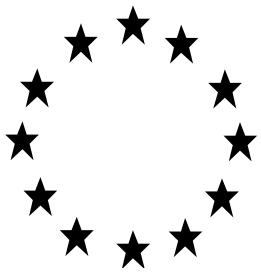
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Polyhexamethylene biguanide (Mn = 1600; PDI =1.8) (PHMB)

Product-type 6
Preservatives for products during storage

June 2015

France

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1 STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1 PROCEDURE FOLLOWED

This Assessment Report has been established as a result of the evaluation of the active substance Polyhexamethylene biguanide with a mean number-average molecular weight (Mn) of 1600 and a mean polydispersity (PDI) of 1.8, i.e. PHMB (1600; 1.8), as product-type 6 (preservatives for products during storage), carried out in the context of the work programme for the review of existing active substances provided for in Article 89 of Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products [1], with a view to the possible approval of this substance.

PHMB (1600; 1.8) (CAS no. 27083-27-8 and 32289-58-0) was notified as an existing active substance, by Lonza (previously Arch Chemicals Ltd.), hereafter referred to as the applicant, in product-type 6.

Commission Regulation (EC) No 1451/2007 of the 4th of December 2007[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process.

In accordance with the provisions of Article 3 paragraph 2 of that Regulation, France was designated as Rapporteur Member State (RMS, hereafter referred to as the evaluating Competent Authority, eCA) to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for PHMB (1600; 1.8) as an active substance in product-type 6 was the 31th of July 2007, in accordance with Article 9 paragraph 2 of Regulation (EC) No 1451/2007.

On the 30th of July 2007, the French Competent Authority received a dossier from Lonza. The evaluating Competent Authority accepted the dossier as complete for the purpose of the evaluation, taking into account the supported uses, and confirmed the acceptance of the dossier on the 18th of February 2008.

On the 14th of February 2014, the evaluating Competent Authority submitted to the European Chemical Agency (ECHA), hereafter referred to as the Agency, and the applicant a copy of the evaluation report, hereafter referred to as the Competent Authority Report.

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

1.2 PURPOSE OF THE ASSESSMENT

The aim of the Assessment Report is to support a decision on the approval of PHMB (1600; 1.8) for product-type 4, and should it be approved, to facilitate the authorisation of individual biocidal products in product-type 4 that contain PHMB (1600; 1.8). 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.

[1] Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products, OJ L 167/1, 27.6.2012, p1.

[2] OJ L 325, 11.12.2007, p. 3

The conclusions of this report were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). 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.

2 OVERALL SUMMARY AND CONCLUSIONS

2.1 GENERAL SUBSTANCE INFORMATION / GENERAL PRODUCT INFORMATION

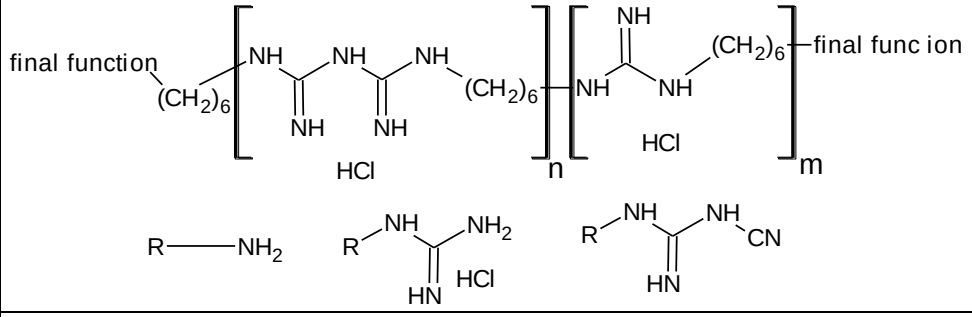
2.1.1 IDENTITY, PHYSICO-CHEMICAL PROPERTIES & METHODS OF ANALYSIS OF THE ACTIVE SUBSTANCE

2.1.1.1 Identity

Table 2.1-1: Identification of the active substance

CAS-No.	CAS-No : 27083-27-8 and 32289-58-0 It must be noted that CAS number 27083-27-8 is not based on characterisation data. In case of a different PHMB (for example with a weigh distribution outside of the specification of the PHMB assessed in this report) the CAS number will not be able to differentiate the PHMB
EINECS-No.	Not listed on the EU (EINECS) inventory because PHMB is a polymer. Polymers are exempt from listing on EINECS if the monomers are listed.
Other No. (CIPAC, ELINCS	None.
IUPAC Name	CoPoly(bisiminoimidocarbonyl,hexamethylenehydrochloride),(iminoimidocarbonyl , hexamethylène hydrochloride) or Copoly(5-imino-7-imino-4,6,8-triazaundecamethylene hydrochloride) (5-imino-4,6-diazanonamethylenehydrochloride)
Common name, synonym	PHMB (1600; 1.8) i.e. polyhexamethylene biguanide with a mean number-average molecular weight (Mn) of 1600 and a mean polydispersity (PDI) of 1.8; Polyhexamethylene biguanide; Poly(hexamethylene) biguanide hydrochloride; polymeric biguanide hydrochloride; "PHMB"; Polyhexanide (International non-proprietary name); Polyaminopropyl Biguanide (INCI)
Molecular formula	Terminal function- $(CH_2)_6$- $[C_8H_{18}N_5Cl]_n$ $[C_7H_{16}N_3Cl]_m$ - terminal function Possible terminal functions: - NH_2 (amine) - $C_2H_3N_4$ (cyanoguanide) - CH_5N_3Cl (guanidine)

		range	average
m+n		2-40	11
n /(m+n) [biguanide %]		90.8 - 91.9%	91.3 %
m /(m+n) [guanide %]		8.1 - 9.2 %	8.6 %
Terminal	amino	35% - 46%	39%
	guanidine	22% - 29%	25%

		function	cyanoguanide	31 - 39%	35%
Structural formula					
Molecular weight	Number average molecular weight (Mn) = 1610 Mass average molecular weight (Mw)= 2986.				

