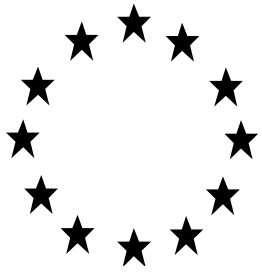
Regulation (EU) n°528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Bromoacetic acid

Product-type 4
(Food and feed area disinfectants)

September 2013

RMS: Spain

Bromoacetic acid (PT4)

Assessment report

Finalised in the Standing Committee on Biocidal Products at its meeting on 27 September 2013

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1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Principle of evaluation

This assessment report has been established as a result of the evaluation of bromoacetic acid product-type 4 (Food and feed area disinfectants), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market1, with the original view to the possible inclusion of this substance into Annex I or IA to that Directive.

The evaluation has therefore been conducted in the view to determine whether it may be expected, in light of the common principles laid down in Annex VI to Directive 98/8/EC, that there are products in product-type 4 containing bromoacetic acid that will fulfil the requirements laid down in Article 5(1) b), c) and d) of that Directive. Those requirements and common principles are very similar to those laid down in Article 19(1), (2) and (5) and Annex VI of Regulation (EU) No 528/2012. At the time of finalisation of this assessment report, there was no indication that the conclusions regarding compliance with Directive 98/8/EC would not be valid for the purpose of establishing compliance with the requirements of Regulation (EU) No 528/2012.

1.2. Purpose of the assessment

The aim of the assessment report is to support a decision on the approval of Bromoacetic acid for product-type 4, and should it be approved, to facilitate the authorisation of individual biocidal products in product-type 4 that contain bromoacetic acid. 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.

The conclusions of this report were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). Extension of the use pattern beyond those described will require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Regulation (EU) No 528/2012.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report 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 has been granted.

1 Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market. OJ L 123, 24.4.98, p.1

1.3. Procedure followed

This assessment report has been established as a result of the evaluation of Bromoacetic acid as product-type 4 (Food and feed area disinfectants), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market, with a view to the possible inclusion of this substance into Annex I or IA to the Directive.

Bromoacetic acid (CAS no. 79-08-3) was notified as an existing active substance, by Albemarle Europe SPRL and Sopura S.A., hereafter referred to as the applicant, in product-type 4.

Regulation (EC) No 1451/2007 of 4 December 20072, which has repealed and replaced Commission Regulation (EC) No 2032/2003 of 4 November 20033, lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive.

In accordance with the provisions of Article 5(2) of Regulation (EC) No 2032/2003, Spain was designated as Rapporteur Member State to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for Bromoacetic acid as an active substance in Product Type 4 was 31.07.2007, in accordance with Annex V of Regulation (EC) No 2032/2003.

On 27th July 2007, Spanish competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 31st January 2008.

On 22nd January 2011, the Rapporteur Member State submitted, in accordance with the provisions of Article 14(4) and (6) of Regulation (EC) No 1451/2007, to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report. The Commission made the report available to all Member States by electronic means on 1st March. The competent authority report included a recommendation for the inclusion of Bromoacetic acid in Annex I to the Directive for PT 4.

In accordance with Article 16 of Regulation (EC) No 1451/2007, the Commission made the competent authority report publicly available by electronic means on 10 March 2011. This report

2 Commission Regulation (EC) No 1451/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L 325, 11.12.2007, p. 3

3 Commission Regulation (EC) No 2032/2003 of 4 November 2003 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/ 8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market, and amending Regulation (EC) No 1896/2000. OJ L307, 24.11.2003, p1

did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.

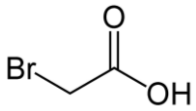
In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the Commission. Revisions agreed upon were presented at technical and competent authority meetings and the competent authority report was amended accordingly.

In accordance with Article 15(4) of Regulation (EC) No 1451/2007, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on 27 September 2013.

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

2.1.1. Identity, Physico-Chemical Properties & Methods of Analysis

CAS-No.	79-08-3
EINECS-No.	201-175-8
Other No. (CIPAC, ELINCS	-
IUPAC Name	2-bromo-ethanoic acid
Common name, synonym	Bromoacetic acid
Molecular formula	$C_2H_3Br\ O_2$
Structural formula	
Molecular weight (g/mol)	138.95 g/mol
Purity of a.s. (% w/w)	94.6% w/w (dry weight basis) - 81.1 % w/w (wet weight basis)
Impurities and additives:	Information on the impurities and additives in the technical grade active substance is confidential and is presented in the confidential attachment

The purified Bromoacetic acid is a solid crystalline and colourless, but Bromoacetic acid as manufactured is an aqueous solution containing 94.6% w/w (dry weight basis) - 81.1% w/w (wet weight basis) according to five batch analysis. At 41°C starting melting and it is completely melted without concurrent decomposition at 46°C The water solubility resulted higher than 1 kg/L at 20°C for the pH range of 1.09–5.69. The partition coefficient of Bromoacetic acid also varies with pH and temperature. The vapour pressure (13.5 Pa at 20°C) and Henry's Law constant is low. Bromoacetic acid is not highly flammable and has no explosive and oxidising properties.

Analysis of active substance as manufactured: The active substance and its identity can be determined by NMR-, IR- and MS-spectroscopy. For determination in mixtures the GLC-chromatography method described below (1.4.2) is recommended. The active substance is not metabolized to toxicological relevant residues, which require a specific analytical method.

Formulation analysis: The active substance and the identity of the active substance in the product are determined by HPLC analysis. No enrichment or cleanup is necessary. The method is calibrated for the range from 624 µg/L to 1029 µg/L for Bromoacetic acid; linearity gives a correlation coefficient of r^2 = 0.9997; recovery rate is >100.0 % and the relative standard deviation is 0.32%; the limit of detection is ca. 10 µg/L.

Residue analysis: For the detection of Bromoacetic acid in beer, the typical application as the biocidal product, an HPLC method has been validated with a detection limit of 0.1µg/L and by an independent laboratory with a detection limit of 0.025µg/L. In addition reference methods

for the detection of Bromoacetic acid in water have been developed. An example is included in the table 1.4.

The application of the SEPTACID S or SEPTACID S PS biocidal products will cause residues in food below the limit of concern provided that appropriate post-use water rinse measures are followed.

2.1.2. Intended Uses and Efficacy

Bromoacetic acid as used for the formulation of biocidal products is an aqueous solution containing 94.6% w/w (dry weight basis) - 81.1% w/w (wet weight basis) a.s. It has to be stored separately from other material.

The biocidal products (SEPTACID S / S PS) are a corrosive solution and must be handled wearing PPE and they are only intended for use in cleaning in place (CIP) systems. The representative products SEPTACID S and SEPTACID S PS contain 8% w/w and 4% w/w Bromoacetic acid, respectively are intended for the disinfection of food processing installations i.e. breweries by means of CIP (cleaning in place) of such installations circulating the biocidal product to clean and disinfect the apparatuses. These end-products are intended for professional users only.

The recommended concentration of the biocidal product SEPTACID S is 1% (v/v) maximum corresponding to 0.13% (w/v) a.s. The bactericidal activity of the biocidal product SEPTACID S is proved at 1% but the fungicidal activity at 1% does not fulfill under obligatory conditions. On the contrary, this product tested at 1% demonstrated fungicidal activity under additional conditions. The recommendation for the concentration of the biocidal product SEPTACID S PS in the treatment solution is 2% (v/v) maximum corresponding to 0.12% (w/v) a.s. The results of the tests for simulated clean and dirty conditions to assess the bactericidal activity at a concentration of 3%v/v under obligatory conditions indicate that the product is effective except for *Enteroccocus hirae* (effective concentration is at 5%v/v). Regarding fungicidal activity at a concentration of 2%v/v, the results indicate that the product is effective.

Bromoacetic acid is a disinfectant for the use in food and feed area. Bromoacetic acid is a bactericide and fungicide with high efficacy against microorganisms known for their potential of beer spoiling effects, e.g. bacteria *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus hirae and fungi Candida albicans, Aspergillus niger.*

In addition, in order to facilitate the work of 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 substance:

- Classification according to Annex I of Council Directive 67/548/EEC

Current classification of a.s.

Classification	as in Directive 67/548/EEC
Class of danger	T (Toxic), C (Corrosive), N (Dangerous for the environment)
R phrases	R23/24/25: Toxic by inhalation, in contact with skin and if swallowed. R35: Causes severe burns. R43: May cause sensitisation by skin contact R50: Very toxic to aquatic organisms
S phrases	S1/2, S26, S36/37/39, S45, S61

Bromoacetic acid is also classified as R41 but according to Dir. 67/548/EEC when a substance or preparation is classified as corrosive and assigned R34 or R35, the risk of severe damage to eyes is considered implicit and R41 is not included in the label

We propose no change the classification and labelling.

- Classification according to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures

Current classification of a.s.

Hazard Class and Category Code(s)		**Hazard Statement Code(s)**	
Acute Tox. 3 Acute Tox. 3 Acute Tox. 3 Skin Corr. 1A Skin Sens. 1 Aquatic acute 1	H331: Toxic if inhaled H311: Toxic in contact with skin H301: Toxic if swallowed H314: Causes severe skin burns and eye damage H317: May cause an allergic skin reaction H400: Very toxic to aquatic life.	**Pictogram, Signal Word Code(s)** GHS06 GHS05 GHS09 Dgr	

Regarding the environment, Bromoacetic acid, the substance is toxic for algae with L(E)C50 less than 1 mg/l and higher than 0.1 mg/l. It is a ready degradable substance and totally soluble in water.

Product Septacid S:

- Classification according to Annex I of Council Directive 67/548/EEC

Current classification of b.p.

Classification	as in Directive 67/548/EEC
Class of danger	C (Corrosive)
R phrases	R20/21/22, R35
S phrases	S20/21, S26, S30, S36/37/39, S45

Proposed classification

Classification	as in Directive 67/548/EEC
Class of danger	T+ (Very toxic); C (Corrosive)
R phrases	R26, R21/22, R35, R43
S phrases	S20/21, S26, S30, S36/37/39, S45

Not classified for the environment. The proposals are based on study results presented in the dossier and the composition of the products.

- Proposed classification according to the Regulation (EC) No 1272/2008 of the European Parliament and of the Council and the Globally Harmonised System of Classification and Labelling of Chemicals (hereinafter referred to as "the GHS"):

Classification	as in Regulation (EC) No 1272/2008
Class of danger	Acute Toxicity Cat. 1 H330; Acute Toxicity Cat. 4 H302; Acute Toxicity Cat. 3 H311; Skin Corrosion Cat. 1A H314; Skin Sensitizer Cat. 1 H317; EUH071

Product Septacid S PS:

- Classification according to Annex I of Council Directive 67/548/EEC

Current classification of b.p.

Classification	as in Directive 67/548/EEC
Class of danger	C (Corrosive)
R phrases	20/21/22, 34
S phrases	23, 26, 28, 36/37/39, 45

Proposed classification

Classification	as in Directive 67/548/EEC
Class of danger	T (Toxic); C (Corrosive)
R phrases	R 23, R 21/22, R 34, R 43
S phrases	23, 26, 28, 36/37/39, 45

Not classified for the environment. The proposals are based on study results presented in the dossier and the composition of the products.

- Classification according to the Regulation (EC) No 1272/2008 of the European Parliament and of the Council and the Globally Harmonised System of Classification and Labelling of Chemicals (hereinafter referred to as "the GHS"):

Classification	as in Regulation (EC) No 1272/2008
Class of danger	Acute Toxicity Cat. 2 H330; Acute Toxicity Cat. 4 H302; Acute Toxicity Cat. 3 H311; Skin Corrosion Cat. 1B H314; Skin Sensitizer Cat. 1 H317; EUH071

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard identification

Metabolism and distribution

A published study of absorption and elimination of several halogenated acetic acids in rats has been submitted (Saghir and Schultz, A6.2.1/01). This study shows that Bromoacetic acid after intravenous (iv) or oral dosing to male Fischer 344 rats could not be detected in the first sample collected 3 min after intravenous dosing and 1 min after oral dosing. This is interpreted as a fast elimination as free compound.

To get additional insight into metabolism a study on the stability of Bromoacetic acid in blood is available (Maas, A6.2.3/01) performed in compliance with GLP but not corresponding to any guideline. In vitro incubations with whole blood and blood plasma obtained from male rats have been performed using [^{14}C]-Bromoacetic acid for analytical sensitivity. In plasma, organic solvent extractable radioactivity (attributable to free Bromoacetic acid) decreased about 42 % or 50% after 120 min when incubated with 10 or 100 µg/ml. In whole blood, after 30 min 1% or 2% were detected after 30 min of incubation with 10 or 100 µg/mL 80 % of the radioactivity was in the blood pellet already after 15 min of incubation..

Absorption

No specific study to determine the oral absorption of Bromoacetic acid is available. The studies of subchronic toxicity dosing Bromoacetic acid via drinking water shows some effect at the low, medium and high dose demonstrating absorption after oral application. For oral application of Bromoacetic acid 30% absorption is assumed for risk characterization according to the estimated oral absorption of dibromoacetic acid (Schultz et al., 1999. Tox Appl Pharmacol 158: 103-114).

