario	$PNEC_{STP}$ = 4.11mg/L	
	PEC_{STP} [mg/L]	$PEC/PNEC_{STP}$
PT5		
Drinking water disinfection (large scale chlorination)	2.80 x 10^{-21}	6.82x 10^{-22}

The above results show that for the application of chlorine released from sodium hypochlorite in PT5 the requirements for acceptable risk according to the TGD on Risk Assessment are met: the PEC/PNEC value is 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 annual average PEC in air after use of chlorine released from sodium hypochlorite in PT5 was calculated to be 3.72 x 10-27 mg/m³.

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

An overview on the results of the soil risk assessment for active chlorine released from sodium hypochlorite is provided in Table 2.2.2.2-04.

Table 2.2.2.2-04: Calculated PEC/PNEC for the soil compartment

Exposure scenario	**$PNEC_{soil}$ = 1.5 x 10^{-5} mg/kg**	
	PEC_{soil} [mg/kg]	**$PEC/PNEC_{soil}$**
PT5		
Drinking water disinfection (large scale chlorination)	3.59 x 10^{-7}	2.39 x 10^{-22}

The above results show that for the application of chlorine released from sodium hypochlorite in PT5 the requirements for acceptable risk according to the TGD on Risk Assessment are met: the PEC/PNEC value is below the trigger value of 1.

The risk assessment for groundwater was based on the limit value of 0.1 µg/L and the product type specific PEC for groundwater as calculated in the exposure assessment (see Doc. IIB, Chapter 3.3.6).

An overview on the results of the soil risk assessment for chlorine released from sodium hypochlorite is provided in Table 2.2.2.2-05.

Table 2.2.2.2-05: Calculated PEC/Limit value for groundwater

Exposure scenario	**Limit value= 0.1 µg/L**	
	PEC_{gw} [µg/L]	**PEC/limit value**
PT5		
Drinking water disinfection (large scale chlorination)	<< 0.1	<< 1

The above results show that for the application of chlorine released from sodium hypochlorite in PT5 the requirements for acceptable risk according to the TGD on Risk Assessment are met.

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 1-5 = 2.4 10^{-15} mg/L	

Aggregate e 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 1-5 = 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 1-5 = 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 1-5 = 8.6 10^{-20} 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

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).
The kinetic model of Vandepitte and Schowanek 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 x 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 in 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 x 10^{-10} µg/L in the river.
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 of hypochlorite in soil is a reduction to chloride.
At environmental pH values (6.5-8.5) half of the active chlorine is present in the un-dissociated 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.

Active 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.

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 sodium hypochlorite.

2.2.3. Assessment of endocrine disruptor properties

Based on the available experimental results, there is no indication that active chlorine released

from sodium hypochlorite affects the endocrine system. Structural characteristics and SAR do not hint to possible effects of active chlorine released from sodium hypochlorite as endocrine disruptor.

2.3. Overall conclusions

The outcome of the assessment for active chlorine released from sodium hypochlorite in product-type 5 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, a full study report on pH and alkalinity are necessary. As regards technical characteristics which are relevant for SL products, also dilution stability should be addressed. Moreover, a long-term storage stability study needs to be provided in support of the shelf-life claim, including the determination prior to and after storage of sodium chlorate (relevant impurity) by a validated method of analysis. Also the effect of temperature, the effect of light, the low temperature stability 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 sodium hypochlorite When diluted in water upon use, sodium hypochlorite 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	5

Identity of the releaser, i.e. sodium hypochlorite

Chemical name (IUPAC)	Sodium hypochlorite
Chemical name (CA)	Hypochlorous acid, sodium salt
CAS No	7681-52-9
EC No	231-668-3
Other substance No.	017-011-00-1 (Index number)
Purity of the active substance as manufactured (g/kg or g/l)	Aqueous solution with an available (active) chlorine concentration ≤18% w/w ([14]), in compliance with the EN 901:2013
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	Sodium chlorate (relevant impurity): ≤5.4% of the active chlorine Sodium hydroxide (additive)
Molecular formula	ClHO.Na
Molecular mass	Na^+ Cl — O^-
Structural formula	74.44 g/mol

([14]) Due to its instability as a pure salt, sodium hypochlorite is manufactured and handled only as aqueous solution, with a pH value greater than 11 at 20°C. Solutions are kept alkaline in order to decrease the degradation rate of the hypochlorite to chloride and chlorate.
Sodium hypochlorite is determined by a titrimetric method. Results are tipically expressed as available (active) chlorine using by convention the molecular weight of elemental chlorine in calculations, but they can be converted into sodium hypochlorite by applying a conversion factor of 1.05 (MW_{NaOCl} /MW_{Cl2} = 74.44/70.91).