The active ingredient (a.i.) Poly Hexa Methylene Biguanide (PHMB) is a small size polymer obtained by the polycondensation of two monomers (1,6-hexanemethylenediamine and N,N'''-1,6-hexanediylbis[N'-cyanoguanidine] (ie. HMBDA)).

As PHMB is a small size polymer, some side reactions that occurred during the manufacturing process could modify significatively the structure of the polymer. The side reaction to obtain the unit guanidine occurred up to 10% in the process. Therefore, it can be considered that the structure of PHMB is not only composed by repetitive unit of guanidine but it is composed by repetitive unit of guanidine and biguanide.

The active substance as manufactured (TK[3]) is a 20% w/w aqueous solution of PHMB. "Purity" is a difficult concept to apply to PHMB which is a mixture of polymers and related substances. Instead the applicant refers to the "strength" of the polymer which is defined as "% total solids" or "dried material". The typical PHMB strength is 20 %.

However, eCA considers more appropriate to use the term "% of active substance (% a.s.)" or "active substance content" instead of "strength". The active substance content being defined as the sum of PHMB and its impurities contents, it can be considered identical to the % total solids and thus to the strength. However, the terms strength or dried PHMB are also used in identity and physico chemical sections and refer to the same thing.

As the technical material is the 20 % PHMB solution obtained directly from the manufacturing process (active substance as manufactured or TK), characterisation data were generated from the dried technical material (TC[4]) using the technique of freeze drying.

The content of PHMB can be calculated by subtracting the total content of impurities in the dried technical material (without residual water) to 100. This value cannot be considered as a real purity but is the closest available data.

The minimum content of PHMB TC was demonstrated > 95.6%.

Since the active substance is a copolymer, identity characterisation criteria (based on % solid, content of PHMB in dried material, Mw, Mn and the biguanide/guanide ratio) as well as limits or range for each criterion are proposed by eCA in the confidential document IIA to characterise the source of PHMB in order to set reference specifications in case of approval of the active substance and future technical equivalence checks. **eCA proposes to rename PHMB considered for approval in this dossier as "PHMB with a mean**

[3] TK: technical concentrate according to GIFAP monograph n°2 nomenclature.

[4] TC: technical material according to GIFAP monograph n°2 nomenclature.

number-average molecular weight (Mn) of 1600 and a mean polydispersity (PDI) of 1.8" i.e. "PHMB (1600; 1.8)". For convenience, PHMB (1600; 1.8) is referred to hereafter as "PHMB" or "a.s.".

There is one relevant impurity, Hexamethylenediamine with a maximal content of 0.4%. All potential impurities have not been looked for and/or quantified. Additional data about impurities and specifications for the active substance and the impurities should be submitted prior to approval.

Quality control data on structural characteristics (2003-2011) are reported in this confidential document to demonstrate that production of TK (liquid form) remained stable during this period of time from a structural point of view. It can be concluded that submitted characterisation data (2011) are representative of current production but also of older production and of active substance material used to perform the toxicological and ecotoxicological studies used to perform the risk assessment (See confidential doc IIA). This statement is only valid for structural data and not for evolution of impurity content in PHMB as no data was submitted to cover this point.

The applicant also manufactures PHMB as a solid material ("Solid PHMB"). Initially the applicant submitted both sources in the dossier. Comparison between liquid and Solid PHMB is discussed in confidential document IIA-02 "Comparison of liquid and solid PHMB". eCA considers that liquid PHMB (VANTOCIL TG) and Solid PHMB are 2 different substances, based on structural considerations. Additional information to demonstrate technical equivalence will be required at product authorisation stage if Applicant claims solid PHMB as a new source. The active substance considered for approval in this dossier is the active substance as manufactured (TK): 20 % w/w aqueous solution of PHMB (VANTOCIL TG) also called liquid PHMB.

Summary of specifications of Lonza PHMB:

Complete specifications are available in confidential part. The summary is reported here.

- Specifications set by eCA:
-

Table 2.1-2: Specifications of PHMB (1600; 1.8) from Lonza

Characterisation specification	
Strength	18-22%
PHMB in dried material	≥ 95.6%
molecular weight by number (Mn)	1449-1771
molecular weight by mass (Mw)	2687-3285
Polydispersity	1.80-1.91
The biguanide / guanide ratio in chain	90/10 to 92/8
Total fraction <1000 Da	16.6-24.5 %
Impurities	
HMD (relevant impurity)	≤ 0.4%
Other impurities	confidential

- (eco)tox batches: Liquid PHMB used to perform (eco)toxicological key studies and efficacy studies is of the same structure than liquid PHMB characterised in this dossier. However, no data on (eco)toxicity of impurities was provided by the applicant. Complementary data about (eco)toxicity of impurities should be submitted for finalisation of specification.