An in-vitro skin permeation study (Maas, A6.2.2/01) shows that Bromoacetic acid is absorbed through intact skin. The mean total absorption including the tape strips was 93.5, 77.9 and 73.9% for high, medium and low concentration, respectively for human skin, and it was 74.9, 64.9 and 46.2% for high, medium and low concentration, respectively for rat skin. For the purpose of risk assessment in this dossier conservative 100% dermal absorption of Bromoacetic acid through the skin will be applied.

No specific study to determine the inhalation absorption of Bromoacetic acid is available. For inhalation application of Bromoacetic acid 100% absorption is assumed for risk characterization.

Acute toxicity

No guideline acute studies are available. This is justified by the corrosive properties of the Bromoacetic acid. According to the report A6.1. 1/01 the LD50 of the Bromoacetic acid for oral acute toxicity in rats is 177 mg/kg bw for males and the Bromoacetic acid have little or no antispermatogenic activity because the reproductive-related parameters were unaffected 2 or 14 days after a single dose of 100 mg MBAA/kg (NOAEL for acute antispermatogenic effects) or after 14 daily doses of 25 mg MBAA/kg/day According to the report A6.1.2/02 the LD50 for dermal toxicity in rabbits is 59.9 mg/kg bw. Bromoacetic acid is classified as corrosive to skin and eyes and as skin sensitizer.

No sublethal or clinical effect data are available in oral, dermal and inhalation pathways in rats or rabbits No specific study to determine the classification of Bromoacetic acid for inhalation route is provided. The exposure times of the data about inhalation toxicity summarized in Document IIA Table 3.2-1 show that they were lower than the period of exposure shown in the Council Regulation EC-No 440/2008 (four hours).

Irritation and Corrosivity

Bromoacetic acid is currently classified as corrosive (R35) under Directive 67/548. No specific study of corrosion and of skin irritation is available. The publication of Eriksson et al. (A6.1.4s/01) is available. This publication reports the LOEC (lowest observed effect concentration; measured for skin corrosion) for Bromoacetic acid, which shows a value of 0.2 M, indicating strong corrosive properties of Bromoacetic acid.

The chicken enucleated eye test (CEET) is available to test the eye irritation properties of Bromoacetic acid. On the basis of the results, Bromoacetic acid is corrosive to the eye.

Sensitisation

Bromoacetic acid is classified as R43: May cause sensitization by skin contact.

A Guinea-Pig Maximisation Test is available. The skin effects observed in the test group animals were considered as positive signs of sensitization. More than 30% of the test animals reacted positively. On the basis of these results, it was concluded that under the conditions of this study Bromoacetic acid is a sensitizer.

Local effects.

On the basis of the irritation effect in the topic dosing of the Guinea-Pig Maximisation Test a LOEC of 1% is proposed. An additional AF is applied for deriving AEC from a LOAEC. A total AF of 20 (2 for NOAEC/LOAEC conversion, and 10 for intraspecies variability) is proposed.

No NOAEC/LOAEC may be deduced for medium or long term exposure. Therefore only risk assessment may be performed for systemic effects for medium and long exposure.

Repeated toxicity

In a 28 day oral toxicity study in rats the NO(A)EL on the basis of reduction of water and food intake and liver relative decreased weight in males and kidney relative increased weight in females is 7 mg/kg bw/day.

In a 90 day oral (drinking water) study, rats displayed signs of toxicity such reduction of food and water intake and body weight in both males and females. Changes in haematological parameters (such as increased mean corpuscular volume, decrease in thrombocyte, increased alkaline phosphatase activity, decreased plasma levels of total protein, cholesterol and phospholipids, increased plasma level of bilirubin in females and increased plasma level of chloride), decreased volume and increased density of the urine, decreased number of crystals in the urinary sediments, and in liver, brain and kidneys weights were also reported. Based on the reduction of food intake and body weight in both males and females, a NOAEL of 10.3 mg/kg bw/day is established for male rats and a NOAEL of 14 mg/kg bw/day is established for females. These NOAELs have been recalculated to get a systemic NOAEL considering an oral absorption of 30% (see Table below).

Genotoxicity and carcinogenicity

Bromoacetic acid did not show any mutagenic activity in any of the in-vitro assay (S. typhimurium strains), either in the absence or in the presence of the S-9 mix. But the Bromoacetic acid was clastogenic according to the studies for chromosomal aberrations in CHO cells in presence and in absence of S-9 mix at cytotoxic concentrations and it is mutagenic in the Ames fluctuation test in presence of S-9 mix at 0.3-300 µg/ml.

From the results obtained in the in-vivo chromosomal aberration test, it is concluded that Bromoacetic acid, close to the lethal dose, was cytotoxic to the bone marrow, but did not induce structural chromosomal aberrations in the bone marrow cells of male rats, under the conditions used in this study.

From the results obtained in the in-vivo “new micronucleus test” (standardised protocol by the French AFNOR) to detect the genotoxic activity of organohalides in erythrocytes of Pleurodeles waltl larvae it is concluded that none of the haloacetic acids (included Bromoacetic acid) except trichloroacetic acid showed any clastogenic activity.

Based on the available information it is concluded that Bromoacetic acid is not genotoxic or mutagenic in-vivo.

No specific carcinogenicity study is available.

Reproductive and developmental toxicity

In a teratogenicity oral (drinking water) study in rat (A6.8.1.1/01), the relevant NOAEL for maternal toxicity adopted was 4.7 mg/kg bw/day on the basis of reduction in body weight or body weight gain observed at medium and high doses. In this study, the highest dose (21.9 mg/kg b w/day) did not produce signs of teratogenic toxicity. This was a range finding study

with 24 animals per group. These NOAELs have been recalculated to get a systemic NOAEL considering an oral absorption of 30% (see Table below).

Considering the two-generation study for the impact of bromoactic acid in fertility, the NOAEL for parental toxicity in rats is 4 mg/kg bw/d in males and 5 mg/kg bw/d in females, based on decreased food and water consumption and lower body weight. The NOAEL for development (F1) is 10 mg/kg bw/d in males and 14 mg/kg bw/d in females, based on decreased food and water consumption and lower body weight.

Bromoacetic acid is not embryo/foetotoxic and does not induce any teratogenic effect and it is unlikely that Bromoacetic acid would cause developmental effects.

2.2.1.2. Effects assessment

The AELs were set as follows:

Exposure	Critical study	Critical NOAEL	Safety Factor	AEL
Short/acute exposure	teratogenicity oral study in rat	NOAELoral: 4.7 mg/kg bw/day NOAELsystemic: 1.5 mg/kg bw/day	100	AELoral: 0.05 mg/kg bw/day AELsystemic: 0.015 mg/kg bw/day
Subchronic exposure	90-day oral rat study	NOAELoral:10.3 mg/kg/day for males NOAELsystemic: 3.09 mg/kg bw/day	200 (100 and additional factor of 2 in order to alleviate uncertainties about the increased alkaline phosphatase activity in females)	AELoral: 0.05 mg/kg bw/day AELsystemic: 0.015 mg/kg bw/day
Chronic exposure	90-day oral rat study	NOAELoral:10.3 mg/kg/day for males NOAELsystemic: 3.09 mg/kg bw/day	400 (200 and additional factor of 2 according to the extrapolation between chronic and subchronic effects)	AELoral: 0.026 mg/kg bw/day AELsystemic: 0.0077 mg/kg bw/day
Short exposure (Local effects)	guinea pig sensitization study	LOAEC 1 %	20	AEC 0.05 %

2.2.1.3. Exposure assessment and Risk characterisation

Human health risk for professional users

The application of biocidal products containing Bromoacetic acid as disinfectant in Cleaning-In-Place (CIP) processes (PT4) in a professional environment can result in direct exposure via skin contact or via inhalation, but the oral ingestion is not considered as a potential direct route for exposure during the use of disinfectant in CIP processes. As there are not measurements of human exposure, exposure has been estimated with the models provided in the TNsG.

The exposure during the production of the active substance and the formulation of the biocidal products are not assessed by the Rapporteur under the requirements of the BPD. However the Rapporteur assumes that the production/formulation is performed in conformity with national and European occupational safety and health regulations.

Due to the hazard properties of the biocidal product the professional working on CIP activities is required to wear appropriate PPE (suitable protective clothing and shoes, chemically resistant gloves (tested to EN374), chemical goggles and face shields) whenever these products are handled in order to avoid contact with eyes or skin. Dermal exposure is prevented by the use of adequate PPE.

Potential inhalation exposure is expected when loading the biocidal products into the system to be disinfected previous to the CIP process although this step occurs in an automated, closed system. Inhalation exposure is estimated using models developed under REACH: Advanced REACH Tool (ART v1). Exposure via the inhalation route is negligible.

Summary of risk assessment for professional use

Exposure Scenario (indicate duration)		**Estimated Internal Exposure**				**Relevant NOAEL/ LOAEL [mg/kg b.w/day] & Reference Value e.g: AEL (acute or medium or chronic)**	**AF MOE ref**	**MOE**	**Exposure /AEL**
		estimated oral uptake [mg/kg b.w]	**estimated inhalation uptake [mg/kg b.w]**	**estimated dermal uptake [mg/kg b.w]**	**estimated total uptake [mg/kg b.w]**				
Tier 2 (PPE no RPE)	Connection of IBC containing biocidal product to CIP installation (5 min)	-	1.73E-05	-	1.73E-05	Acute exposure NOAELsystemic 1.5 mg/kg bw/d & AELsystemic 0.015 mg/kg bw	100	86705	0.00115

The only relevant MOE to be considered is a short term inhalation exposure. This MOE is above the minimal short term exposure MOE of 100.

Human health risk for non professional users

Not applicable since the biocidal products are not intended for non professional uses.

Human health risk from indirect exposure as a result of use

During application in disinfection of food processing installations i.e. breweries no secondary exposure of the general public takes place.

Bromoacetic acid residues in beverages are expected after the use of the biocidal products to clean and disinfect the drinks producing tank. Secondary exposure scenario is expected for consumers due to the ingestion of Bromoacetic acid residues beverages.

Indirect exposure has been assessed for the use of Bromoacetic acid in CIP systems during the production of beer. Practical measurements of Bromoacetic acid residues in beer show that the dietary exposure of consumers to residues of Bromoacetic acid in beer is not a concern. With regard to the use of biocidal products containing Bromoacetic acid in CIP systems for applications other than breweries, practical measurements of residue is needed at product authorisation level.

Human health risk for combined exposure

The potential for combined exposure for the professional user is expected considering the dietary exposure due to the consumption of beer containing Bromoacetic acid residues and the potential exposure expected for a professional who is exposed to Bromoacetic acid directly while at work.

Combined exposure is considered acceptable.

Conclusion

Based on the inherent hazard profile and the intended use of Bromoacetic acid in CIP (closed systems) exposure is controlled and limited.

Dermal exposure is prevented by the use of adequate PPE. Taking into account that the product is classified as corrosive it is not necessary to assess the risk from dermal exposure (TGD part I Exposure Assessment pp.63).

Inhalation exposure is restricted by the use pattern and further limited by short duration of handling the biocidal product. In addition exposure via the inhalation route is negligible.

2.2.2. Environmental Risk Assessment

The information submitted in the dossier was evaluated and interpreted in the light of the existing Scenario Documents for PT-4 (disinfectants used in food and feed areas). The Supplement to the methodology for risk evaluation of biocides endorsed during the 34th CA meeting was the version applied. In addition, the ECB Technical Guidance Document on Risk Assessment (TGD), together with the knowledge from experts in the Technical Meetings where this assessment was discussed, were supporting the evaluation.

Consequently, from the dossier presented by the applicant to comply the requirements of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market, it has been elaborated the present report.

Two products were evaluated, Septacid S and Septacid SPS. The first had 8% of Bromoacetic acid in its formulation and the second a 4%. Both are intended for *Disinfection of food processing installations i.e. breweries which are closed systems to prevent contamination with microorganisms. CIP (cleaning in place) of such installations by circulation of the biocidal product to clean and disinfect the apparatuses* and use is only made by professionals in this context.

2.2.2.1. Fate and distribution in the environment

Biodegradation.

Bromoacetic acid was considered as readily biodegradable. Two tests were submitted to assess this endpoint. The first test, A7.1.1.2.1/01, was according the OECD 301B guideline, performed with GLPs and provided evidence of biodegradation for the 57 mg/l flasks, that were 7.76, 81.26, 88.49, 81.46 (percentage) for days 6, 13, 20 and 28. Analogously, for the 115 mg/l flasks it was 8.64, 75.39, 88.49 and 84.36 (percentage) respectively. Test A7.1.1.2.1/02 was according to the same guidance but was rated for reliability 3. It evidenced biodegradability for Bromoacetic acid but ready biodegradation could not be established under the test conditions. Manometric measures, not performed with GLP, were appended which evidenced ready biodegradability for the Bromoacetic acid. On the other hand, QSAR estimation together with available scientific literature for monochloroacetic acid, which passes tests for ready biodegradability (EU risk assessment report, final report, 2005), is also supporting these evidences.