Physical and chemical properties of the releaser, i.e. sodium hypochlorite

Freezing point (state purity)	-28.9±0.5 °C (24.3% w/w active chlorine)
Boiling point (state purity)	Water evaporated when heating the sodium hypochlorite aqueous solution (24.3% w/w active chlorine), white crystals were observed on the bottom of the test vessel
Thermal stability / Temperature of decomposition	Not determined, since sodium hypochlorite in its pure form is highly unstable
Appearance (state purity)	Yellow limpid liquid (24.3% w/w active chlorine), with faint chlorinous odour (according to EN 901:2013)
Relative density (state purity)	$D^{21.2}_4$ = 1.300 ± 0.001 (24.3% w/w active chlorine)
Surface tension (state temperature and concentration of the test solution)	82.4 ± 0.8 mN/m at 20.2-20.3 °C (24.3% w/w active chlorine)
Vapour pressure (in Pa, state temperature)	ca. 2.5 x 10^3 Pa at 20°C for sodium hypochlorite aqueous solutions (according to EN 901:2003) At pH >11 the hypochlorite anion is the predominant species. As an ionic species, the hypochlorite anion has high water solubility and is unlikely to evaporate from the aqueous solution. Thus, it can be assumed that the hypochlorite anion has a vapour pressure significantly less than 10^{-5} Pa
Henry's law constant (Pa m^3 mol^{-1})	Not derived for sodium hypochlorite (expected to be negligible, based on vapour pressure and solubility in water) 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 PT 5
Solubility in water (g/l or mg/l, state temperature)	26 g sodium hypochlorite/100 g H_2O at 0°C (CRC Handbook of Chemistry and Physics)
Solubility in organic solvents (in g/l or mg/l, state temperature)	Not relevant. Sodium hypochlorite is not used in organic solvents, due to its nature as a strong oxidant
Stability in organic solvents used in biocidal products including relevant breakdown products	Not relevant. Sodium hypochlorite is not used in organic solvents, due to its nature as a strong oxidant
Partition coefficient (log P_{OW}) (state temperature)	Not required for inorganic substances such as sodium hypochlorite

Dissociation constant	In water, sodium hypochlorite hydrolyses according to: $NaClO + H_2O \leftrightarrow Na^+ + HClO + OH^-$ $K_{hydrolysis}(ClO^-) = K_w/K_a$ where $K_a(HClO) = 3.5 \times 10^{-8}$ mol/dm^3 at 20°C Further, the hypochlorous acid (HClO) participates in the following equilibrium: $HClO + H_3O^+ + Cl^- \leftrightarrow Cl_2 + 2H_2O$ $K_{hydrolysis}(Cl_2) = 3.2 \times 10^{-4}$ mol/dm^3 at 20°C
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Not determined, since sodium hypochlorite in its pure form is highly unstable
Flammability or flash point	Flash-point > 110°C (24.3% w/w active chlorine) Sodium hypochlorite solutions are not known to spontaneously ignite when exposed to air or to emit flammable gases
Explosive properties	New test for explosives according to the UN Recommendation on the Transport of Dangerous Goods, Manual of Tests and Criteria needs to be provided (at the maximum available concentration of sodium hypochlorite in water), at the latest six months before the date of approval
Oxidising properties	New test for oxidising liquids according to the UN Recommendation on the Transport of Dangerous Goods, Manual of Tests and Criteria needs to be provided (at the maximum available concentration of sodium hypochlorite in water), at the latest six months before the date of approval
Auto-ignition or relative self ignition temperature	Not required for liquids non flammable in air such as sodium hypochlorite aqueous solutions

Classification and proposed labelling, of the releaser, i.e. sodium hypochlorite

In June 2016, RAC decided to change the harmonized classification (acc. to Annex VI to CLP) with respect to the aquatic endpoints:

- for Aquatic Acute 1 (H400), an M-factor of 10 was assigned;
- classification as Aquatic Chronic 1 (H410) with M-factor of 1 was added.

with regard to physical hazards	No classification
with regard to human health hazards	Danger GHS05 H314: Causes severe skin burns and eye damage
	EUH031: Contact with acids liberates toxic gas C ≥ 5 %

with regard to environmental hazards	Danger GHS09 H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long-lasting effects
	M=10 (H400) M=1 (H410)

Chapter 2: Methods of Analysis

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

Active substance (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). Results expressed as active chlorine can be converted into sodium hypochlorite by applying a conversion factor of 1.05
Impurities in the releaser (principle of method)	Fully-validated analytical methods are to be provided to the eCA-IT at the latest six months before the date of approval

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)	Not required. In case of accidental release of chlorine, analytical methods for the monitoring of chlorine in workplace air (a, b) are available: 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)	In principle, under PT5 fully-validated analytical methods for residues of both the active chlorine ($HClO/ClO^-$) and the relevant metabolite chlorate (ClO_3^-) are requested for monitoring purposes in various matrices and for the estimation of human and animal exposure. Nevertheless, active chlorine degrades rapidly in contact with food/feed matrices, hence the request cannot be met, but for chlorate only. Methods should be submitted at the latest six months before the active substance approval
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	In principle, under PT5 fully-validated analytical methods for residues of both active chlorine ($HClO/ClO^-$) and the relevant metabolite chlorate (ClO_3^-) are requested for monitoring purposes in various matrices and for the estimation of human and animal exposure. Nevertheless, active chlorine degrades rapidly in contact with food/feed matrices, hence the request cannot be met, but for chlorate only. Methods should be submitted at the latest six months before the active substance approval