- Criterion data to be used to differentiate PHMB from different origins: All of presented caracterisation data are important to differentiate PHMB assessed in this dossier and other PHMB. However, some of those criterion data could be found difficult for control (biguanide / guanide ratio quantified by NMR) or not selective (strength). eCA is of the opinion that Mn and polydipersity would be the most convenient property for the control of the identity of PHMB used in biocidal products.

2.1.1.2 Physico-chemical properties

TC (dried PHMB) is a dusty solid/powder, off white with a strong ammonia smell. It has a glass transition temperature of 90-91°C (non crystalline polymer) and decomposes at 205-210°C before boiling. The TK (PHMB as manufactured, 20% in water) has a boiling point of 100.2°C. The relative density of TC is 1.20 at 20°C and the relative density of the TK is 1.04 at 20°C. As a polymer, PHMB is not considered to be volatile. Henry's Law Constant is not applicable as PHMB is not considered to be volatile and is present in ionic form at neutral pH. It is assumed that PHMB has only slight possibility to go from water to air. It is very soluble in water (426 g/L). It is also soluble in methanol (41%), in ethanol (0.5%) and sparingly soluble in organic solvents (10-3 g/L). The pKa is calculated as approximately 4.4 at 25°C. Log Pow is -2.3 at pH=7.4 and 25°C. TC is not highly flammable, and does not have oxidising and explosive properties. A surface tension study should be performed but PHMB is not expected to be surface active based on structural considerations.

2.1.1.3 Methods of analysis

It is impossible to determine directly PHMB since it is not a single chemical entity but a polymeric mixture with a range of molecular weight. Adequate methodology exists for the characterisation of the active ingredient and the determination of the known impurities in TC but more validation data are required.

Justifications for non submission of analytical methods for residues of the active substance in soil, water, air and body fluids and tissues, in food or feedstuffs were submitted.

For polymeric substances it may be difficult to develop an adequate residue analytical method. A limited residue definition in form of a marker will be required if PHMB is proposed for approval

Residue definition: a proposal of residue definition for drinking water, body fluid and tissues and food and feeding stuff is required 6 months before the date of approval

Monitoring methods:

- Based on the bibliography and the nature of the active ingredient, determination of PHMB in soil is currently not technically feasible. Moreover, eCA considers that if a method could allow to quantify PHMB in soil, this method could probably not be considered as enforcement method.
- The non submission is acceptable for air because occurrence in air is not probable.

- The non submission is acceptable for surface water, as eCA considers that the issue is the same than in soil. However, determination of PHMB in drinking water should be technically feasible. Therefore, a validated method for determination of PHMB would be required
- The justification for non submission submitted by the applicant is not acceptable for body fluids and tissues as PHMB is classifed as very toxic. An analytical method for determination of PHMB in body fluids and tissues or another justification of non submission of data would be required.
- The justificatification for non submission submitted by the applicant is not acceptable for food and feeding stuff as the justification based on the non exposure of food or feedstuffs is not acceptable. Methods for the determination of PHMB and residues in food and feedstuffs would be required.

2.1.2 IDENTITY, PHYSICO-CHEMICAL PROPERTIES & METHODS OF ANALYSIS OF THE BIOCIDAL PRODUCT

2.1.2.1 Identity

Table 2.1-3: Identification of the biocidal product

Trade name	VANTOCIL™ TG	
Manufacturer's development code number(s)		
Ingredient of preparation	**Function**	**Content** (strength % w/w)
PHMB	Active Substance	20
Physical state of preparation	*Liquid*	
Nature of preparation	SL (Soluble concentrate): A liquid homogenous preparation to be applied as a true solution of the active substance after dilution with water.	

2.1.2.2 Physico-chemical properties

VANTOCIL TG is a very pale yellow liquid without odour. Its pH is acid (pH=5.7). It has a relative density of 1.04 at 20 °C. The product is a free flowing mobile liquid with a low viscosity of 4.15 mPa.s. Experience in use indicates that the product does not foam. A study should be provided at the product authorisation stage for confirmation. Data on the surface tension measured with VANTOCIL TG is required at the product authorisation stage.

VANTOCIL TG is stable 14 days at 54°C. Low temperature stability (7 days at 0°C) and a shelf life study (2 years at ambient temperature) including measure of PHMB adsorbed on container after storage were not submitted and should be required. VANTOCIL TG is not flammable and has neither oxidising nor explosive properties.

Experience in use indicates no reactivity with High Density Polyethylene (PE-HD) and lacquer lined steel.

2.1.2.3 Methods of analysis

Adequate methodology exists for the characterisation of the active ingredient in biocidal product.

2.1.3 INTENDED USES AND EFFICACY

2.1.3.1 Field of use envisaged

Main group: 2 – Preservative

Product type 6 – Preservatives for products during storage

2.1.3.2 Function

Polyhexamethylene biguanide (PHMB) is an antimicrobial preservative for aqueous manufactured products in cans, tanks or other closed containers. The preservative must prevent the bio-deterioration of these systems until they are used. In this dossier, the submitted tests showed that PHMB has an efficacy that lasts up to 3 weeks. A longer lasting effect should be proven at product authorisation stage.