Abiotic degradation

Regarding the hydrolysis, the substance is stable being half-lives in a range of 9.17 - 21.25 days at 40 °C and 29.17 - 78.75 days at 30 °C, depending on the pH. DT50 at 12ºC were recalculated based on the TGD eq. #25 and were ranging from 86.08 - 199.63 days at 40ºC in different pH and 123.08 - 325.33 days in different pH.

No specific breakdown products were identified. From the structure of Bromoacetic acid it can be deducted that it is likely that a bromine ion is released resulting in acetic acid according to the reference Concurrent Exchange and Hydrolysis Reactions of Bromoacetic acid. Specific Cation Effect. J.F. Hinton and F.J. Johnoston. J. Phys. Chem. 1996. 70 (3), 841-844.

Negligible photo reactivity in water of Bromoacetic acid is expected given the analysis of photo reactivity in air as Bromoacetic acid does not contain any functional group or reactive centre which could be excited by UV irradiation or will react with hydroxyl radicals formed in low amounts under certain conditions of sunlight.

The reaction with hydroxy- radicals in the atmosphere can be estimates using QSAR models. The reaction rate and half-life resulted in an OVERALL OH Rate Constant 0.7161 E-12 cm3/molecule-sec during 24 hours of daylight and a half-life of 22.40 Days (24-hr day; 0.5E6 OH/cm3).

Distribution

Regarding distribution, Bromoacetic acid did not bind significantly to soil. This was tested in an absorption/desorption test according to the edition of 1981 of OECD guideline 106 encoded A7.1.3. Koc were determined at pH 4.2 (Koc 0) at pH 5.3 (Koc 1.3) and pH 5.7 (Koc 32.5).

Bioaccumulation.

Bromoacetic acid

No measured data on bioaccumulation potential was supplied by the applicant but being Bromoacetic with an expected logPow= -0.3 at pH 5, logPow= -2.3 at pH 7 and logPow= -2.3 at pH 9, at 22ºC, this suggests a low potential to accumulate in environmental compartments. With limited exposure under practical use pattern and its low partition withoctanol, the potential for biomagnification of Bromoacetic acid in the food chain was considered negligible. A QSAR result supported that the test was not necessary given the cited circumstances with a BCF for fish of 3.16 calculated with EPI suite from EPA USA (2000) BCF Program version 2.17.

Sodium Bromide

Regarding Sodium Bromide, the Core data of the active substance was consulted. In the CAR it is stated "*Because a log Kow is not relevant for inorganic substances such as HOBr and NaBr, estimation of the BCF using QSARs is not applicable. HOBr rapidly reacts with organic molecules. NaBr is not expected to have a potential to accumulate in biota. This is confirmed by the limited experimental data on Artemia salina*." The data was extracted from the public article *"Effects of Selected Biocides Used in the Disinfection of Cooling Towers on Toxicity and Bioaccumulation in Artemia Larvae"4*

Therefore Sodium bromide is considered as not bioaccumulable in biota.

4 *Bartolomé M.C. and Sánchez-Fortún S. (2005) Effects of Selected Biocides Used in the Disinfection of Cooling Towers on Toxicity and Bioaccumulation in Artemia Larvae, Environmental Toxicology and Chemistry, Vol. 24, No. 12, pp. 3137-3142.*

2.2.2.2. Effects assessment

Bromoacetic acid.

Aquatic effects

Studies on Bromoacetic acid together with studies on Sodium bromide were provided by the applicant. The latter were responding to the fact that Bromide ion is formed from the hydrolysis reaction in equimolar ratio. As the extent of this transformation was not measured by the applicant in the fate and behaviour section, data on bromide ecotoxicity was submitted as was available in the scientific literature.

The Bromoacetic acid ecotoxicological data available for aquatic organisms is displayed in the following table:

Table 2.2.2.2-1 Ecotoxicological data set for Bromoacetic acid for aquatic biota

Type of Organisms	Species	Study Type	LC50 or EC50 (acute) [mg/L]	NOEC (chronic) [mg/L]	Reference	Reliability
Fish	*Brachydanio rerio*	Semi-static 96 h -acute	103 (96h) 134 (48h)		A7.4.1.1/01	2
	Brachydanio rerio	Semi-static chronic 28 d		77	A7.4.3.2/01	2
Crustaceans	*Daphnia magna*	Acute 48 h	42		A7.4.1.2	2
		Chronic 21 d		1.6	A7.4.3.4/01	3
Algae	*Selenastrum capricornutum*	72 h	E_bC_{50}[1] 0.29 E_rC_{50}[2] 0.28	0.10 (NOErC)	A7.4.1.3/01	2
	Scenedesmus subspicatus	72h	E_bC_{50}[1] 0.20 E_rC_{50}[2] 1.4	E_rC_{10} (72h) =0.10 mg/l	A7.4.1.3/02	3

[1] calculated from the area under the growth curve; [2] calculated from growth rate

Being algae the most sensitive taxa for short term test the NOEC value for algae should be supported by the result of a test on a second species of algae (TGD, pag 100). This was carried out by further data by Kühn and Pattard (1990) as summarised in document IIIA7.4.1.3/02. The reliability of the test was ranked to 3 due to the fact that in scientific literature the reporting is not subject to GLP rules and raw data to trace the results are lacking but, being this work published in an international scientific journal, the data are valuable and will be considered as evidence of multigenerational and acute effects on green algae. Then, the study was considered acceptable to inform for the chronic data of green algae other than the formerly named *S. capricornutum* in spite of the Reliability ranked to 3 because the aim of it was to support the toxicity data of NOEC for algae with other toxicity data. The study did not supply another NOEC but provided an EC_r10 which is recommended in some instances (TGD, OECD guideline 201) to assess multigenerational effect in algae instead of NOEC.

Therefore, when applying the assessment factors, the surrogate that should be applied is surrogate d) from TGD or surrogate A4 from the Appendix 1 (Decision table for additional aquatic toxicity testing) in the *Guidance on data requirements for active substances and biocidal products*. The AF applied was 10 to the lowest data covering multigenerational effects.

Consequently, 0.10 mg/l was the lowest toxicity data for multigenerational effects (that is the reason ErC10 at 48 h for *S. subspicatus* was not used although is lower), generated in algae. Then, the **aquatic PNEC is 0.10/10 = 0.010 mg/l**

No data was presented for sediment dwelling organisms. Bromoacetic acid has a Kow far lower than 500 l/kg, and therefore is not likely sorbed to sediments (TGD part II, point 3.2.5). Bromide anion is expected to be highly mobile as well. Therefore ecotoxicity data from sediment dwelling organisms is not relevant in this case.

Microorganisms

The toxicity data for microorganisms in water is summarized in the following table,

Table 2.2.2.2-2. Ecotoxicological data set for Bromoacetic acid for microorganisms

Guideline / Test method	Species / Inoculum	Endpoint / Type of test	Exposure		Results			Remarks	Reference
			design	duration	EC_{10}	EC_{50}	EC_{80}		
OECD 209	Mixture of activated sludge and synthetic sewage feed	Respiration rate	Decrease in oxygen conc.	3 h	256 (NOEC)	> 800 mg a.i./L			A7.4.1.4/01, 2001

To calculate the PNEC for microorganisms an AF of 100 is applied to the EC50 following TGD. This results in **Bromoacetic acid PNECmicroorganisms of 8 mg a.i./l**

Bromide.

Due to the fact that this is an identified subproduct of hydrolysis from Bromoacetic acid, effects were assessed considering a worst case of every molecule releasing a bromide ion. Public literature was used to support it.

Aquatic effects

Regarding Bromide, this is the summary of ecotoxicological data considered to calculate PNEC

Table 2.2.2.2-3. Ecotoxicological data set for Bromide for aquatic biota

Type of Organisms	Species	Study Type	LC50 or EC50 (acute) [mg/L]	NOEC (chronic) [mg/L]	Reference
Fish	*Fathead Minnows*	Static 96 h -acute	16479 (96h) (NaBr) (Equivalent to 12796 mg(Br-)/L 17757 (48h) (NaBr) (Equivalent to 13788.3 mg(Br-)/L		Alexander H.C., 1981. Bull. Environm. Contam. Toxicol., 27, 326-331.
	Poecilia reticulate	Semi-static renewal every 7 days;124 days-chronic		7.8 mg (Br^-)/L	Canton J. H., Fd. Chem. Toxic., 1983, Vol. 21, No. 4, 369-378.
Crustaceans	*Daphnia magna*	Acute 48 h	6.7-9.3 g (NaBr)/l (Equivalent to 5.2- 7.22 mg(Br-)/L		Baird D.J., (1991)
		Acute 48 h	8.9 g (NaBr)/l (Equivalent to 6.9 mg(Br-)/L		Allen Y., (1995)
		Chronic Semi-static 16 days		2.8 mg/L (equivalent to 2.2 mg (Br-)/L)	Deneer J.W., et al., Ecotoxicological and Environmental Safety, 1988, 15, 72-77.
		Chronic Semi-static 21 days		7.5 mg/L (Equivalent to 5.8 mg (Br-)/L)	Guilhermino L, et al., Ecotoxicology and Environmental Safety 42, 67-74 (1999).
		Chronic Semi-static 21 days		14.3 mg (Br-)/L	Van Leeuwen C.J., (1986) Hydrobiologica, 133, 277-285.
		Chronic Semi-static 19days		<3 to 19 (NaBr) mg/L (Equivalent to <2.33 to 14.75 mg(Br-)/L	Soares A.M.V.M. (1992) Environmental Toxicology and Chemistry, Vol. 11, pp. 1477-1483.
Algae	Scenedesmus subspicatus	72 h	E_bC_{50}[1] 8000 mg NaBr/L (Equivalent to 6212 mg(Br-)/L		Kühn R., (1990) Wat. Res., Vol. 24. No. 1, 31- 38.

Type of Organisms	Species	Study Type	LC50 or EC50 (acute) [mg/L]	NOEC (chronic) [mg/L]	Reference
			E_rC_{50}[2] 20000 mg NaBr/L (Equivalent to 15533 mg(Br-)/L		

Sodium Bromide PNEC for aquatic organisms.

Acute and chronic toxicity data are available for three trophic levels, fish, invertebrates and algae. Data is from scientific articles and in most of them procedures similar to the OECD corresponding guideline has been followed. The PNEC was calculated on the basis of the lowest of the available NOEC results, being the 2.2 mg (Br-)/L in Daphnia. Using an assessment factor of 10 as appropriate given the chronic and acute data-set available for three trophic levels (fish, invertebrate and algae), the PNEC is 0.22 mg (Br-)/L. This value is only a little bit lower than the value found in naturally occurring river waters in the EU (which happens to be 0.27 mg/l , for River Ijssel in the Netherlands, Flury and Papritz, 1993). Therefore, given this background concentration of 0.27 mg/L for Br- in river waters, the use of the assessment factor 10 and the public available literature data is justified. Therefore, PNEC for aquatic organisms was set from toxicity data at **PNECaquatic = 0.22 mg/L for Br^-**.

Microorganisms

The toxicity data for microorganisms in water is summarized in the following table,

Table 2.2.2.2-4. Ecotoxicological data set for Bromide for microorganisms

Guideline / Test method	Test substance	Species / Inoculum	Endpoint / Type of test	Exposure design	Exposure Duration	Results EC_{50}	Remarks	Reference
OECD 209	Sodium bromide	Activated sewage sludge micro-organisms	Respiration rate	Decrease in oxygen conc.	3 h	> 776 mg (Br^-)/L	Reliability 2	A7.4.1.4/02, 2009

The results of the activated sludge respiration inhibition test on sodium bromide indicated that the NOEC is 1000 mg/L (equivalent to 776 mg Br-/L). An assessment factor of 10 appropriate for a NOEC according to the TGD derived from such a study leads to the following result: **Bromide PNECmicroorganisms of 77.6 mg/L.**

Atmosphere

There are no data on biotic effects of Bromoacetic acid in atmosphere. No significant volatilization is expected from Bromoacetic acid and has a predicted half-life in the atmosphere (AOP program (v1.91)) of 22.4 days based on a 24-hour day. Given its Henry constant and Vapour pressure, it is not likely that Bromoacetic acid will enter in the atmosphere and contribute to global warming, ozone depletion in the stratosphere, or acidification on the basis of its physical and chemical properties.

Additionally, all the operations with Bromoacetic acid based products are carried out in closed systems, so the emission is only to water. Therefore, volatilization from facilities to air is not assessed.

Related to the volatilization from water, the calculated Kair-water for Bromoacetic is 5.67 E-06 and regarding the fraction of a.s. associated to particles, this is 5.94 E-06 (from TGD). The fraction emited to air estimated by SimpleTreat is 5.83E-03 %.

Regarding sodium bromide, the very low vapour pressure measured for sodium bromide indicates that the volatilisation of the ion into the atmosphere in quantities of concern will not occur.

Terrestrial compartment

There is no ecotoxicological data on the terrestrial compartment. The PNECsoil was calculated using the equilibrium partitioning method described in the TGD.

Table 2.2.2.2-5. PNEC calculation for the terrestrial compartment.