Chapter 3: Impact on Human Health

In water, sodium hypochlorite dissociates into the sodium cation (Na^+) and hypochlorite anion (ClO^-), which is characterised by its well-known irritating/corrosive effects. Further, hypochlorite is in equilibrium with hypochlorous acid (HClO) and chlorine (Cl_2). The remaining sodium cation is a physiologically-essential element and required in the intermediary metabolism. Hence, it cannot be regarded as a typical xenobiotic when entering the body.
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:	The BPC TOX-WGIII-2016 agreed that human health effects are primarily due to the local mode of action of hypochlorite and potential systemic effects are secondary to its direct irritating reactivity Consequently, oral absorption of sodium hypochlorite is not relevant Regarding oral absorption of sodium ions, high sodium intakes are not expected to be associated with severe health effects as sodium ions are natural physiological metabolites
Rate and extent of dermal absorption*:	The BPC TOX-WGIII-2016 agreed that human health effects are primarily due to the local mode of action of hypochlorite and potential systemic effects are secondary to its direct irritating reactivity Consequently, dermal absorption of sodium hypochlorite is not relevant
Distribution:	The BPC TOX-WGIII-2016 agreed that human health effects are primarily due to the local mode of action of hypochlorite and potential systemic effects are secondary to its direct irritating reactivity In water, different chlorine species are available. The final metabolites in physiological systems are most likely the sodium and chloride ion, which are physiologically essential metabolites
Potential for accumulation:	The BPC TOX-WGIII-2016 agreed that human health effects are primarily due to the local mode of action of hypochlorite 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 96h 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 the sodium and chloride ion, 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	LD_{50}>2000 mg avCl/kg bw No classification for acute toxicity (oral) warranted
Rat LD_{50} dermal	LD_{50}>2000 mg avCl/kg bw No classification for acute toxicity (dermal) warranted
Rat LC_{50} inhalation	$LC_{50(1h)}$>10.5 mg avCl/L 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 hypochlorite exerts only local effects at the side of first contact, such conversion is not considered necessary No classification for acute toxicity (inhalation) warranted

Skin corrosion/irritation	With sodium hypochlorite solutions ≥5% avCl, skin irritating properties were shown Sodium hypochlorite is classified as Skin Corr. 1B, H314, according to Annex VI, Regulation (EC) 1272/2008 (harmonised classification)

Eye irritation	With sodium hypochlorite solutions ≥5% avCl, eye irritation properties were shown Sodium hypochlorite is classified as Skin Corr. 1B, H314, according to Annex VI, Regulation (EC) 1272/2008 (harmonised

	classification), covering also eye irritation effects
Respiratory tract irritation	Sodium hypochlorite can be expected to be irritant to the respiratory tract due to the corrosive character of the substance. According to the Guidance on the Application of the CLP Criteria (Version 4.1, 2015, Chapter 3.8.2.5), a classification for corrosivity is considered to implicitly cover the potential to cause RTI. Consequently, no additional classification is required
Skin sensitisation (test method used and result)	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 sodium hypochlorite, 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	LOAEC: not detected NOAEC: >7500 ppm avCl
Relevant dermal NOAEC / LOAEC	No dermal repeated dose studies are available for sodium hypochlorite Human data is available for sodium hypochlorite (see below)
Relevant inhalation NOAEC / LOAEC	No inhalation repeated dose study is available for sodium hypochlorite Read-across to chlorine: 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	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 sodium hypochlorite Human data is available for sodium hypochlorite (see below)
Relevant inhalation NOAEC / LOAEC	No inhalation repeated dose studies are available for sodium hypochlorite Read-across to chlorine: 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	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 sodium hypochlorite Human data is available for sodium hypochlorite (see below)
Relevant inhalation NOAEC / LOAEC	No inhalation repeated dose studies are available for sodium hypochlorite Read-across to chlorine: LOAEC: 0.4 ppm avCl (1.2 mg/m³) NOAEC: <0.4 ppm avCl (<1.2 mg/m³)

Genotoxicity

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; there were no treatment related increases in non-neoplastic lesions or tumour incidence

Relevant NOAEC/LOAEC	Studies performed with sodium hypochlorite (oral): LOAEC: 0.2 % avCl NOAEC: between 0.0275 % avCl (highest dose tested) and 0.1 % avCl Read-across to chlorine (inhalation): LOAEC: 0.4 ppm avCl (1.2 mg/m³) NOAEC: <0.4 ppm avCl (<1.2 mg/m³)

Reproductive toxicity

Developmental toxicity

Species/ Developmental target / critical effect	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 sodium hypochlorite 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