2.1.3.3 Mode of action

The lethal action of PHMB is an irreversible loss of essential cellular components as a direct consequence of cytoplasmic membrane damage. Cytoplasmic precipitation is a secondary event to the death of the bacterial cell.

It has been shown that the lethal sequence consists of a series of cytological and physiological changes - some of which are reversible - which culminate in the death of the cell. The important steps are:

- binding to a receptive site on the surface
- leakage of low molecular weight cytoplasmic components
- precipitation of cell contents.

The molecular interaction between PHMB and bacterial membranes has been deduced by over laying this lethal sequence with the findings of experiments modelling the possible interactions of polymeric biguanides and membrane components - particularly phospholipids.

2.1.3.4 Objects to be protected, target organisms

The efficacy of PHMB has been achieved against bacteria for the following applications:

- Preservatives for detergents. The example selected in this dossier is a fabric conditioner.
- Preservatives for fluids used in paper, textile and leather production. The example selected in this dossier is a polymer emulsion.

The list of all the intended uses and application rates are presented in Appendix II.

Table 2.1-4: Intended uses for which efficacy of the active substance PHMB has been proved sufficiently

Uses	a.s rate	Application mode	Effect	Target organisms
Preservatives for detergents.	0.04% w/w (claimed rate: 0.01 % up to 0.08% w/w)	Addition to aqueous manufactured products during their production in the manufacturing plant	Preservative antimicrobial efficacy against potentially harmful and spoilage microorganisms	Bacteria
Preservatives for fluids used in paper, textile and leather production.	0.02 % w/w (claimed rate: 0.01% up to 0.06% w/w)			

NOTE: 0.04% w/w is the highest minimal active concentration provided in the studies of the dossier (in challenge tests). Some Gram positive bacterial species have shown MIC (minimal inhibitory concentration) as high as 0.05% w/w active substance PHMB. Efficacy would have to be demonstrated for each claimed organisms at product authorisation stage.

Note that preservative efficacy of the active substance against bacteria has been demonstrated for detergents, with the example of a fabric conditioner but not for wet wipes liquor, preservation of timber products or glues and adhesives. No risk assessment was therefore performed for these use patterns.

2.1.3.5 Resistance

The evaluation of the literature studies provided does not show particular resistance to PHMB by bacteria. Nevertheless it is not appropriate to conclude that PHMB resistance is not an issue and that a resistance management strategy is not required. In particular, the description in the literature of cross resistances and modifications of the expression of genes as a mechanism of tolerance to sublethal concentrations of PHMB should be taken into account in the strategy of resistance management.

Indeed Standard methods of measuring resistance brought about by biocide use are not available and should be developed for all types of biocides (Assessment of the Antibiotic Resistance Effects of Biocides, Scenihr 2009).

2.1.4 CLASSIFICATION AND LABELLING

2.1.4.1 Proposed classification of the active substance as manufactured: PHMB 20% in water and of the product VANTOCIL TG

Classification according to Regulation (EC) No 1272/2008 (CLP)		
Class of danger	Acute Tox 4	Warning
	Skin Sens 1B	Warning
	STOT Rep 1	Danger
	Carc. 2	Warning
	Aquatic Acute 1	Danger
	Aquatic Chronic 1	Danger
Hazard statement	H332	Harmful if inhaled.
	H317	May cause an allergic skin reaction.
	H372	Causes damage to organs through prolonged or repeated exposure by inhalation.
	H351	Suspected of causing cancer.
	H400	Very toxic to aquatic life.
	H410	Very toxic to aquatic life with long lasting effects.

2.1.4.2 Harmonised classification for the active substance: PHMB

Classification according to Regulation (EC) No 1272/2008 (CLP)		
Class of danger	Acute Tox 4	Warning
	Eye dam 1	Danger
	Skin Sens 1B	Warning
	STOT Rep 1	Danger
	Carc. 2	Warning
	Aquatic Acute 1	Danger
	Aquatic Chronic 1	Danger
Hazard statement	H302	Harmful if swallowed.
	H318	Causes serious eye damage.
	H317	May cause an allergic skin reaction.
	H372	Causes damage to organs through prolonged or repeated exposure by inhalation.
	H351	Suspected of causing cancer.
	H400 (M-factor =10)	Very toxic to aquatic life.
	H410 (M-factor =10)	Very toxic to aquatic life with long lasting effects.

A RAC opinion (March 2014) is also available for the acute inhalation toxicity endpoint:

- Acute Tox. 2; H330: Fatal if inhaled.

2.2 SUMMARY OF THE RISK ASSESSMENT

2.2.1 SUMMARY OF HUMAN HEALTH RISK ASSESSMENTS

2.2.1.1 Hazard identification

- **Toxicokinetic:**

Oral absorption of PHMB ranges approximately from 0.3 to 8% but the value of 4% is retained based on the oral absorption of PHMB from diet at the lower dose tested. This value was selected as it corresponds to the closest conditions to the experimental conditions of the study in which the relevant oral NOAEL was determined.

A dermal absorption of PHMB was determined to be 4% by default based on EFSA guidance on dermal absorption (2012), corresponding to the oral absorption value.