Symbol	Definition	Unit	Value	Source
PNEClocal$_{soil}$	predicted no effect concentration in soil	[mg/kgwwt]	**0.00694**	Output
$K_{soil.-water}$	partitioning coefficient soil water	[m^3/m^3]	1.18	Calculated
RHO_{soil}	bulk density of wet soil	[kg/m]	1700	Default
$PNEClocal_{water}$	predicted no effect concentration in surface water	[mg/L]	0.01	Calculated

$$PNEC_{soil} = \frac{\mathrm{PNEC_{water}} \cdot \mathrm{K_{soil\text{-}water}} \cdot 1{,}000}{\mathrm{RHO_{soil}}} = \frac{0.01 \cdot 1.18 \cdot 1{,}000}{1700} = 0.00694\ mg/kg_{wwt}$$

Sediment compartment

There is no ecotoxicological data on the sediment dwelling organisms. The PNECsediment has been calculated using the equilibrium partitioning method described in the TGD.

Table 2.2.2.2-6. PNEC calculation for the sediment compartment

Symbol	Definition	Unit	Value	Source
***PNEClocal*$_{sediment}$**	predicted no effect concentration in soil	[mg/kgwwt]	**0.33**	Output
$K_{susp.-water}$	Suspended matter-water partition coefficient	[m3/m3]	1.712	Calculated
RHO_{ssup}	bulk density of wet suspended matter	[kg/m]	1150	Default
$PNEClocal_{water}$	predicted no effect concentration in surface water	[mg/L]	0.22	Calculated

$$PNEC_{soil} = \frac{\mathrm{PNEC_{water}} \cdot \mathrm{K_{susp\text{-}water}} \cdot 1{,}000}{\mathrm{RHO_{susp}}} = \frac{0.22 \cdot 1.712 \cdot 1{,}000}{1150} = 0.32751\, mg/kg_{wwt}$$

Non compartment specific effects relevant to the food chain (secondary poisoning)

Bromoacetic acid (log P_{ow} negative at 25 ˚C) has a low potential to accumulate in environmental compartments. With limited exposure under practical use pattern, the potential for biomagnification of this active substance in the food chain is considered as not of concern. Regarding sodium bromide, the very high water solubility of sodium bromide suggests that the log Pow is very low. This, together with the measured low BCF of 0.23 indicates that secondary poisoning through the food chain is unlikely to be a problem for the bromide ion.

2.2.2.3. PBT, CMR and ER assessment

P criterion.

Bromoacetic acid half life at 12ºC and pH 7 is 327d in the hydrolysis test A7.1.1.1.1. However, the substance is readily biodegradable and therefore is considered as not persistent in the PBT assessment.

B criterion.

As above stated, bioaccumulation is not foreseen due to the low partition with octanol of the active ingredient.

T criterium: Chronic NOEC<0.01 mg/l

The more sensitive taxa is algae, and its NOECr is 0.10 mg/l. Therefore the Bromoacetic acid does not fulfil the T criterium.

CMR Assessment

In addition, Bromoacetic acid does not accomplish the criteria for CMR substances.

Assessment of Endocrine Disruption (ED)

The RMS performed a search in the list included in the web link http://ec.europa.eu/environment/docum/01262_en.htm, (September 2010) which contains the Commission of a Communication to Council and European Parliament on a Community Strategy for Endocrine Disrupters in December 1999 (COM(1999)706), and the substance was not found in the list. Analogously, the RMS performed a search in the PubMed (http://www.ncbi.nlm.nih.gov/sites/entrez) in September 2010 with the terms: "Bromoacetic acid" and no result related to endocrine disruption or hormone synthesis was found.

2.2.2.4. Exposure assessment

Two stages have been considered in order to assess the exposure. One stage concerns to the formulation of the two biocide products submitted in this application, which takes place within the UE and the other stage concerns to the use itself as PT-4. For the formulation stage confidential data from the applicant has been used to carry out calculations for the exposure. As regards the use, what has been evaluated in this dossier is the use of the Bromoacetic acid in products as disinfectant in breweries in a CIP process. The calculation followed the guideline of the Technical Notes for Guidance endorsed during the 34th CA meeting for biocides PT-4. The emission estimation is based on defaults proposed in the scenario document.

Bromide ion is a main degradation product of Bromoacetic acid by hydrolysis in water, predicted by the applicant and in scientific literature. No quantification has been performed in any of the fate and behaviour assays and as toxicity data were provided by the applicant, therefore a worst case PEC has been calculated assuming an equimolar decomposition and corrected by mass ratio and also assuming that no elimination occurs in the STP and all the bromide remains in water without being distributed in sludge or sediment.

Regarding the coformulants exposure assessment, only sulphate (Septacid S) and phosphate (Septacid S PS) have been considered in the PEC calculations. The waste water from the different plant units is collected in a collecting tank and the pH is adapted before release either to the public sewer system or to an onsite STP (WWTP). Therefore, sulphuric and phosphoric acid will be in the sodium salt form prior emission and directing to the facility WWTP. Sulphate and Phosphate PECs have been calculated. For the manufacture, data from the industry were used, but for the use, a gross worst case estimation has been made assuming 100% of Bromoacetic acid consumed in average per plant (pick list from the Emission Scenario Documentfor PT-4) was formulated either with sulphate or phosphate.

Although Bromoacetic acid is produced in Europe, this stage has not been addressed here. The modelling of exposure and the risk assessment during the production of Bromoacetic acid should be addressed under other EU legislation and not repeated under Directive 98/8/EC.

Exposure to the aquatic compartment, sediment and the STP.

Manufacture

Product B1.

Considering the above stated, the predicted environmental concentrations (PECs) for the manufacture were calculated and, according to data submitted by the applicant and the TGD equations #32 and 45 and that all loses are directed to the WWTP. The calculations in the manufacture process can be found in the confidential annex.

Table 2.2.2.4-1 Calculated PECs water for Bromoacetic acid during manufacture

Bromoacetic acid

Category	Compartment	Value
Manufacture of Product B1	Local PEC in surface water during emission episode (dissolved) (mg/l)	1.11E-03
	Local PEC in fresh-water sediment during emission episode (mg/kg wwt)	1.65E-03
	PEC for micro-organisms in the STP (mg/l)	0.0111

PEC for Bromide can be calculated from these figures, correcting the STP elimination factor (Fstp) to Fstp=1 (no STP elimination) and the mass ratio.

Table 2.2.2.4-2 Calculated PECs water for sodium bromide during manufacture

Sodium Bromide

Category	Compartment	Value
Manufacture of Product B1	Local PEC in surface water during emission episode (dissolved) (mg/l)	0.0050
	Local PEC in fresh-water sediment during emission episode (mg/kg wwt)	9,49E-04
	PEC for micro-organisms in the STP (mg/l)	0.0507

Sulphuric acid was the main coformulant. To calculate PEC of sulphate, as there was no data of loss reported, the fraction of loss when manufacturing the product for Bromoacetic acid was applied to the loss of sulphuric acid. Then from the total production declared by the applicant in

the confidential statement, the loss of Bromoacetic acid was applied to the total and the percentage of acid was also considered and that 100% of the salt is passing to water upon STP.

Table 2.2.2.4-3 Calculated PECs water for sulphate during manufacture

Sulphate

Category	Compartment	Value
Manufacture of Product B1	Local PEC in surface water during emission episode (dissolved) (mg/l)	0.071
	PEC for micro-organisms in the STP (mg/l)	0.706

Product B2

The calculations were analogous to B1.

Table 2.2.2.4-4 Calculated PECs water for Bromoacetic acid during manufacture

Bromoacetic acid

Category	Compartment	Value
Manufacture of Product B2	Local PEC in surface water during emission episode (dissolved) (mg/l)	1.03E-03
	Local PEC in fresh-water sediment during emission episode (mg/kg wwt)	1.53E-03
	PEC for micro-organisms in the STP (mg/l)	0.0103

PEC for Bromide can be calculated from the same figures as Bromoacetic acid, correcting the STP elimination factor (Fstp) and the mass ratio.

Table 2.2.2.4-5 Calculated PECs water for sodium bromide during manufacture

Sodium Bromide

Category	Compartment	Value
Manufacture of Product B2	Local PEC in surface water during emission episode (dissolved) (mg/l)	0.0045
	Local PEC in fresh-water sediment during emission episode (mg/kg wwt)	8E-04
	PEC for micro-organisms in the STP (mg/l)	0.0449

Only the PEC for the phosphate anion was calculated. To this aim, as there was no data reported, the fraction of loss when manufacturing the product for Bromoacetic acid was applied to the loss of phosphoric acid. Then from the total production declared by the applicant in the confidential statement, the loss of Bromoacetic acid was applied to the total and the percentage of acid was also considered and 100% of salt passing to water upon STP treatment, to yield a phosphate $PEC_{manufacture, surface\_water}$ and a phosphate $PEC_{manufacture, STP}$.

Table 2.2.2.4-6 Calculated PECs water for phosphate during manufacture

Phosphate

Category	Compartment	Value
Manufacture of Product B2	Local PEC in surface water during emission episode (dissolved) (mg/l)	0.117
	PEC for micro-organisms in the STP (mg/l)	1.17

Use

Since the values used for the calculation of the exposure during professional use are default values, the PECs for product B1 and B2 are the same**.**

Bromoacetic acid.

PECs in the aquatic compartment were calculated according to generic model as explained before, resulting in a **PECuse,surface_water for Bromoacetic acid of 0.0099 mg/l.** The **Bromoacetic acid $PEC_{use,STP}$ is 0.0987 mg/l.**

Sodium bromide

The harmonized ESD used for Bromoacetic acid PECuse calculation was applied here, only Felim was set to 0. Considering the Qai of 362 Kg/yr from the escenario, and an equimolar Bromide release and a molar mass ratio Br-/ Bromoacetic acid =0.575, then bromide **Ceffluent**

or PECsurfacewater = 0.045 mg/l and a **Cinfluent (off site**) or **bromide $PEC_{use,STP}$= 0.45 mg/l**

Sulphate anion.

Calculations were done using the harmonized ESD and considering the formulation, provided in a confidential annex. The details can be followed in the annexed calculations to DocIIB. 100% of the salts were considered as passing to water during the STP treatment. The outcome was a **Sulphate PECuse, surface_water of 0. 628 mg/l and PECuse,STP of 6.28 mg/l**

Phosphate anion.

The same procedure and reasoning was followed than for the sulphate anion. The outcome was a **phosphate PECuse,surface_water of 1.227 mg/l and a phosphate PECuse, STP of 11.753 mg/l.**

It is not foreseen that sulphate or phosphate to be emitted to soil and, as 100% of the salts were considered as passing to water during the STP treatment, only direct emission to water was considered. In such case, the sludge will not be retaining the salt according to the TGD and the Simple Treat model. Therefore, PEC in soil and in groundwater were assumed to be not relevant.

Exposure to the Groundwater compartment

The fate and behaviour profile for Bromoacetic acid suggests that it is not expected to reach groundwater since this compound has a low Koc. Nevertheless the estimation made using SimpleTreat model (Doc IIB table 10.1.2-1) shows a percentage of the a.s. leading to sludge and therefore to soil after sludge application in agricultural soils and afterwards to groundwater.

The PECgroundwater was first calculated using EUSES 2.1 giving a value of PEC in groundwater under agricultural soil of 2.79×10^{-4} mg/l (manufacturing of biocidal product) and 2.69×10^{-3} mg/l (professional use). These values are above the limit established in Drinking Water Directive (0.1 µg/l).

A more realistic, higher-tier assessment of the potential for ground water contamination associated with soil applications of Bromoacetic acid has also been carried out using the simulation model FOCUS-PEARL 3.3.3.

Simulations were carried out for scenarios representing a wide range of psdo-climatological conditions in the European Union. The model was parameterised according to the standardised

guidance provided by FOCUS (2000) and German documents. FOCUS was used on the worst case assumption of arable land.

The results showed that the concentration in the majority of the scenarios is lower than 0.1 µg/l for grassland and arable lands, therefore according to the conclusions of different TM (TM I 2010 and TM II 2010), one scenario below the Drinking Water Directive limit (0.1 µg/l) is enough for the annex I inclusion to directive 98/8/EC.

Therefore **no unacceptable risk was found for the groundwater compartment.**

Sodium bromide

According to the behaviour of the bromoacetic acid. Aquatic solution is necessary to produce the bromide, therefore we suppose that the all the parent produced in ground water is going to be transformed into bromide.

There are no legal standards for Br- from the Directive 2000/60/EC (Water Framework Directive). Part C of Directive 98/83/EC gives an indicator value of 200 mg/L for sodium. The general standard of 0.1 µg/L for pesticides does not apply, since Br- is inorganic compound. As a standard is not available, testing of Br- concentrations in ground water is considered not possible.

Exposure to the soil compartment

During the life cycle of the biocidal product SEPTACIP S PS and SEPTACID S, potential indirect exposure of soil exists only during the waste disposal stage via application of contaminated sewage sludge from an STP. No direct exposure of soil is envisaged.

The predicted environmental concentration in soil receiving applications of sludge from an STP is dependant upon the fraction directed to effluent, the fraction of this directed to sludge and the rate of sewage sludge production. For sludge application to agricultural soils an application rate of 5,000 kg/ha/y dry weight is assumed while for grassland a rate of 1,000 kg/ha/y should be used.