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

<u>Oral exposure towards hypochlorite solutions</u>

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

<u>Dermal exposure towards hypochlorite solutions</u>

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

<u>Inhalation of chlorine gas</u>

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	-
$NOAEC_{oral}$	1000 ppm avCl (0.1 % avCl)	rat 90-d subchronic repeated dose oral (drinking water) study rat 104-wks chronic repeated dose oral (drinking water) study	1
$NOAEC_{dermal}$	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)
$AEC_{inhalat\ on}$ (NaOCl)	No repeated dose inhalation toxicity study on NaOCl is available. In the absence of data, the BPC TOX-WGIII-2016 agreed to derive an $AEC_{inhalat\ on}$ based on chlorine data (please see above) $AEC_{inhalat\ on}$ (NaOCl) = 0.5 mg avCl/m³		
$AEC_{inhalat\ on}$ (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) $AEC_{inhalat\ on}$ (HClO) = 0.5 mg avCl/m³		

MRLs

Relevant commodities	Not relevant for substances such as NaOCl which act by a local mode of action only For chlorate (stable relevant 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)
Depration time (DT_{50})	Not applicable: no test performed
Depration 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	
Drinking water disinfection (large scale chlorination) (professional use)	Sodium hypochlorite 14%	Bacteria, fungi, viruses, spores	Aqueous solution	14 % w/w	Dissolution in water (automated dosing for large scale disinfection)	--	Continuously	0.5 mg/L	--	--	The frame legislation regime at EU level (98/83/EC), sets minimum standards for certain ingredients in water for human consumption, including drinking water. Depending on the specific National Regulations, chlorinations should range between 0.3-0.7 mg/L. The amount of chlorine added to water depends on the specific content of oxidizable

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	
											compounds, the amount needed to kill the microorganisms, plus a sufficient reserve to maintain a minimum concentration of free available chlorine at each point in the water pipe.

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 3.1.1/01 NaOCl	Tieche A	2007	Melting point and boiling point of liquids (bs dsc) on the sodium hypochlorite 24% Source: Defitraces Defitraces Report No.: 07-905015-001 GLP; (unpublished) Doc. No.: 112-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 3.1.3/01 NaOCl	Tieche A	2007	Relative density of liquids on the sodium hypochlorite 24% Source: DefitracesDefitraces Report No.: 07-905015-002 GLP; (unpublished) Doc. No.: 113-003	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 3.2.1/01 (ALL)	Holzwarth 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.
III-A 3.2/01 NaOCl	Anonymous	1999	Nf en 901 european standard chemicals used for treatment of water intended for human consumption sodium hypochlorite Source: Associoation Francaise de Normalisation Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 031-004	No	N.R.
III-A 3.6/01 NaOCl +	Pinto G, Rohrig B	2003	Use of chloroisocyanuarates for disinfection of water Source:	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
CaOCl			JChemEd.chem.wisc.edu, January 2003, 80, 1, 41-44 Report No.: Not applicable Not GLP; (published) Doc. No.: 192-003		
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 3.10/01 NaOCl	White GC	1972	Handbook of chlorination Source: Handbook of Chlorination , pp. 627-675 Report No.: Not applicable Not GLP; (published) Doc. No.: 031-001	No	N.R.
III-A 3.12/01 NaOCl	Ferron N	2007	Flash point on the sodium hypochlorite 24% Source: Defitraces Report No.: 07-905015-003 GLP; (unpublished) Doc. No.: 142-001	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: Defitraces 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 3.13/01 NaOCl	Ferron N	2007	Surface tension on the sodium hypochlorite 24% Source: Defitraces Report No.: 07-905015-004 GLP; (unpublished) Doc. No.: 116-006	Yes (Data on existing a.s. submitted for the first time for entry	Euro Chlor

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
				into Annex I)	
III-A 3.14/01 NaOCl	Tieche A	2007	Viscosity on the sodium hypochlorite 24% Source: Defitraces Report No.: 07-905015-005 GLP; (unpublished) Doc. No.: 116-005	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 4.1/01 NaOCl III-A 4.1/02 Ca(OCl)2	Anonymous	1999	Nf en 901 european standard chemicals used for treatment of water intended for human consumption sodium hypochlorite Source: Associoation Francaise de Normalisation Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 031-004	No	N.R.
III-A 4.1/02 NaOCl III-A 4.1/07 Ca(OCl)2	Anonymous	N.I.	Free alkali in sodium hypochlorite Source: Not indicated Report No.: Not indicated Not GLP; (published) Doc. No.: 492-007	No	N.R.
III-A 4.1/03 NaOCl+ Ca(OCl)2	USP 24	N.I.	Sodium chloride Source: Official Monographs USP 24, 1528-1529 Report No.: Not applicable Not GLP; (published) Doc. No.: 492-008	No	N.R.
III-A 4.1/05 NaOCl	Anonymous	2007	Chemicals used for treatment of water intended for human consumption - sodium hypochlorite Source: Associoation Francaise de Normalisation Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 031-006	No	N.R.
III-A 4.1/06 NaOCl	Anonymous	2000	German standard methods for the examination of water, waste water and sludge cations (group e) - determination of iron by atomic absorption	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
			spectrometry (AAS) (E32) Source: Deutsche Norm, May 2000, DIN 38406-32 : 2000-05 Report No.: DIN 38406-32 : 2000-05 Not GLP; (published) Doc. No.: 492-009		
III-A 4.1/07 NaOCl	Anonymous	1998	Standardization of methods for the determination of traces of mercury Source: Euro Chlor Report No.: Analytical 3-7 Not GLP; (published) Doc. No.: 412-005	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-1,4phenylenediamine Source: Deutsche Norm, April 2000, DIN EN ISO 7393-1 Report No.: Not indicated Not GLP; (published) Doc. No.: 435-001	No	N.R.
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	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
			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		
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.
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) Doc. No.: 392-022	No	N.R.
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	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
			foodborne spoilage microbes Source: Z Lebensm. Unters Forsch A, 1999, 289-298 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-041		
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 etal.	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.
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-	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
			125 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-021		
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.
A5.3.1/15 (ALL)	Jones MV, Wood MA, Herd TM	1992	Comparative sensitivity of Vibrio cholerae 01 el tor and Escherichia coli to disinfectants Source: Letters in Applied Microbiology, 1992, 14, 51-53 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-045	No	N.R.
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)	No	N.R.