Since no information is available on absorption of PHMB by inhalation, an absorption of 100% is retained.

- **Acute toxicity:**

A classification for acute oral or dermal toxicity is not justified for the active substance as manufactured, PHMB 20% in water. For respiratory route, a classification Xn; R20 or Acute Tox 4 – H332 is proposed based on the RAC opinion for PHMB.

- **Irritation/Sensitisation:**

PHMB is not irritant by dermal contact. For eye irritation, classification is not justified based on the data of the PHMB 20% w/w. PHMB is considered as a moderate to strong potency skin sensitizer based on animal data. Human studies indicate that PHMB is a skin sensitizer in humans, although with a rare frequency of sensitisation in the current conditions of consumer uses. Classification Xi; R43 (may cause sensitisation by skin contact) or Skin sens 1 – H317 for CLP, is therefore warranted. Relatively low incidences from human data support classification as CLP Skin Sens **1B** – H317 according to the 2nd ATP to CLP Regulation.

- **Repeated toxicity:**

On the basis of the severity of the effects caused by inhalation of PHMB (mortality and to a lesser extent histopathological changes in the respiratory tract and in the thymus), the absence of reversibility of inflammation in the respiratory tract and the very low doses causing these effects, classification T; R48/23 is warranted (CLP STOT RE 1 - H 372). By inhalation the primary target organ is the respiratory tract and no effect warranting classification are identified by oral and dermal route. The target organs are kidneys and liver via oral route. By dermal contact, local effects are expected.

- **Genotoxicity:**

PHMB is not considered to be mutagenic or genotoxic, according to the results of the *in vitro* (Ames test and chromosomal aberration test) and *in vivo* studies (mouse bone marrow micronucleus test and UDS assay).

- **Carcinogenicity:**

PHMB increases the incidence of benign and malign vascular tumours in female rats by oral route and in male and female mice by oral and dermal route. The tumours are induced mainly in the liver, which is one of the target organ of PHMB and the increase is clearly seen at doses above the MTD. However, it is also observed more equivocally at doses below MTD (mouse oral study at mid-dose and rat oral study at high dose). These increases are not considered incidental when considering the clear induction of vascular tumours at higher doses and they are considered biologically significant and attributed to treatment.

A classification as carcinogenic category 3; R40 or Carc 2 – H351 for CLP, is warranted. In absence of carcinogenicity data by inhalation, it is proposed to allocate the general hazard statement H351 without indication of the route of exposure.

- **Reprotoxicity:**

PHMB has no teratogenic effect and has no effect on fertility or reproductive performance at dose levels up to 2000 ppm.

Determination of AEL/AEC/ADI/ARfD

- Systemic effects

The lowest NOAEL from any oral studies is 13 mg/kg bw/day from the rat developmental toxicity study (Doc IIIA 6.8.1/01). This value is based on reduced maternal food consumption and body weight (-23% of controls) seen at the next higher dose. The choice of this value is also supported by the rabbit developmental toxicity study, in which increased mortality and reduced bodyweight with associated reduced food consumption were seen at the same level of doses.

The absorption rate following administration in the diet for females is 4%. Hence, internal NOAEL is 0.52 mg a.s./kg bw/day.

The default assessment factors are 10 for inter-species variation and 10 for intra-species variation in the case of the systemic effects. The inter-species factor consists of 2.5 for toxicodynamic- and 4.0 for toxicokinetic variability, while the inter-individual factor consists of 3.2 for toxicokinetic and 3.2 for toxicodynamic variability.

Although the selected NOAEL is based on a short duration of exposure (22 days in the rat teratogenicity study), no assessment factor will be applied to take into account the medium and chronic exposure because the NOAEL from teratogenicity is in the same order of magnitude or lower than NOAEL from sub-chronic or chronic studies. Consequently, it means that effects are not more severe with longer exposure of PHMB. The NOAEL from teratogenicity is therefore, sufficiently conservative for these longer exposures and no additional assessment factors to extrapolate NOAEL of the teratogenicity study to longer duration is justified.

The MOE_{ref} is therefore 100 for acute-term, medium-term and long-term exposure.

An acute, medium-term and long-term AEL of 5.2×10^{-3} mg a.s./kg bw/day is proposed.

- Respiratory exposure, local effects

The relevant study for respiratory exposure is the 28-day inhalation study. The NOAEC from this study is 0.024 mg/m^3 (Document IIIA 6.3.3).

The MOE_{ref} is therefore 25, 75, 150 for local effects for acute, medium and long-term respiratory exposure.

An acute respiratory AEC of 0.96 µg/m^3 a.s. is proposed.

A medium-term respiratory AEC of 0.32 µg/m^3 a.s. is proposed.

A long-term respiratory AEC of 0.16 µg/m^3 a.s. is proposed.

According to the TNsG on Annex I inclusion, chapter 4.1: quantitative risk characterisation (2008), ADI and ARfD are usually based on the same NOAEL as the $AEL_{chronic}$ and AEL_{acute} respectively. They are external reference doses.

A value of 0.13 mg/kg is proposed for ADI and ARfD.