Table 2.2.2.4-7 Predicted environmental concentrations of Bromoacetic acid in agricultural soil and grassland following the use of the biocidal products.

			Manufacturing of biocidal product	Manufacturing of biocidal product	Professional use

			Septacid S	Septacid S PS	(off-site plant)
Parameter	Soil type	Averaging time (d)	Value [mg a.s./kg_{wwt}]	Value [mg a.s./kg_{wwt}]	Value [mg a.s./kg_{wwt}]
PEClocal	Agriculture	30	6.91×10^{-4}	6.4×10^{-4}	6.15×10^{-3}
		180	2.08×10^{-4}	1.93×10^{-4}	1.86×10^{-3}
	Grassland	180	7.43×10^{-5}	6.88×10^{-5}	6.61×10^{-4}

Bromide:

According to the behaviour of the bromoacetic acid. Aquatic solution is necessary to produce the bromide, therefore it is supposed that no Bromide will be present in the soil compartment.

Exposure to the atmosphere.

Manufacturing of biocidal product:

The production installation is closed during operation. Therefore the only emission to air of Bromoacetic acid takes place within the STP. EUSES was used to estimate the emission. Please refer to EUSES files annexed to the CAR.

Product B1

$PECair_{Manufacture}$ = 2.85E-09 mg/m3

Product B2

$PECair_{Manufacture}$ = 2.85E-09 mg/m3

Professional use of biocidal product for product B1 and B2:

The emission was calculated analougsly to the $PECair_{Manufacture}$.

$PECair_{Use}$ = 1.61E-08 mg/m3

As the exposure is negligible for the atmosphere compartment, **risk was considered not of concern for this compartment**.

Non compartment specific exposure relevant to the food chain (secondary poisoning).

Based on the use of the biocidal product, exposure to Bromoacetic acid from accumulation in the food chain is not expected because the substance is readily biodegradable and has a very low Kow.

2.2.2.5. Risk characterisation

The risk characterization for the use in CIP of Bromoacetic acid based products will be based on two stages: manufacturing and use in CIP processes in breweries. The products are used exclusively by workers in breweries by performing cleaning in place (CIP) and this is the use evaluated in this dossier. Further use in the food industry by professionals has not been evaluated here.

Regarding the manufacturing, during which the mix of the components of the formulation takes place, this proceed in a closed system (A2_10) then releases to the atmosphere have been considered irrelevant. Direct releases to the aquatic compartment have been considered.

Regarding the use, products B1 and B2 are only sold for the purpose of cleaning process equipment in the food industry. Here the CIP process has been evaluated and it can be considered as completely closed. Emissions were considered only to off-site STP. After a disinfection-cycle the solution is recuperated and finally controlled released to a sewage treatment plant previous neutralization.

For the risk assessment purposes, data from the applicant and also from the harmonized scenario were used. The scenario was described in the document "Technical Notes for Guidance. Supplement to the methodology for risk evaluation of biocides. Emission scenario documents for product type 4: Disinfectants used in food and feed areas".

Considering effects and exposure of the active substance Bromoacetic acid, bromide and coformulants, the risk was quantified for the relevant compartments by means of the PEC/PNEC ratio.

Bromoacetic acid Risk for the surface water

The risk ratios for Bromoacetic acid regarding the surface water were calculated in the following table:

Table 2.2.2.5-1 Risk ratios for the surface water compartment and different scenarios for Bromoacetic acid.

Exposure scenario	Bromoacetic acid PECsw [mg/l]	Bromoacetic acid PNECw [mg/l]	PEC/PNEC
Manufacture Septacid S	1.11E-03	0.010	**0.111**
Manufacture Septacid S PS	1.03E-03		**0.103**

Use Septacid S and S PS	0.0099		**0.99**

All PEC/PNEC ratios are below 1 in the surface water compartment. Therefore **no unacceptable risk** was encountered for the aquatic compartment regarding use of Bromoacetic acid.

Bromoacetic acid Risk for sediment

Table 2.2.2.5-2 Risk ratios for the sediment compartment and different scenarios for Bromoacetic acid.

Exposure scenario	Bromoacetic acid PECsediment [mg/kg wwt]	Bromoacetic acid PNECw [mg/l]	PEC/PNEC
Manufacture Septacid S	1.65E-03	0.33	**0.005**
Manufacture Septacid S PS	1.53E-03		**0.0046**
Use Septacid S and S PS (off-site)	0.0147		**0.0445**

Therefore **no unacceptable risk for the sediment compartment regarding use of Bromoacetic acid.**

Bromoacetic acid **Risk** for **STP**

The risk ratios for Bromoacetic acid regarding the STP compartment were calculated in the following table:

Table 2.2.2.5-3 Risk ratios for the STP compartment and different scenarios for Bromoacetic acid.

Exposure scenario	Bromoacetic acid PEC_{STP} [mg/l]	Bromoacetic acid PNECmicroorganisms [mg/l]	PEC/PNEC
Manufacture Septacid S	0.0111	8	**0.00138**
Manufacture Septacid S PS	0.0103		**0.00129**
Use Septacid S and S PS	0.0987		**0.0123**

All PEC/PNEC ratios are below 1. Therefore, risk of Bromoacetic acid for the STP compartment **is not of concern** for any of the studied scenarios**.**

Bromoacetic acid Risk for Soil

Table 2.2.2.5-4 Risk ratios for the Soil compartment and different scenarios for Bromoacetic acid.

Exposure scenario	Bromoacetic acid PEC_{soil} [mg/l]	Bromoacetic acid PNECmicroorganisms [mg/l]	PEC/PNEC
Manufacture Septacid S	6.91×10^{-4}	0.00694	**$9{,}96 \times 10^{-2}$**
Manufacture Septacid S PS	6.4		**$9{,}22 \times 10^{-2}$**
Use Septacid S and S PS	6.15×10^{-3}		**$8{,}86 \times 10^{-1}$**

The results show that the PEc/PNEC ratios in the all the scenarios is below 1. Therefore **no unacceptable risk was found for the soil compartment.**

Bromoacetic acid Risk for Groundwater

Concerning the risk to the groundwater simulations were carried out for scenarios representing a wide range of psdo-climatological conditions in the European Union. The model was parameterised according to the standardised guidance provided by FOCUS (2000) and German documents. FOCUS was used on the worst case assumption of arable land.

The results showed that the concentration in the majority of the scenarios is lower than 0.1 µg/l for grassland and arable lands, therefore according to the conclusions of different TM (TM I 2010 and TM II 2010), one scenario below the Drinking Water Directive limit (0.1 µg/l) is enough for the annex I inclusion to directive 98/8/EC.

Therefore **no unacceptable risk was found for the groundwater compartment.**

Risk derived from the relevant metabolites.

Bromide Risk for surface water

The risk ratios for Bromide concerning the water compartment are collected in the following risk table.

Table 2.2.2.5-5 Risk ratios for the surface water compartment and different scenarios for Bromide

Exposure scenario	Bromide PECsw [mg/l]	Bromide PNECw [mg/l]	PEC/PNEC
Manufacture Septacid S	0.0050	0.22	**0.023**
Manufacture Septacid S PS	0.0045		**0.020**
Use Septacid S and S PS	0.045		**0.205**

Bromide Risk for sediment

Bromide anion is expected to be highly mobile as **well. Therefore PEC/PNEC derivation is not considered in this case.**

Bromide Risk for STP

The resulting risk ratios of Bromide for the STP compartment are shown in the following table.

Table 2.2.2.5-6 Risk ratios for the STP compartment and different scenarios for Bromide

Exposure scenario	Bromide PEC_{STP} [mg/l]	Bromide PNECmicroorganisms [mg/l]	PEC/PNEC
Manufacture Septacid S	0.0507	77.6	**6.53E-04**
Manufacture Septacid S PS	0.0449		**5.78E-04**
Use Septacid S and S PS	0.45		**0.0058**

Therefore, risk of bromide for the water and STP compartment **is not of concern** for any of the studied scenarios**.**

Bromide Risk for Groundwater

Concerning the risk to the groundwater simulations were carried out for scenarios representing a wide range of psdo-climatological conditions in the European Union. The model was parameterised according to the standardised guidance provided by FOCUS (2000) and German documents. FOCUS was used on the worst case assumption of arable land.

Additionally, there are no legal standards for Br- from the Directive 2000/60/EC (Water Framework Directive). Part C of Directive 98/83/EC gives an indicator value of 200 mg/L for sodium. The general standard of 0.1 ug/L for pesticides does not apply, since Br- is inorganic compound. As a standard is not available, testing of Br- concentrations in ground water is considered not possible.

Risk derived from the relevant coformulants.

Sulphate.

Risk can be regarded as not of concern for the sulphate anion. From the Screening information Data Set for HPV chemicals **Initial Assessment Report, *2005,***
http://www.inchem.org/documents/sids/sids/7757826.pdf *(July, 2010): Algae were shown to be the most sensitive to sodium sulphate; EC50 120h = 1900 mg/l. The acute studies all show a toxicity of sodium sulphate higher than 100mg/l, no bioaccumulation is expected, therefore it can be considered that no further chronic studies are required. Sediment dwelling organisms were not very sensitive either, with an LC5096h = 660 mg/l for Trycorythus sp. Overall it can be concluded that sodium sulphate has no acute adverse effect on aquatic and sediment dwelling organisms. Toxicity to terrestrial plants is also low.*

Phosphate

No risk has been calculated. Only PECs were calculated here in order to have them into account in those regions where **eutrophication** can be of concern or specific regulations should be followed at the product authorization stage.

2.2.3. List of endpoints

In order to facilitate the work of Member States in granting or reviewing authorisations, the most important endpoints, as identified during the evaluation process, are listed in Appendix I.

3. PROPOSED DECISION

3.1. Background to the proposed decision

Regarding efficacy, the active substance Bromoacetic acid has demonstrated a bactericide and fungicide activity against microorganisms known for their potential of beer spoiling effects.

The specific use being supported is the use of Bromoacetic acid as active biocidal substance in product formulations to act as PT 04 Food and Feed area disinfectants for equipment of the food processing industry at use concentrations ranging from 1%v/v (SEPTACID S) to 2% v/v (SEPTACID S PS) that is 0.13%w/v and 0.12%w/v active ingredient Bromoacetic acid, respectively. The use is limited to automatic cleaning and sanitizing in closed circuits (CIP) and for professional use only. The use in breweries has been specifically assessed for two products in the CAR.

The exposure during the production of the active substance and the formulation of the biocidal products are not assessed by the Rapporteur under the requirements of the BPD.

Based on the inherent hazard profile and the intended use of Bromoacetic acid during CIP processes (closed systems) professional exposure is controlled and limited. Professionals must wear suitable protective clothing and shoes, chemically resistant gloves (tested to EN374) and eye/ face protection adequate to handle corrosive chemicals.

During application in disinfection of food processing installations (as assessed for breweries in this submission) no secondary exposure of the general public takes place.

Indirect exposure is expected for adults due to the ingestion of Bromoacetic acid residues due to the consumption of beer by adults. This exposure is assumed to be chronic. Analysis of beer samples for disinfectant content shows that residues of Bromoacetic acid in beer as a result of its use are negligible. Hence the dietary exposure of consumers to residues of Bromoacetic acid in beer is not a concern. For other potential applications in PT4 for CIP uses in the food processing industry the assessment of indirect exposure needs to be performed at product authorization level.

Regarding the Environment, Bromoacetic acid was evaluated in the presented formulates and under the considered dose and pattern of use it does not pose risk of concern for the aquatic compartment and was considered safe.

Bromoacetic acid does not meet neither POP / vPvB-criteria nor PBT criteria and is therefore not a potential PBT substance. Regarding Endocrine disruption, no further data than those used for Human Toxicology are available. No known Endocrine Disruption effect is however reported in literature.

3.2. Proposed decision

The overall conclusion from the evaluation of Bromoacetic acid for use in Product Type 4 (food and feed area disinfectants), is that it may be possible to issue authorisations of products containing Bromoacetic acid in accordance with the conditions laid down in Article 5(1) b), c) and d) of Dir. 98/8/EC.

At the time of finalisation of this assessment report, there is no indication that this conclusion would not be valid with regard to compliance with Article 19(1), (2) and (5), and the common principles of Annex VI of Regulation (EU) No 528/2012. As consequence, it can also be concluded that it may be possible to issue authorisations of products containing Bromoacetic acid in accordance with Article 19(1), (2) and (5), and the common principles of Annex VI of Regulation (EU) No 528/2012.

There is no indication that Bromoacetic acid would fulfil the exclusion criteria specified in article 5(1), nor the substitution criteria specified in Article 10 (1) of Regulation (EU) No 528/2012.

It is therefore proposed to approve Bromoacetic acid is an active substance for use in product-type 4 (food and feed area disinfectants), subject to the following specific conditions:

1. The active substance, Bromoacetic acid, as manufactured, shall have a minimum purity of 94.6%w/w dry weight basis.- 81.1% w/w wet weight basis..

2. The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.

3. Authorisations are also subject to the following particular conditions:

   1) For industrial or professional users, safe operational procedures and appropriate organizational measures shall be established. Where exposure cannot be reduced to an acceptable level by other means, products shall be used with appropriate personal protective equipment.