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			Doc. No.: 392-047		
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 5.3.1/20 (ALL)	El-Kest SE Marth EH	1988	Inactivation of listeria monocytogenes by chlorine Source: Journal of Food Protection, 1988, 51, 520-524 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-038	No	N.R.
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.

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 5.3.1/23 (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 RL 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 5.3.1/25 (ALL)	Tanner RS	1989	Comparative testing and 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	No	N.R.
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	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.: 392-029		
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 Not GLP; (published) Doc. No.: 392-060	No	N.R.
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	Bond WW	1983	Inactivation of hepatitis b	No	N.R.

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5.3.1/33 (ALL)	et al.		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		
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 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-056	No	N.R.
III-A 5.3.1/35 (ALL)	Prince DL, Prince RN, Prince HN	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	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
			Report No.: Not applicable Not GLP; (published) Doc. No.: 391-001		
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.
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	No	N.R.

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			Source: www.ifh-homehygiene.org Report No.: Not applicable Not GLP; (published) Doc. No.: 392-069		
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) Source: International Scientific Forum on Home Hygiene (IFH), October 2003 Report No.: Not applicable Not GLP; (published) Doc. No.: 392-070	No	N.R.
III-A 6.1.1/01 III-A 6.1.2/01 III-A 6.1.3/02 III-A 6.1.4/01 III-A 6.1.4/02 Ca(OCl)2	[redacted]	1975	Acute oral LD 50 in rats using calcium hypochlorite [redacted] Not GLP; (unpublished) Doc. No.: 521-004	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	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	BioFax	1970	Bio - fax -sodium	Yes	Euro Chlor

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6.1.3/01 NaOCl			hypochlorite Source: Industrial Bio-Test Laboratories Inc. Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 581-001	(Data on existing a.s. submitted for the first time for entry into Annex I)	
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] Not GLP; (unpublished) Doc. No.: 567-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-A 6.1.5/01 Ca(OCl)2	[redacted]	2000	Delayed contact dermal sensitization test - buehler method	Yes (Data on existing	Euro Chlor

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			[redacted] GLP; (unpublished) Doc. No.: 567-004	a.s. submitted for the first time for entry into Annex I)	
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 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 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	Yes (Data on existing	Euro Chlor

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			Laboratories Inc. Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 581-001	a.s. submitted for the first time for entry into Annex I)	
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) Doc. No.: 592-052	No	N.R.
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]	Yes (Data on existing a.s.	Euro Chlor

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			[redacted] Not GLP; (unpublished) Doc. No.: 592-113	submitted for the first time for entry into Annex I)	
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 NaOCl	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.
A6.5/02 (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	Ishidate M et al.	1994	Primary mutagenicity screening of food additives	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
(ALL)			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		
III-A 6.6.1/02 (ALL)	Kawachi T et al.	1980	Results of recent studies on the relevance of various short-term screening tests in Japan Source: Applied Methods in Oncology, Bd. 3, 1980, pp. 253-267 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-054	No	N.R.
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	No	N.R.

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			Source: La Kromosomo II-20, 31.12.1980, pp. 574-584 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-057		
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 Not GLP; (published) Doc. No.: 592-114	No	N.R.
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	No	N.R.

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			Not GLP; (published) Doc. No.: 592-091		
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.
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)	No	N.R.

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			Doc. No.: 592-016		
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 Not GLP; (published) Doc. No.: 592-017	No	N.R.
III-A 6.12.2/01 CI2	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 etal.	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)	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
			Doc. No.: 592-134		
III-A 612.2/03 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 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-178	No	N.R.
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	Weill 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 6.12.2/05 NaOCl	Habets JMW et al.	1986	Sensitization to sodium hypochlorite causing hand dermatitis Contact Dermatitis 15, Vol. 1986, pp. 140-142	No	N.R.