Table 2.2-1: Summary of the values of AEL and MOE_{ref}

Systemic effects		
	AEL	**MOE_{ref}**
acute, medium and long-term	5.2 µg a.s./kg bw/d	100
	ADI - ARfD	**MOE_{ref}**
Chronic and acute	0.13 mg a.s./kg bw/d	100
Local effects by inhalation		
	AEC	**MOE_{ref}**
acute	0.96 µg/m^3	25
medium-term	0.32 µg/m^3	75
long-term	0.16 µg/m^3	150

2.2.1.2 Exposure assessment and risk characterisation

PHMB is intended to be incorporated into aqueous products to prevent spoilage during shipping and storage prior to use. For certain uses (e.g. wallpaper adhesives, timber preservatives) it also acts as a wet state preservative to prevent spoilage once the product has been diluted prior to application or whilst drying following application.

Efficacy was demonstrated for the uses of preservation of polymer emulsions used in the production of paper, textile and leather, and preservation of detergents (fabric conditioner). A risk assessment was performed for these uses summarised in the table below:

Table 2.2-2: Overview: use of VANTOCIL TG containing 20% w/w a.s. (primary exposure)

Scenario	**In use concentration** (% v/v a.s. in the preserved product)	**Application method**	**User**
Preservation of detergents	0.04% v/v to 0.08% v/v (400 to 800 ppm)	Charging to a mixing vessel by manual pouring (small scale) or, semi/automated pumping system (large scale)	Industrial
		Representative worst case uses: Use of preserved liquid detergent for manual laundry washing; Use of preserved liquid detergent for cloth pre-treatment; Use of preserved liquid detergent for manual dishwashing; Use of preserved liquid detergent for surface cleaning.	Industrial, professional or non professional / domestic
Preservation of Polymer Emulsions.	0.02% v/v to 0.06% v/v (200 to 600 ppm v/v)	Charging to a mixing vessel by manual pouring (small scale) or, semi/automated pumping system (large scale)	Industrial
		Representative worst case use: Use of preserved polymer emulsions in paper, textile and leather industries.	Industrial, professional

Primary exposure

The following representative worst case uses were assessed:

- Addition of biocidal product into product to be preserved (detergents and polymer emulsions);
- Use of polymer emulsions in paper, textile and leather industries;
- Use of liquid detergent for manual laundry washing;
- Use of liquid detergent for cloth pre-treatment;
- Use of liquid detergent for manual dishwashing;
- Use of liquid detergent for surface cleaning.

Secondary exposure

Representative worst cases were defined as follows:

- Dermal exposure from contact with processed leather
- Dermal exposure of general public from contact with leather/textile
- Dermal exposure from handling dry paper
- Oral exposure to paper by an infant (ingestion of paper)
- Dermal exposure from dish washed with preserved product

- Dermal exposure from wearing clothes washed with preserved product
- Oral and dermal exposure for an infant crawling on surface cleaned with preserved product
- Exposure via food in contact with utensils or surface cleaned with preserved product, or in contact with paper.

Table 2.2-3: Summary of main paths of human exposure

Exposure path	Industrial use	Professional use	General public	Via the environment
Inhalation	No	No	No	Negligible
Dermal	Yes	Yes	Yes	Negligible
Oral	No	No	Yes	Negligible

Quantitative risk assessment was performed for systemic effects, comparing the estimated exposure with relevant reference value (AEL).

2.2.1.2.1 Primary exposure of professional users and risk characterisation

Most of the information on exposure scenarios assumptions and indicative values are coming from the Technical Notes for Guidance (TNsG) on Human Exposure to Biocidal Products, either its first version (2002), including the User guidance (2002) or its second version (2007), including the database BEAT.

2.2.1.2.1.1 Formulation of biocidal product into end-use applications (addition of biocides into products to be preserved)

The primary exposure to PHMB during formulation of biocidal product into the **polymer emulsions used in paper, textile and leather production** at final concentration of 0.02 to 0.06 %w/w a.s., and into **detergent** to be preserved at final concentration of 0.04 to 0.08 % w/w a.s. was evaluated.

The scenario of manual addition of VANTOCIL TG to detergent product to be preserved was chosen as a worst case.

Scenario Description

The scenario for the pumping of VANTOCIL TG is adopted using the efficacious final concentration PHMB of 0.08 % in the detergent product.

According to the recommendation by the Human Exposure Expert Group (HEEG), the most relevant model for simple manual loading of liquids is the Model 7, TNsG part.2 (Professional pouring and pumping liquid, and dumping solids into systems).

The mixing and loading tasks involve the removal of the product from its container and introduction to the system and may be conducted by automation or manually. In the automated process, the biocide is metered directly into the sump from a holding tank or other type of bulk container. The manual process involves a worker dispensing (via a tap

or by pouring) a measured quantity of product into a jug and manually pouring the product into the sump.

The addition is typically done by operators usually involved in the detergent fabric and formed for the handling of dangerous products. A higher dosage range and/or increased treatment frequency may be required depending upon a number of factors including the rate of dilution of the preservative within the makeup fluid, the nature and severity of contamination, levels of control required, filtration effectiveness and system design. Regardless of the manner of incorporation, the total active substance concentration of PHMB in the system should not exceed 800 ppm (0.08% w/v) in the final use dilution.