   2) For products that may lead to residues in food or feed, the need to set new or to amend existing maximum residue levels (MRLs) in accordance with Regulation (EC) No 470/2009 or Regulation (EC) No 396/2005 shall be verified, and any appropriate risk mitigation measures shall be taken to ensure that the applicable MRLs are not exceeded.

   3) Products containing bromoacetic acid shall not be incorporated in materials and articles intended to come into contact with food within the meaning of Article 1(1) of Regulation (EC) No 1935/2004, unless the Commission has established specific limits on the migration of bromoacetic acid into food or it has been established pursuant to that Regulation that such limits are not necessary.

Where a treated article has been treated with or intentionally incorporates bromoacetic acid, and where necessary due to the possibility of skin contact as well as the release of bromoacetic acid under normal conditions of use, the person responsible for placing the treated article on the market shall ensure that the label provides information on the risk of skin sensitisation, as well as the information referred to in the second subparagraph of Article 58(3) of Regulation (EU) No 528/2012.

3.3. Elements to be taken into account when authorising products

Further efficacy data will be required to support authorisation of the biocidal product at the Member State level in accordance with the claims.

The use of Bromoacetic acid as active biocidal substance in product formulations to act as PT04 Food and Feed area disinfectant is limited to automatic cleaning and sanitizing in closed circuits (CIP) and for professional use only. For the approval, the use in breweries has been specifically assessed for two products. Other potential applications need to be assessed at product authorization level.

When professional workers handle the concentrated biocidal products and use it for cleaning - in-place (CIP) processes in the food industry the use of personal protective equipment including respiratory protection is mandatory (suitable protective clothing and shoes, chemically resistant gloves (tested to EN374) and eye/ face protection appropriate to handle corrosive chemicals).

The reference product was only assessed for use by professional users only. Non-professional use is not envisaged by the applicant at the approval stage.

It seems that use of the Bromoacetic acid is always combined with high concentrations of mineral acids. This fact should be taken into consideration for the authorization of the product.

Finally, it will have to be taken into account that the application of the SEPTACID S or SEPTACID S PS biocidal products does not lead to significant concerns in terms of dietary risk assessment if appropriate post-use water rinse measures are followed and show a no relevant residue situation in beer. This issue and the need to establish MRLs should be further considered when agreed guidelines are in place.

Regarding the Environment, other pattern of use, doses and formulates containing Bromoacetic acid as a.i. different of what assessed here should be assessed in order to ensure a safe use under National Authorization.

Products formulated with phosphoric acid in order to maintain low pH should be controlled in order to avoid water eutrophication or meet National Regulations.

Dermal absorption values used in the applications for product authorisation should be justified, if available by the submission of specific dermal absorption data on the product, or by read-across to existing data if scientifically justified, or by using default values.

3.4. Requirement for further information

It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit the proposal for the approval of Bromoacetic acid in accordance with Article 9 of Regulation No 528/2012.

3.5. Updating this Assessment Report

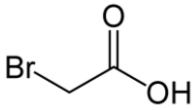
This Assessment Report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information submitted in relation with Regulation (EU) No 528/2012. Such adaptations will be examined and finalised in connection with any amendment of the conditions for the approval of Bromoacetic acid.

Appendix I: List of endpoints

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

Active substance (ISO Common Name)	Bromoacetic acid
Product-type	Food and feed area disinfectants

Identity

Chemical name (IUPAC)	2-bromo-ethanoic acid
Chemical name (CA)	Bromoacetic acid
CAS No	79-08-3
EC No	201-175-8
Other substance No.	None
Minimum purity of the active substance as manufactured (g/kg or g/l)	94.6%w/w dry weight basis.- 81.1% w/w wet weight basis.
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	None
Molecular formula	$C_2H_3BrO_2$
Molecular mass	138.95 g/mol
Structural formula	

Physical and chemical properties

Melting point (state purity)	41-46 °C (99.6%)
Boiling point (state purity)	206-208 °C (99.6%)
Temperature of decomposition	371.2 °C
Appearance (state purity)	Solid (100%); yellowish liquid (80%)
Relative density (state purity)	1.5865 g/cm^3 at 20 ^{o}C (80% solution in water)
Surface tension	67.86 mN/m 20 ^{o}C
Vapour pressure (in Pa, state temperature)	20.2 Pa 25°C
Henry's law constant (Pa m^3 mol $^{-1}$)	Bond est: 0.006393 Pa m3/mol at 25 ºC Group est: 0.008998 Pa m3/mol at 25ºC
Solubility in water (g/l or mg/l, state temperature)	pH__5____: completely soluble
	pH__9____: completely soluble
	pH__7____: completely soluble
Solubility in organic solvents (in g/l or mg/l, state temperature)	Solubility in methanol:> 250g/L at 22ºC Solubility in n-hexane:10 - 20 g/L at 22ºC
Stability in organic solvents used in biocidal products including relevant breakdown products	Not available
Partition coefficient (log P_{OW}) (state temperature)	pH 5 log Pow = -0.29
	pH 7 log Pow < -2.31
	pH 9 log Pow < -2.30
Hydrolytic stability (DT_{50}) (state pH and temperature)	pH 4.0 = 220 h, pH 7.0 = 510 h, pH 9.0 =310h at 40ºC pH 4.0 =710-700 h, pH 7.0 =1890-1850 h, pH 9.0 = 910-920 h at 30°C
Dissociation constant	pKa = 3.3 at 22 °C
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	The test substance shows absorption below 280 nm with no maximum in double distilled water. In 1N HCl/water (90/10 v/v/) the test substance shows absorption below 280 nm with no maximum
Photostability (DT_{50}) (aqueous, sunlight, state pH)	14.9 days (12-h sunlight)
Quantum yield of direct phototransformation in water at □ > 290 nm	Not available
Oxidizing properties	Bromoacetic acid doesn´t show oxidizing properties
Reactivity towards containers material	Bromoacetic acid is incompatible with metals, but stable with appropriate container materials such as plastic containers made of polyethylene or polypropylene certified for use with acid and glass bottle with screw cap.
Flammability	Bromoacetic acid is not highly flammable
Explosive properties	Bromoacetic acid doesn´t show explosive properties

Classification and proposed labelling

with regard to physical/chemical data	None
with regard to toxicological data	Toxic, Corrosive; R23/24/25-35-43
with regard to fate and behaviour data	-
with regard to ecotoxicological data	N; R50

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	HPLC with a column "Prevail Organic Acid" ALLTECH. UV detector at 210 nm
Impurities in technical active substance (principle of method)	IC(Ionic chromatography) /conductimetric detector

Analytical methods for residues

Soil (principle of method and LOQ)	Based on the use of the A.S. in CIP, there is inherently negligible emission to the environment, therefore development of an analytical method for soil is not necessary.
Air (principle of method and LOQ)	GC/MS LOQ = $2 \cdot 10^{-5}$ µg/m^3
Water (principle of method and LOQ)	Surface water GC (electron capture), LOQ=0.25 µg/L Drinking water GC/MS, LOQ=0.02µg/L
Body fluids and tissues (principle of method and LOQ)	Plasma GC/MS 0.02µg/L Urine GC/MS 0.02µg/L.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Residues in beer GC (electron capture) LOQ=0.1µg/mL Independent Laboratory Validation of r**esidues in beer** GC (electron capture) LOQ=$4 \cdot 10^{-3}$ µg/mL
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	N.a.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	30% is assumed
Rate and extent of dermal absorption:	100% is assumed
Rate and extent of inhalation absorption:	100% is assumed
Distribution:	Highly distributed
Potential for accumulation:	No data
Rate and extent of excretion:	The free substance and metabolites are not detected in blood/urine after 3 min.
Toxicologically significant metabolite(s)	No data

Acute toxicity

Rat LD_{50} oral	177 mg/kg bw (only for males)
Rabbit LD_{50} dermal	59.9 mg/kg bw
Rat LC_{50} inhalation	No data
Skin irritation	Corrosive
Eye irritation	Corrosive
Skin sensitization (test method used and result)	Sensitizer (Guinea-Pig Maximisation Test; more than 30% of the test animals reacted positively)

Repeated dose toxicity

Species/ target / critical effect	Rats/-/ /-/ reduction of the food intake and body weight
Lowest relevant oral NOAEL / LOAEL	For rats NOAELsystemic = 3.09 mg/kg bw/day (90-day oral study) LOAELoral = 20.7 mg/kg bw/day (90-day oral study)
Lowest relevant dermal NOAEL / LOAEL	No data
Lowest relevant inhalation NOAEL / LOAEL	No data

Genotoxicity	In vitro Bromoacetic acid shows clastogenic and mutagenic effects in some in vitro studies In vivo

	Bromoacetic acid is not genotoxic or mutagenic in vivo.

Carcinogenicity

Species/type of tumour	No data
lowest dose with tumours	No data

Reproductive toxicity

Species/ Reproduction target / critical effect	Rat/ No recorded effect on reproductive parameters/ reduction in body weight or body weight gain
Parental NOAEL / LOAEL	LOAELoral = 11.6 mg / kg bw / day NOAELsystemic = 1.5 mg / kg bw / day
Lowest relevant reproductive NOAEL / LOAEL	Not observed at the highest dose: 21.9 mg/kg bw
Species/Developmental target / critical effect	Rats/ No recorded effect on development parameters/ decreased food and water consumption and lower body weight
Developmental toxicity	
Lowest relevant developmental NOAEL / LOAEL	NOAEL (F1)oral = 10 mg / kg bw / day (males), 14 mg / kg bw / day (females)

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	No data
Lowest relevant developmental NOAEL / LOAEL.	No data

Other toxicological studies

.....	No data

Medical data

.....	No data

Summary	Value	Study	Safety factor
ADI (if residues in food or feed))	0.026 mg/kg bw/day	90-day rat oral study	400
AELsystemic (Operator/Worker Exposure, short term)	0.015 mg/kg bw/day	teratogenicity oral study in rat	100
AELsystemic (Operator/Worker Exposure, medium term)	0.015 mg/kg bw/day	90-day oral rat study	200
AELsystemic (Operator/Worker Exposure, long term)	0.0077 mg/kg bw/day	90-day oral rat study	400

AEC_{local}	0.05%	Guinea Pig Maximisation Test	20
ARfD (acute reference dose)	0.05 mg/kg bw/day	teratogenicity oral study in rat	100
Drinking water limit	No relevant		

Acceptable exposure scenarios (including method of calculation)

Professional users	The biocidal products are only intended for use in cleaning in place (CIP) systems and for professional use only. The loading of the biocidal products into the system to be disinfected occurs in an automated, closed system. No risk is envisaged. See details in Doc IIB.
Production of active substance:	Not applicable
Formulation of biocidal product	Not applicable
Secondary exposure	Not applicable
Non-professional users	Not applicable
Indirect exposure as a result of use	Ingestion of Bromoacetic acid residues is expected after the use of the biocidal products to clean and disinfect the drinks producing tank. No risk is envisaged. See details in Doc IIB.

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)

Bromoacetic acid

pH	Temperature [°C]	Reaction rate constant, K_h [1/s x 10^5]	Half-life, DT_{50} [h]	Half-life, DT_{50} [h] for 12ºC (1)	Reference
4.0	40	$8.7*10^{-7}$ (sec^{-1})	220	2066	A7.1.1.1.1/01
7.0		$3.8*10^{-7}$ (sec^{-1})	510	4791	
9.0		$6.2*10^{-7}$ (sec^{-1})	310	2912	
4.0	30	$2.7*10^{-7}$ (sec^{-1})	710	2997	
		$2.7*10^{-7}$ (sec^{-1})	700	2954	
7.0		$1.0*10^{-7}$ (sec^{-1})	1890	7977	
		$1.0*10^{-7}$ (sec^{-1})	1850	7808	
9.0		$2.1*10^{-7}$ (sec^{-1})	910	3841	
		$2.1*10^{-7}$ (sec^{-1})	920	3883	

Photolytic / photo-oxidative degradation of active substance and resulting relevant

Negligible photo reactivity of Bromoacetic acid is expected given the analysis of photo reactivity in air (please see bellow).

metabolites	
Readily biodegradable (yes/no)	Yes
Biodegradation in seawater	n.d.
Non-extractable residues	n.d.
Distribution in water / sediment systems (active substance)	n.d.
Distribution in water / sediment systems (metabolites)	n.d.

Route and rate of degradation in soil

Mineralization (aerobic)	
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (20°C, aerobic): n.d.
	DT_{90lab} (20°C, aerobic): n.d.
	DT_{50lab} (10°C, aerobic): n.d.
	DT_{50lab} (20°C, anaerobic): n.d.
	degradation in the saturated zone: n.d.
Field studies (state location, range or median with number of measurements)	DT_{50f}: n.d.
	DT_{90f}:
Anaerobic degradation	n.d.
Soil photolysis	Negligible photo reactivity of Bromoacetic acid is expected given the analysis of photo reactivity in air (please see bellow).
Non-extractable residues	n.d.
Relevant metabolites - name and/or code, % of applied active ingredient (range and maximum)	Not determined. Bromide ion is released from Bromoacetic acid acid hydrolysed in equimolar ratio, as described before in *Concurrent Exchange and Hydrolysis Reactions of Bromoacetic Acid. Specific Cation Effect*. J.F. Hinton and F.J. Johnoston. J. Phys. Chem. 1996. 70 (3), 841-844.
Soil accumulation and plateau concentration	n.d.