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			Report No.: na Not GLP, published Doc. No.: 592-101		
III-A 6.12.2/06 NaOCl	Rotman HH et al.	1983	Effects of low concentrations of chlorine on pulmonary function in humans American Physiological Society, (1983), pp. 1120-1124 Report No.: na Not GLP, published Doc. No.: 592-077	No	N.R.
III-A 6.12.2/07 NaOCl	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.

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 6.12.5/02 NaOCl	Tanyel FC, Büyükpamukcu N, Hicsönmez A	1988	Chlorine bleach ingestion in children - a review of 80 cases Source: Inc. Türkish Journal of Pediatrics 30, (1988), pp. 105-106 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-119	No	N.R.
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 6.12.2/03 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)	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
			Doc. No.: 592-135		
III-A 6.12.2/05 Cl2	Weill 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 6.12.3/01 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 Journal 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, Hicsönmez A	1988	Chlorine bleach ingestion in children - a review of 80 cases Source: Inc. Türkish Journal of Pediatrics 30, (1988), pp. 105-106 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-119	No	N.R.
III-A 6.12.5/03 NaOCl	Strange DC et al.	1951	Corrosive injury of the stomach Source: A.M.A. Archives of	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
			Surgery 62, (1951) pp. 350-357 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-009		
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 NaOCl	Hostynek JJ et al.	1990	Irritation factors of sodium hypochlorite solutions in human skin Source: Contact Dermatitis 1990, pp. 316-324 Report No.: Not applicable Not GLP; (published) Doc. No.: 592-136	No	N.R.
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	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
			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		
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) Doc. No.: 989-003	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
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 7.4.1.1/0	Heath J	1977	Toxicity of intermittent chlorination to freshwater	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
1 (ALL)			fish - influence of temperature and chlorine for Source: Hydrobiologia Vol. 56, 1, (1977), pp. 39-47 Report No.: Not applicable Not GLP; (published) Doc. No.: 892-012		
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)	[redacted]	1978	The relative sensitivity of pacific northwest fishes and invertebrates to chlorination sea water [redacted] 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 Report No.: Not applicable Not GLP; (published) Doc. No.: 892-022	No	N.R.
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	Yes (Data on existing	Euro Chlor

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
			cladoceran (*Daphnia magna*) Source: Wildlife International Ltd, Easton, Maryland, USA Report N.: 676A-101; 2009-03-26 GLP: yes; (unpublished) Doc. No. 822-001	a.s. submitted for the first time for entry into Annex I)	
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 Ltd, Zelgliweg, Switzerland; Report No.: D62230; 18.07.2013 GLP: yes; (unpublished). Doc No. 823-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
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	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
			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		
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.
III-B 3.1.1/01 NaOCl	Tieche A	2007	Relative density of liquids on the sodium hypochlorite 14% Source: Defitraces Report No.: 07-905015-007 GLP; (unpublished) Doc. No.: 113-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-B 3.1.1/01 NaOCl	Ferron N	2007	Relative density of liquids on the sodium hypochlorite 5% Source: Defitraces Report No.: 07-905015-011 GLP; (unpublished) Doc. No.: 112-002	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-B 3.4/01 NaOCl	Ferron N	2007	Flash point on the sodium hypochlorite 24% Source: Defitraces Report No.: 07-905015-003 GLP; (unpublished) Doc. No.: 142-001	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-B 3.5/01	Ferron N	2007	Determination of ph values on the sodium hypochlorite	Yes (Data on	Euro Chlor

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			5% Source: Defitraces Report No.: 07-905015-014 Not GLP; (unpublished) Doc. No.: 215-001	existing a.s. submitted for the first time for entry into Annex I)	
III-B 3.7/01 NaOCl	White GC	1972	HANDBOOK OF chlorination Source: Handbook of Chlorination , pp. 627-675 Report No.: Not applicable Not GLP; (published) Doc. No.: 031-001	No	Euro Chlor
III-B 3.7/02 NaOCl	Anonymous	1999	Nf en 901 european standard chemicals used for treatment of water intended for human consumption sodium hypochlorite Source: Associoation Francaise de Normalisation Report No.: Not applicable Not GLP; (unpublished) Doc. No.: 031-004	No	Euro Chlor
III-B 3.10/01 (ALL)	Ferron N	2007	Surface tension on the sodium hypochlorite 5% Source: Defitraces 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-B 3.10/01 NaOCl	Ferron N	2007	Surface tension on the sodium hypochlorite 14% Source: Defitraces Report No.: 07-905015-008 Not GLP; (unpublished) Doc. No.: 116-003	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor
III-B 3.11/01 NaOCl	Tieche A	2007	Viscosity on the sodium hypochlorite 14% Source: Defitraces Report No.: 07-905015-009 GLP; (unpublished)	Yes (Data on existing a.s. submitted	Euro Chlor

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
			Doc. No.: 116-004	for the first time for entry into Annex I)	
III-B 3.11/01 NaOCl	Tieche A	2007	Viscosity on the sodium hypochlorite 5% Source: Defitraces Report No.: 07-905015-013 GLP; (unpublished) Doc. No.: 116-007	Yes (Data on existing a.s. submitted for the first time for entry into Annex I)	Euro Chlor

Annex - Livestock exposure assessment

It has to be noted that the "Guidance on Estimating Livestock Exposure to Active Substances used in Biocidal Products" of Dec. 2010 is currently under revision by ARTFood and should normally not be used. Moreover, ARTFood noted in their project plan of Feb. 2014 that it will be closely linked to the EMA "Guideline on risk characterization and assessment of maximum residue limits (MRL) for biocides" (2015). However, the practical implementation remains still unclear.