Table 2.2-4: Formulation into product to be preserved – professional primary exposure summary (Chronic exposure)

Tier	Dermal exposure	
	Deposit on skin (hands)	Systemic dose
	%	mg a.s. / kg bw /day
Task:	**Addition of biocidal product into product to be preserved – Mixing and loading phase**	
Tier 1: Without PPE[5]	20	2.69×10^{-1}
Tier 2: Gloves and protective clothes	20	2.69×10^{-3}

Risk characterisation for formulation into product to be preserved

Summaries of the risk characterisation for formulation of VANTOCIL TG into PT 6 products for the professional user scenarios are shown in the following tables.

- Quantitative risk assessment for systemic effects

Table 2.2-5: Summary of risk assessment for professionals during the formulation of biocidal product into product to be preserved.

	Total exposure (mg a.s./kg bw/d)	Relevant NOAEL (mg a.s./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.s./kg bw/d)	%AEL
Task:	**Addition of product into product to be preserved – Mixing and loading phase**					
Tier 1: Without PPE	2.69×10^{-1}	0.52	100	2	5.20×10^{-3}	**5179**
Tier 2: Gloves and protective clothes	2.69×10^{-3}	0.52	100	193	5.20×10^{-3}	52

[5] Personal protective equipment.

The risk for systemic exposure during the manual mixing and loading of the biocidal product is only acceptable in Tier 2 (with gloves and protective clothes) with a MOE (193) higher than MOE_{ref} (100) and a %AEL (52%) below 100%.

- Risk assessment for local effects

As the product is classified as skin sensitiser, a qualitative assessment was performed.

PPE for dermal protection will not decrease the concentration of exposure but the occurrence of the event of skin contact with the active substance. PPE for dermal protection is therefore only taken into account on a qualitative basis and the wearing of PPE did not change the value of the local dermal exposure.

The concentrated product containing 20% of PHMB in water is classified as sensitising and as carcinogenic category 2 according to CLP, thus, PPE are required during manipulation of the product. Indeed, this risk of skin sensitization and carcinogenicity from PHMB is readily controllable through the use of proper risk mitigation measures, gloves and suitable protective clothing, when handling formulations. Besides, the use of concentrated product (20% in water) is restrained to professional operators. Providing adapted PPE are worn, the occurrence of exposure should be considered as accidental and manageable as such. Therefore, packaging, equipments and procedures, e.g. automated dosing systems, should be designed to prevent exposure as much as possible. MSDS and product use instructions shall inform the users of the potential risks and prevention measures.

By using adapted processes, protective equipments and respecting good professional practices, the exposure potential to PHMB based products can be avoided and the risk of adverse health effects can be reduced to an acceptable level.

In such conditions, it may be assumed that dermal exposure would occur only under accidental circumstances during the different tasks.

2.2.1.2.1.2 Professional user's application: polymer emulsion (paper, textile, leather production)

2.2.1.2.1.2.1 Mixing and loading exposure

The scenario for the pumping of polymer emulsion is adopted using the efficacy final concentration PHMB of 0.06 % in the production system (leather, textile and paper), following the Model 7, TNsG part.2.

The mixing and loading tasks involve the removal of the polymer emulsion from its container and introduction to the system and may be conducted by automation or manually. In the automated process, the biocide is metered directly into the sump from a holding tank or other type of bulk container. The manual process involves a worker dispensing (via a tap or by pouring) a measured quantity of product into a jug and manually pouring the product into the sump.

Manual pouring is considered as a worst case scenario compared to the automated transfer. The exposure will be assessed following this scenario.

2.2.1.2.1.2.2 Application exposure

No specific assessment for human exposure has been made, since the application is the mixing and loading phase of the product.

It should be noted that the active substance is not volatile; therefore exposure via inhalation succeptible to intervene during application is not considered to be relevant.

2.2.1.2.1.2.3 Post-application exposure

Post-application scenario corresponds to the cleaning of the dispensing pumps.

The most adequate model in the BEAT database (2008) is 'Cleaning of spray equipment', which includes rinsing and rubbing (with paper, rag or brush) tasks, which are similar in cleaning dispensing pumps or fouled system.

2.2.1.2.1.2.4 Combined exposure

Table 2.2-6: Combined exposure for primary exposure for workers - preservatives for polymer emulsion used in paper/leather/textile production

Tier	Dermal exposure	
PPE	Deposit on skin (hands)	Systemic dose
	%	mg a.s. / kg bw /day
Task:	**Addition of the polymer emulsion into the production system – Mixing and loading phase**	
Tier 1: Without PPE	0.06	8.08×10^{-4}
Tier 2: Gloves and protective clothes	0.06	8.08×10^{-6}
Task:	**Pump cleaning- Post application**	
Tier 1: Without PPE	0.06	4.40×10^{-4}
Tier 2: without PPE With a previous rinsing	0.0006	4.40×10^{-6}
Task:	**Professional – Total combined exposure (mixing loading and post application)**	
Tier 1: Without PPE	Not relevant*	1.25×10^{-3}
Tier 2: without PPE With a previous rinsing for postapplication	Not relevant*	1.25×10^{-5}

*As for local dermal effect it is the concentration of the PHMB during the event of contact that is relevant, combined exposures have only been assessed for systemic exposure.