Adsorption/desorption

Ka , Kd

Ka_{oc} , Kd_{oc}

pH dependence (yes / no) (if yes type of dependence)

Guideline / Test method	K_a [1]	K_{aOC} [2]	Reference
Soil 1 pH 4.2 Soil 2 pH 5.3 Soil 3 pH 5.7	0 0.04 0.19	0 1.3 32.5	A7.1.3/01

	K_d [3] and K_{dOC} [4] not determined. Degradation products not measured and not identified.

Fate and behaviour in air

Direct photolysis in air	OVERALL OH Rate Constant 0.7161 E-12 cm3/molecule-sec during 24 hours of daylight and a half-life of 22.40 Days (24-hr day; 0.5E6 OH/cm3).
Quantum yield of direct photolysis	
Photo-oxidative degradation in air	Latitude: ..... Season: ..... DT_{50} .....
Volatilization	

Monitoring data, if available

Soil (indicate location and type of study)	
Surface water (indicate location and type of study)	
Ground water (indicate location and type of study)	
Air (indicate location and type of study)	

Chapter 5: Effects on Non-target Species

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Brachydanio rerio	96h	LC50 (48h)	134 mg/l (A7.4.1.1/01)
Brachydanio rerio	28d	NOEC	77 mg/l (A7.4.3.2/01)
Invertebrates			
Daphnia magna	48h	LC50	42 mg/l (A7.4.1.2)
Daphnia magna	21d	NOEC	1.6 mg/l (A7.4.3.4/01)
Algae			
Selenastrum capricornutum	72h	LCr50 LCb50 NOECr	0.29 mg/l (A7.4.1.3/01) 0.28 mg/l (A7.4.1.3/01) 0.10 mg/l (A7.4.1.3/01)
Scenedesmus subspicatus	72h	ECr50 ECb50 ECr10	1.4 mg/l (A7.4.1.3/02) 0.20 mg/l (A7.4.1.3/02) 0.10 mg/l (A7.4.1.3/02)
Microorganisms			
		NOEC	776 mg Br-/L

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Fathead Minnows	96h	LC50(96h)	16479 mg/l (NaBr)
Poecilia reticulata	124d	NOEC	7.8 mg (Br^-)/l
Invertebrates			
Daphnia magna	48h	LC50	6.7-9.3 g (NaBr)/l
	48h	LC50	8.9 g (NaBr)/l
	16d	NOEC	2.2 mg (Br-)/L)
	16d	NOEC	5.8 mg (Br-)/L
	21d	NOEC	14.3 mg (Br-)/L
	21d	NOEC	<3 to 19 (NaBr) mg/L
	19d	NOEC	2.2 mg (Br-)/L)
Algae			
Scenedesmus subspicatus	72h	E_bC_{50}[1] E_rC_{50}[2]	8000 mg NaBr/L 20000 mg NaBr/L
Microorganisms			
activated sludge respiration inhibition test		NOEC	776 mg Br-/L

Effects on earthworms or other soil non-target organisms

Acute toxicity to ……..	n.d.
Reproductive toxicity to ……	n.d.

Effects on soil micro-organisms

Nitrogen mineralization	n.d.
Carbon mineralization	n.d.

Effects on terrestrial vertebrates

Acute toxicity to mammals	n.d.
Acute toxicity to birds	n.d.
Dietary toxicity to birds	n.d.
Reproductive toxicity to birds	n.d.

Effects on honeybees

Acute oral toxicity	n.d.
Acute contact toxicity	n.d.

Effects on other beneficial arthropods

Acute oral toxicity	n.d.
Acute contact toxicity	n.d.
Acute toxicity to ……..	n.d.

Bioconcentration

Bioconcentration factor (BCF)	Bromoacetic acid has a mean expected logPow= -0.3 at pH 5, logPow= -2.3 at pH 7 and logPow= -2.3 at pH 9, at 22ºC, what suggests a low potential to accumulate in environmental compartments. A QSAR estimate was performed and the BCF for fish was 3.16, EPI suite from EPA USA (2000):BCF Program version 2.17
Depration time (DT_{50}) (DT_{90})	n.d.
Level of metabolites (%) in organisms accounting for > 10 % of residues	n.d.

Chapter 6: Other End Points

Appendix II: List of Intended Uses

Object and/or situation (a)	Member State or Country	Product name	Organisms controlled (c)	Formulation		Application			Applied amount per treatment			Remarks: (m)
				Type (d-f)	Conc. of as (i)	Method kind (f-h)	Number min max (k)	interval between applications (hours)	g as/L min max	water L/m^2 min max	g as/m^2 min max	
CIP cleaning in place	All	SEPTACIDS	Bacteria: *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus hirae* Fungi: *Candida albicans, Aspergillus niger*	LIQUID	8 % (w/w)	CIP	1	24	0.13 % (w/v)	N.a.	N.a.	PPE mandatory
CIP cleaning in place	All	SEPTACIDS PS	Bacteria: *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus hirae* Fungi: *Candida albicans, Aspergillus niger*	LIQUID	4% (w/w)	CIP	1	24	0.12 % (w/v)	N.a.	N.a.	PPE mandatory

(a) *e.g.* biting and suckling insects, fungi, molds; (b) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(c) GCPF Codes - GIFAP Technical Monograph No 2, 1989 ISBN 3-8263-3152-4); (d) All abbreviations used must be explained
(e) g/kg or g/l;(f) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench;
(g) Kind, *e.g.* overall, broadcast, aerial spraying, row, bait, crack and crevice equipment used must be indicated;
(h) Indicate the minimum and maximum number of application possible under practical conditions of use;
(i) Remarks may include: Extent of use/economic importance/restrictions

1 adapted from: EU (1998a): European Commission: Guidelines and criteria for the preparation of complete dossiers and of summary dossiers for the inclusion of active substances in Annex I of Directive 91/414/EC (Article 5.3 and 8,2). Document 1663/VI/94 Rev 8, 22 April 1998

Appendix III: List of studies

Data protection is claimed by the applicant in accordance with Article 12.1(c) (i) and (ii) of Council Directive 98/8/EC for all study reports marked "Y" in the "Data Protection Claimed" column of the table below. These claims are based on information from the applicant. It is assumed that the relevant studies are not already protected in any other Member State of the European Union under existing national rules relating to biocidal products. It was however not possible to confirm the accuracy of this information.

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	Key study
A2.10/01	Albemarle	2007	Production of monobromoacetic acid as 80% solution in water used for the formulation of biocidal products Albemarle Unpublished	Y	Albemarle SPRL	Y
A2.10/02	Verschaeve, S.	2007	Final concentration of MBAA in biocidal product Sopura N.V. Unpublished	Y	Sopura N.V.	Y
A2.10/02PS	Verschaeve, S.	2007	Final concentration of MBAA in biocidal product Sopura N.V. Unpublished	Y	Sopura N.V.	Y
A2.10/03	Verschaeve, S.	2007	Cleaning and disinfecting using a CIP-system Sopura N.V Unpublished.	Y	Sopura N.V.	Y
A2.10/04	Verschaeve, S.	2007	Method to calculate the unavoidable residue Sopura N.V. Unpublished	Y	Sopura N.V.	Y
A2.10/04PS	Verschaeve, S.	2007	Method to calculate the unavoidable residue Sopura N.V. Unpublished	Y	Sopura N.V.	Y
A2.10/05	Verschaeve, S.	2007	Notification of monobromacetic acid Manufacturing process of the biocidal preparations Sopura N.V. Unpublished	Y	Sopura N.V.	Y
A2.10/05PS	Verschaeve, S.	2007	Notification of monobromacetic acid Manufacturing process of the biocidal preparations Sopura N.V. Unpublished	Y	Sopura N.V.	Y

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	Key study
A2.10/06	Verschaeve, S.	2007	Quantitative evaluation of monobromacetic acid likely to be found back in the environment after application//SEPTCID S Sopura N.V. Unpublished	Y	Sopura N.V.	Y
A2.10/06PS	Verschaeve, S.	2007	Quantitative evaluation of monobromacetic acid likely to be found back in the environment after application//SEPTCID S PS Sopura N.V. Unpublished	Y	Sopura N.V.	Y
A3/01	Garofani, S.	2008	Monobromoacetic Acid (MBAA 100%) Determination of the Melting Point Chem Service S r.l ChemService Study No. CH-260/2008 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A3/02	Lewis Sr., Richard J.	2002	Hawley's Condensed Chemical Dictionary (14th Edition) John Wiley & Sons Published	N	Published	Y
A3/03	Gangolli, S.	2005	Dictionary of Substances and Their Effects (DOSE, 3rd Electronic Edition) Royal Society of Chemistry Published	N	Published	Y
A3/04	Garofani, S.	2008	Monobromoacetic Acid (MBAA 100%) Determination of the Boiling Point Chem Service S r.l ChemService Study No. CH-261/2008 Unpublished	Y	Sopura N.V. Albemarle SPRL.	Y
A3/05	Cordia, J.A.	1999	Determination of some physico-chemical properties of Monobromoacetic acid; TNO PML Report no PML-1999-C86 Unpublishe	Y	Sopura N.V. Albemarle SPRL	Y
A3/06	Gaisser, H.-D.	2007	Calculation of the Henry Law Constant for bromoacetic acid with the Program HENRYWIN v3.10	Y	MCF-Consultancy GmbH	Y

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	Key study
A3/07	Staudinger, J., Roberts, P.V.	2001	A critical compilation of Henry's law constant temperature dependence relations for organic compounds in dilute aqueous solutions Pergamon; Chemosphere 44 (2001) 561-576 Published	N	Published	Y
A3/08	Garofani, S.	2008	Monobromacetic Acid 80% Solution in Water: Determination of the Relative Density Chem Service S r.l ChemService Study No. CH-262/2008 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A3/09	Garofani, S.	2008	Monobromacetic Acid 80% Solution in Water: Determination of the Partition Coefficient (N-Octanol/Water) also as a Function of the PH Value Chem Service S r.l ChemService Study No. CH-263/2008 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A3/10	Garofani, S.	2008	Monobromacetic Acid 80% Solution in Water: Determination of the Water Solubility also as a Function of the PH Value Chem Service S r.l ChemService Study No. CH-264/2008 Unpublished	Y	Sopura N.V. Albemarle SPRL.	Y
A3/11	Gaisser, H.-D	2007	Expert Statement Thermal stability of bromoacetic acid	Y	MCF-Consultancy GmbH	Y
A3/12	Gaisser, H.-D	2007	Expert Statement Flammability of bromoacetic acid	Y	MCF-Consultancy GmbH	Y
A3/13	Verschaeve, S.	2007	Physico-chemical Parameters Sopura N.V. Unpublished	Y	Sopura N.V.	Y
A3/14	Verschaeve, S.	2005	Surface Tension Measurement Sopura N.V. Unpublished	Y	Sopura N.V.	Y
A3/15	Gaisser, H.-D	2007	Expert Statement Explosive properties of bromoacetic acid	Y	MCF-Consultancy GmbH	Y
A3/16	Gaisser, H.-D	2007	Expert Statement Oxidizing properties of bromoacetic acid	Y	MCF-Consultancy GmbH	Y

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	Key study
A3/17	Gaisser, H.-D	2007	Expert Statement Reactivity of bromoacetic acid towards container materials	Y	MCF-Consultancy GmbH	Y
A3/18	Garofani, S.	2008	Monobromacetic Acid 80% Solution in Water: Determination of the Dissociation Constant in Water Chem Service S r.l ChemService Study No. CH-266/2008 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A3/19	Garofani, S.	2008	Monobromoacetic Acid (MBAA 100%): Determination of the Solubility in Organic Solvents (Methanol and N-Hexane) Chem Service S r.l ChemService Study No. CH-265/2008 Unpublished	Y	Sopura N.V. Albemarle SPRL.	Y
A3/20	Ticco S.P.	2012	Monobromacetic acid 80% solution: complete analysis of five batch samples; Chem Service S r.l. Report No CH-130/2012; Sopura S.A. Unpublished	Y	Sopura N.V. Albemarle SPRL	y
A3/21	Mazzei N.	2012	Flash point on the sample *Monobromacetic acid 80 % solution*; INNOVHUB, Stationi Sperimentali per l'Industria Report No 201201753; Sopura S.A. Unpublished	Y	Sopura N.V. Albemarle SPRL	
A3/22	Ticco S.P.	2012	Monobromacetic acid 80% solution: determination of the viscosity; Chem Service S r.l. Report No CH-126/2012; Sopura S.A. Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A3/23	Ticco S.P.	2012	Monobromacetic acid 80% solution: determination of the accelerated storage stability and corrosion characteristics; Chem Service S r.l. Report No CH-127/2012; Sopura S.A. Unpublished	Y	Sopura N.V. Albemarle SPRL	Y