A preliminary livestock exposure and dietary risk assessment for chlorate for intended uses in PT5 has been performed according to the "Guidance on Estimating Livestock Exposure to Active Substances used in Biocidal Products" (CA-Dec10-Doc.6.2b).

Livestock exposure was calculated using the "BfR Livestock Exposure Calculator" (2012; http://www.bfr.bund.de/en/assessment___residue_analytics-54528.html). The assessment includes a screening step as well as a realistic worst-case scenario. The subsequent dietary exposure assessment has been performed according to the EMA "Guideline on risk characterization and assessment of maximum residue limits (MRL) for biocides" (2015) taking into account the standard EMA food basket.

Livestock exposure was calculated with the "BfR Livestock Exposure Calculator" in accordance with the "Guidance on Estimating Livestock Exposure" (2010) for the following use:

- *Drinking water disinfection (large scale chlorination) – professional use*

As proposed in the "Guidance on Estimating Livestock Exposure" (2010), a worst-case screening scenario was performed. For "treatment of drinking water", no further refinement options are given in the "BfR Livestock Exposure Calculator". Details on input parameters and scenarios are provided in the "Read me" spreadsheet of the "BfR Livestock Exposure Calculator".

It is noticed that chlorate residue formation may depend on the formulation of the products as well as on the storage conditions of the product. No measured data on chlorate residues after application of the theoretical product are available. In the absence of measured residue data, the chlorate content according to sodium hypochlorite specification was used for estimation of chlorate contents in the application solution. However, according to EN 901:2013, Chapter 6.5.2, sodium chlorate content of NaOCl solutions increases over time, i.e. during storage. Thus, residue transfer via livestock into food should be assessed in detail at product authorization.

According to the specification criteria for the active chlorine releaser NaOCl sodium chlorate is present at concentrations ≤5.4% of available chlorine. For an in-use concentration of 0.5 mg avCl/L (human drinking water), this results in an in-use concentration of 0.027 mg sodium chlorate/L and 0.021 mg chlorate/L (**Error! Reference source not found.**). The calculations of in use concentrations assume zero demand. All values should be less than or equal to.

Table 2.2.2.4-1: Overview on in-use concentrations of avCl, sodium chlorate and chlorate.

	Units	
In-use concentration avCl	mg/L	0.5
Content sodium chlorate	%	5.4
In-use concentration sodium chlorate	mg/L	0.027
In-use concentration chlorate ("application rate of a.s.")	**mg/L**	**0.021**

In the screening scenario the trigger value of 0.004 mg/kg bw was exceeded only for rabbits.

A subsequent worst case consumer exposure estimate (WCCE) was performed (**Error! Reference source not found.**). For this purpose, the standard EMA food basket (according to the EMA Guideline on MRLs (2011a and 2015)) was taken into account.

Table 2.2.2.4-2: Worst case consumer exposure (WCCE) estimation.

Worst case consumer exposure from animals exposed to chlorate by drinking water consumption

Livestock exposure results from screening scenario			Standard food basket *					
Animal Species		Sum of all routes of exposure [mg chlorate/kg bw/d]	amount meat eaten (muscle, kidney, liver, fat) [kg]	milk [kg]	eggs [kg]	dietary exposure by meat [mg chlorate]	dietary exposure by milk [mg chlorate]	dietary exposure by eggs [mg chlorate]
Beef cattle		0.0021	0.5			0.0011		
Dairy cattle		0.0037		1.5			0.0056	
Calf		0.0021	0.5			0.0011		
Fattening pig		0.0021	0.5			0.0011		
Breeding pig		0.0012						
Breeding pig	individual housing							
Breeding pig	group housing							
Sheep		0.0028	0.5			0.0014		
Lamb		0.0026	0.5			0.0013		
Slaughter goat (= goat kids)		0.0021	0.5			0.0011		
Lactating goat		0.0021		1.5			0.0032	
Broilers		0.0031	0.5			0.0015		
Broilers	free range, litter floor		0.5					
Broilers	parent broilers, free range (grating floor)							
Broilers	parent broilers in rearing, free range (grating floor)							
Laying hen		0.0028			0.1			0.0003
Laying hen	battery				0.1			
Laying hen	free range (litter floor)				0.1			
Laying hen	free range (grating floor)				0.1			
Turkey		0.0030	0.5			0.0015		
Horse		0.0021	0.5			0.0011		
Rabbit		0.0042	0.5			0.0021		
MAXIMUM						0.0021	0.01	0.0003