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	Key study
A4.1/01	Servais, D., Vandermarliere, M.	2006	Method for the monobromoacetic acid determination by hplc; Report no it.lma.37 ; Validation report of the analytical method of monobromoacetic acid determination by hplc; Sopura s.a.; Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A4.1/01a	Ticco S.P.	2012	Monobromacetic Acid 80% Solution: Validation Of The Analytical Method For The Determination Of The Active Ingredient Content; Chem Service S r.l. Report No CH-128/2012; Sopura S.A. Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A4.1/01b	Ticco S.P.	2012	Monobromacetic acid 80% solution: validation of the analytical method for the determination of the significant impurities content; Chem Service S r.l. Report No CH-129/2012; Sopura S.A. Unpublished	Y	Sopura N.V. Albemarle SPRL	
A4.1/01c	Ticco S.P.	2012	Monobromacetic acid 80% solution: complete analysis of five batch samples; Chem Service S r.l. Report No CH-130/2012; Sopura S.A. Unpublished	Y	Sopura N.V. Albemarle SPRL	
A4.2/02	Zazzi, B.C. et al.	2006	Method of Analysis at the U.S. Geological Survey California Water Science Center; Sacramento Laboratory; Govt Reports Announcements & Index (GRA&I), Issue 01, 2006; Published	N	Published	Y
A4.3/01	D. Servais, M., Vandermarliere,.	2006	Method for the monobromacetic acid determination in water or beer by gaseous chromatography Sopura N.V. IT-LMA 20 Unpublished	Y	Sopura N.V.	Y

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	Key study
A4.3/01a	Ticco S.P.	2012	Monobromacetic acid 100%: independent laboratory validation of the analytical method it-lma-20 for the determination of residues in beer; Chem Service S r.l. Report No CH-124/2012 Unpublished	Y	Sopura N.V. Albemarle SPRL	
A5/01	S. Verschaeve	2007	Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies Sopura N.V. Unpublished	Y	Sopura N.V.	Y
A5.3/01	P. Maurer, R. Coomans	2007	Evaluation of the microbicidal activity according to the European standard test methods monobromoacetic acid; Haute Ecole Lucia de Brouckère Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A6.1.1/01	R.E. Linder et al.	2003	Acute Spermatogenic Effects of Bromoacetic Acids; Fund. Appl. Toxicol. 22, P 422-430; Published	N	Published	Y
A6.1.2/01	Anonymus	1993	RTECS Database	Y	NIOSH	Y
A6.1.2/02	Anonymus	1977	EPA	Y	Eastman Kodak CO	Y
A6.1.4e/01	M.K. Prinsen	1992	Chicken Enucleated Eye Test (CEET) with monobromoacetic acid; an alternative to the Draize eye irritation test with rabbits. TNO Nutrition and food Research; Report no. V92.244/352069	Y	Sopura N.V. Albemarle SPRL	Y
A6.1.4s/01	L. Eriksson et al.	1993	A multivariate quantitative structure-activity relationship for corrosive carboxylic acids Chemometrics and Intelligent Laboratory Systems 23 (1994) 235-245	N	Elsevier	Y
A6.1.5/01	Prinsen M.K.	1992	Sensitization study with monobromoacetic acid in guinea pigs (maximization test); TNO Nutrition and Food Research Report no. V 92.202 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y

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	Key study
A6.2.2/01	W.J.M. Maas	2007	In vitro percutaneous absorption of Monobromoacetic acid (MBAA) in three concentrations through human and rat skin membranes using flow-through diffusion cells TNO Quality of Life Report no V7008 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A6.2.3/01	W.J.M. Maas	2008	Stability test with Monobromoacetic acid (MBAA) TNO Quality of Life Report no V7540 Unpublished	Y	Sopura N.V. Albemarle SPRL	**Y**
A6.2.1/01	Saghir and Schultz	2005	Toxicokinetics and Oral Bioavailability of Halogenated Acetic Acids Mixtures in Naïve and GSTzeta-Depleted Rats Toxicological science 84, 214-224 (2005) Published	N	Published	Y
A6.3.1/01	D. Jonker	1990	Sub-acute (28—day) oral toxicity study with bromoacetic acid in rats (range-finding study); TNO-CIVO Institutes; Report no: 89.578 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A6.4.1.1/01	D. Jonker	1998	Sub-chronic (13-week) oral toxicity study with monobromoacetic acid in rats; TNO Nutrition and food Research; Report no. V98.848 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A6.6.1/01	J.W.G.M.Wilmer	1985	Examination of bromoacetic acid for mutagenic activity in the Ames test; CIVO-TNO; Report no V 85.285/250064; Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A6.6.2/01	J.W.G.M. Wilmer	1985	Chromosome Analysis of cultured Chinese hamster ovary cells treated with monobromoacetic acid; CIVO-TNO Report no: V 85.322 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A6.6.2/02	Van Delft J.H.M. N. de Vogel	1999	Chromosomal aberration test with monobromoacetic acid in cultured Chinese hamster ovary cells; TNO Nutrition and Food Research Institute; Report no. V98.1246	Y	Sopura N.V. Albemarle SPRL	Y

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	Key study
A6.6.3/01	P.B. Davis	1987	An Investigation into the possible induction of point mutations at the HGPRT Locus of chinese hamster ovary cells by monobromoacetic acid TNO Report no 87/025 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A6.6.4/01	N. de Vogel	1990	Chromosome analysis in bone marrow cells of rats after oral administration of Bromoacetic acid; TNO-CIVO Institutes Report no. V90.215 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A6.6.4/02	N. de Vogel	2006	In-vivo Chromosomal Aberration Test in bone marrow cells of male rats treated with Monobromoacetic acid TNO Report no V 6802/01	Y	Sopura N.V. Albemarle SPRL	Y
A6.6.5/01	S. Giller et al.	1997	Comparative genotoxicity of halogenated acetic acids found in drinking water UK Environmental Mutagen Society Mutagenis vol 12 pp 321-328 Published	N	Published	
A6.7.1/01	WHO	2000	Disinfectants and disinfectant by-products, IPCS INCHEM Environmental Health Criteria 216 Published	N	Published	
A6.7.1/02	Federal-Provincial-Territorial Committee on Drinking Water	2006	Haloacetic Acids in Drinking Water; Publication of Health Canada Published	N	Published	
A6.7.1/03	Anonymus		NTP 11th Report on Carcinogens U.S. Department of Health and Human Services Published	N	Published	
A6.7.1/04	EPA	2006	National Primary Drinking Water Regulations: Stage 2 Disinfectants and Disinfection Byproducts Rule; U.S. Environmental Protection Agency, Federal Register: January 4, 2006, Volume 71, Number 2; Published	N	Published	
A6.8.1.1/01	A.E. Smits-van Prooije, D.H. Waalkens-Berendsen	1993	Oral embryotoxicity/teratogenicity study with bromoacetic acid in rats TNO Nutrition and Food Research Report no V 93.479 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y

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	Key study
A6.8.2/01	D. Jonker, D.H. Waalkens-Berendsen	1994	Oral two-generation reproduction stuy with bromoacetic acid in rats; TNO Nutrition and food Research, Report no: V 93.564 Unpublished	Y	Sopura N.V. Albemarle SPRL	
A7.1.1.1.1/01	A. Schouten	1999	Abiotic degradation of monobromoacetic acid according to OECD guideline 111; TNO Nutrition and Food Research Institute: Report no: V99.243 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A7.1.1.2.1/01	J. Hemmink, A.J.M. Blom	1992	Ready biodegradability of monobromoacetic acid according to EEC Directive 79/831 Annex V Part C (CO2 Evolution Test) TNO; Report no: R32/032; Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A7.1.1.2.1/02	Neri, MC	2010	Ready Biodegradability of Monobromoacetic acid (MBAA) solution in a carbon dioxide evolution test ChemService S r.l. Testing Laboratory; CH-E - 028/2009;	Y	Sopura N.V. Albemarle SPRL	
A7.1.3/01	K. van der Kerken	1997	Adsorption/desorption test on monobromacetic acid LISEC, studiecentrum voor ecologie en bosbouwv.z.w. BB-03-005 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A7.4.1.1/01	R.N. Hooftman, J.A. Kauffman-van Bommel	1991	The acute toxicity of monobromoacetic acid to *Brachydanio rerio* (OECD Guideline No. 203); TNO Environmental and Energy Research; Report no R91/249	Y	Sopura N.V. Albemarle SPRL	Y
A7.4.1.2/01	R.N. Hooftman, J.A. Kauffman-van Bommel	1991	The acute toxicity of monobromoacetic acid to *Daphnia magna* (OECD Guideline No. 202,48h); TNO Environmental and Energy Research; Report no R91/248	Y	Sopura N.V. Albemarle SPRL	Y

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	Key study
A7.4.1.3/01	A.O. Hanstveit, H. Oldersma	1992	Effects of monobromoacetic acid on the growth of the algae *Selenastrum capricornum* (OECD 201); TNO Environmental and Energy Research; Report no R91/238; Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A7.4.1.3/02	R. Kühn and M. Pattard.	1990	Results of the harmful effects of water pollutants t o green algae (*Scenedesmus subspicatus*) in the cell multiplication inhibition test. Wat. Res. Vol 24, No. 1, pp. 31-38	N	Open Source Literature.	
A7.4.1.4./01	Ph. Mayer et al.	2001	Screening of the effect of monobromoacetic acid on the respiration of activated sludge (OECD Guideline No 209) TNO Nutrition and Food Research Report no V2391/03 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A7.4.1.4/02	Clarke N, and Azarnia F. D.	2009	Sodium Bromide: Assessment of the Inhibitory Effect on the Respiration of Activated Sewage Sludge, Harlan Laboratories Ltd, Project Number 1193/0017; A7.4.1.4/02. Final Report for Determination of the Purity and Water Content of Sodium Bromide, Albemarle Corporation, Reference Protocol: NaBr-012109; A7.4.1.4/03.	Y	Sopura N.V. Albemarle SPRL	
A7.4.2/01	H.D. Gaisser	2007	Calculation of the BCF for bromoacetic acid with the US-EPA program “BCF program (v2.17)” Unpublished	Y	MCF-Consultancy GmbH.	Y
A7.4.3.2/01	R.N. Hooftman	2001	28d fish juvenile growth test with monobromoacetic acid and the zebra fish Brachydanio rerio (Guideline: OECD 215 “Fish Juvenile growth Test”); TNO nutrition and Food Research Report no V2391/01 Unpublished	Y	Sopura N.V. Albemarle SPRL	Y
A7.4.3.4./01	R. Kühn et al	1989	Results of the harmful effects of pollutants to *Daphnia magna* in 21 day; Water Research Vol. 23 p. 501-510; Published	N	Published	Y
	Alexander H.C.	1981	Static Acute Toxicity of Sodium Bromide to Fathead Minnows,. Bull. Environm. Contam. Toxicol., 27, 326-331.	N		

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	Key study
	Canton J. H.	1983	Study on the Toxicity of Sodium Bromide to Different Freshwater Organisms, Fd, Fd. Chem. Toxic., , Vol. 21, No. 4, 369-378.	N		
	Allen Y, Calow P, Baird D J,	1995	A Mechanistic Model of Contaminant-Induced Feeding Inhibition in *Daphnia magna*, Environmental Toxicology and Chemistry, ,14 (9) 1625 – 1630	N		
	Baird D J, Barber I, Bradley M, Soares A M V M, Calow P A	1991	Comparative Study of Genotype Sensitivity to Acute Toxic Stress Using Clones of Daphnia magna straus, Ecotoxicology and Environmental Safety, 21: 257 – 265.	N		
	Clarke	2009	Harlan Laboratories Ltd, Sodium bromide: Assessment of the inhibitory efffect onm the respiration of activated sludge Project Number 1193/0017 Sponsor: Albemarle.	N		
	Deneer J W, Seinen W, Hermens J L M.	1988	Growth of Daphnia magna Exposed to Mixtures of Chemicals with Diverse Modes of Action, Ecotoxicology and Environmental Safety, 15: 72 – 77.	N		
	Guilhermino L, Sobral O, Chastinet C, Ribero R, Gonçalves F, Silva M C, Soares A M V M A	1999	*Daphnia magna* First Brood Chronic Test: An Alternative to the Conventional 21-day Chronic Bioassay?, Ecotoxicology and Environmental Safety, 42: 67 – 74.	N		
	Kühn R, Pattard M,	1990	Results of the Harmful Effects of Water Pollutants to Green Algae (*Scenedesmus subspicatus*) in the Cell Multiplication Inhibition Test, Wat. Res., 24 (1) 31-38	N		
	Soares A M V M, Baird D J, Calow P.	1992	Interclonal Variations in the Performance of *Daphnia magna* straus in Chronic Bioassays, Environmental Toxicology and Chemistry, 11: 1477 – 1483	N		
	Van Leeuwen C J, Rijkeboer M, Niebeek G..	1986	Population Dynamics of *Daphnia magna* as Modified by Chronic Bromide Stress, Hydrobiologica, 133: 277 – 285.	N		

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	Key study
	Wester P W, Canton J H, Dormans J A M A.	1988	Pathological Effects in Freshwater Fish *Poecilia retculata* (Guppy) and *Oryzias latipes* (Medaka) following Methyl Bromide and Sodium Bromide Exposure, Aquatic Toxicology, 12: 323 – 344	N		