Systemic chlorate exposure via animal products

Products consumed	chlorate taken up via diet [mg]	body weight [kg]	systemic exposure to chlorate [mg/kg bw]	ADI [mg/kg bw] 0.003 % ADI	> 30% ADI?
meat	0.002	60	0.0000	1.2	no
milk	0.01	60	0.0001	3.1	no
eggs	0.00	60	0.0000	0.2	no
meat + milk + eggs	0.01	60	0.0001	4.4	no

* The **standard food basket** proposed in the EMA guidance on MRL setting (2010) contains: muscle 300 g, liver 100 g, fat 50 g, kidney 50 g, milk 1500 g, eggs 100 g, honey 20 g.
For calculations, amounts of muscle, liver, kidney and fat were added, resulting in 500 g of animal tissue eaten.

With the exposure values obtained from the BfR Livestock Exposure Calculator scenario, consumption of eggs, meat and milk from livestock potentially in contact with chlorate residues in drinking water is below the $ADI_{chlorate}$=0.003 mg/kg bw. Moreover, values are below 30% ADI, thus no MRL setting is required according to EMA Guidance on MRL setting.

To be noted that the assessment was based on the concentration of chlorate according to the sodium hypochlorite specification, but the potential generation of chlorate during or post application was not considered.

Dietary risk assessment

Currently, no agreed and published guidance is available for the estimation of dietary risk from transfer of biocidal active substances into food in professional settings. Thus, no dietary risk assessment can be provided at this stage for the intended uses of the active chlorine releaser NaOCl in PT5.

Instead, reference is made to the EFSA Scientific Opinion of the EFSA CONTAM Panel on "Risks for public health related to the presence of chlorate in food" (EFSA Journal 2015; 13:4135) which includes a comprehensive dietary exposure and risk assessment for chlorate residues in food and drinking water based on occurrence data.

In brief, the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) evaluated the exposure and risk arising from chlorate residues found in food and drinking water. Occurrence data from European national food authorities and similar bodies was collected and approximately 8000 samples were analysed for chlorate contents (e.g. grains and grain-based products, vegetables and vegetable products, legumes, fruit and fruit products, herbs and spices, milk and dairy products, (non-)alcoholic beverages, composition food, and drinking water). Chlorate content in all food commodities assessed ranged from 3 µg/kg (alcoholic beverages) to 417 µg/kg (herbs and spices) (mean upper bound values). The mean chlorate value for drinking water was 39 µg/L (mean upper bound).

An acute and chronic exposure assessment was performed for different population groups, using consumption data from the EFSA Comprehensive Database and the measured chlorate levels. According to the Scientific Opinion, "mean and 95th percentile acute exposures were below the ARfD [36 µg chlorate/kg bw] for all age groups indicating no concern". Moreover it is stated that, "chronic exposure of adolescent and adult age classes did not exceed the TDI [3 µg chlorate/kg bw]. However, at the 95th percentile, the TDI was exceeded in all surveys for 'Infants' and 'Toddlers', and in some surveys in 'Other children'", indicating that "chronic exposures are of concern in particular in younger age groups with mild or moderate iodine deficiency."

Chlorate is no longer used as pesticide (according to Commission Decision No 2008/865/EC). Thus, chlorate contamination in food is likely to be mainly derived from biocidal uses of chlorine and hypochlorite. Both substances are widely used for disinfection of surfaces and equipment in food and feed processing areas as well as for disinfection of drinking water (i.e. as biocidal products in PTs 4 and 5), and thus, chlorate residues can be carried-over into food and feed during cleaning, washing and processing steps. Accordingly, "CONTAM Panel assumes that chlorate residues in food result mainly form the use of chlorinated water for food processing (e.g. washing) and from the disinfection of surfaces and food processing equipment coming into contact with food."

Potential chlorate residues from the application of chlorine and hypochlorite in PTs 4 and 5 are considered to be included in the measured chlorate residue values, and the conclusions drawn by the EFSA CONTAM Panel on chlorate residues cover thus also the dietary risk arising from PT4 and PT5 uses of chlorine and hypochlorite. Since the EFSA Scientific Opinion on chlorate residues provides actual measured data for chlorate residues in food and an exhaustive exposure and risk assessment based on consumption data, the

conclusions drawn in the EFSA Scientific Opinion are superior to any dietary risk assessment based on exposure models.

Consequently, no dietary risk assessment is deemed necessary for the intended professional uses of the active chlorine releaser NaOCl in PT5.

Additional considerations on chlorate residues in drinking water

The provisional guideline value WHO for drinking water for chlorate is 0.7 mg/L.

According to the conclusions of the BPC TOX-WG-IV-2016, it has to be demonstrated at product authorisation stage that disinfection of drinking water with sodium hypochlorite would not lead to a concentration of chlorate that will exceed the drinking water limit.

In this respect, it has to be noted that sodium chlorate is a by-product of the manufacturing process and can be formed from hypochlorite in aqueous solutions of sodium hypochlorite during storage.