Risk characterisation for workers during use of polymer emulsion

- Quantitative risk assessment for systemic effects

Table 2.2-7: Summary of risk assessment for systemic effects

	Total exposure (mg a.s./kg bw/d)	Relevant NOAEL (mg a.s./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.s./kg bw/d)	%AEL
Task:	**Addition of the polymers emulsion into the system of production – Mixing and loading phase**					
Tier 1: Without PPE	8.08×10^{-4}	0.52	100	644	5.20×10^{-3}	16
Tier 2: Gloves and protective clothes	8.08×10^{-6}	0.52	100	64356	5.20×10^{-3}	< 1
Task:	**Pump cleaning- Post application**					
Tier 1: Without PPE	4.40×10^{-4}	0.52	100	1182	5.20×10^{-3}	8
Tier 2: without PPE With a previous rinsing	4.40×10^{-6}	0.52	100	118182	5.20×10^{-3}	0.08
Task:	**Professional– Total combined exposure (mixing loading and post application)**					
Tier 1: Without PPE	1.25×10^{-3}	0.52	100	417	5.20×10^{-3}	24
Tier 2: without PPE With a previous rinsing for post-application	1.25×10^{-5}	0.52	100	41667	5.20×10^{-3}	< 1

The risk for systemic effects is considered to be acceptable for professionals without PPE, since the MOE (417) is higher than the MOE_{ref} and the % AEL (< 1) is below 100 %.

- Quantitative risk assessment for dermal local effects

The content of PHMB in the end use product is below classification limits of skin irritation and sensitisation. As the product is not classified for its sensitisation and irritations properties, the risk for dermal local effects is considered to be acceptable.

2.2.1.2.1.3 Professional user's applications: liquid detergent

Professional user's applications have been identified as follow:

- Hand washed laundry

- Pre-treatment of clothes
- Hand dishwashing
- Surface cleaning (household)

2.2.1.2.1.3.1 Liquid detergents for hand wash laundry, pre-treatment of clothes and hand dishwashing – professional exposure

VANTOCIL TG is incorporated into liquid detergents at a maximum final a.s. concentration of 0.08%.
Exposure to PHMB may occur when people use liquid detergent products containing the active substance.

As no specific data and models can be found in the Technical Notes for Guidance (TNsG 2008), it has been considered that ConsExpo is the best available tool for this assessment, provided some parameters (from ConsExpo's Cleaning product factsheet, RIVM 2006) are modified as explained for each scenario according the Technical Meeting II 2008 agreements and the HEEG opinion.

Summaries of the risk characterisation for the professional using liquid detergents are shown in the following tables.

Table 2.2-8: Liquid detergents uses professional primary exposure summary (Chronic exposure)

Tier	Dermal exposure	
PPE	Deposit on skin (hands)	Systemic dose
	%	mg a.s. / kg bw /day
Task :	**Professional hand washing laundry/machine wash – Mixing and loading phase**	
Tier 1: Without PPE	0.08	8.53×10^{-5}
Task:	**Professional hand washing laundry – Application phase**	
Tier 1: Without PPE	0.0008	1.62×10^{-3}
Task:	**Professional hand washing laundry – combined exposure (mixing and loading phase + application phase)**	
Tier 1: Without PPE	Not relevant*	1.71×10^{-3}
Task:	**Professional spot pre-treatment of clothes – application phase**	
Tier 1: Without PPE	0.08	5.55×10^{-4}
Task:	**Professional hand dishwashing/machine wash – Mixing and loading phase**	
Tier 1: Without PPE	0.08	1.28×10^{-4}
Task:	**Professional hand dishwashing – Application phase**	
Tier 1: Without PPE	0.000112	1.54×10^{-4}
Task:	**Professional hand dishwashing – combined exposure (mixing and loading phase + application phase)**	
Tier 1: Without PPE	Not relevant*	2.82×10^{-4}
Task:	**Professional– Total combined exposure (hand washing clothes + spot pre-treatment + hand dishwashing)**	
Tier 1: Without PPE	Not relevant*	2.54×10^{-3}

*As for local dermal effect it is the concentration of the PHMB during the event of contact that is relevant, combined exposures have only been assessed for systemic exposure.

Risk characterisation for liquid detergents

- Quantitative risk assessment for systemic effects

Table 2.2-9: Summary of risk assessment for professional using liquid detergents

	Total exposure (mg a.s./kg bw/d)	Relevant NOAEL (mg a.s./kg bw/d)	MOEref (sum of AFs)	MOE	AEL (mg a.s./kg bw/d)	%AEL
Task :	**Professional hand washing laundry/machine wash – Mixing and loading phase**					
Tier 1 : Without PPE	8.53×10^{-5}	0.52	100	6096	5.20×10^{-3}	2
Task:	**Professional hand washing laundry – Application phase**					
Tier 1: Without PPE	1.62×10^{-3}	0.52	100	321	5.20×10^{-3}	31
Task:	**Professional hand washing laundry – combined exposure (mixing and loading phase + application phase)**					
Tier 1: Without PPE	1.71×10^{-4}	0.52	100	305	5.20×10^{-3}	33
Task:	**Professional spot pre-treatment of clothes – application phase**					
Tier 1 : Without PPE	5.55×10^{-4}	0.52	100	937	5.20×10^{-3}	11
Task:	**Professional hand dishwashing/machine wash – mixing and loading phase**					
Tier 1 : Without PPE	1.28×10^{-4}	0.52	100	4063	5.20×10^{-3}	2
Task:	**Professional hand dishwashing – application phase**					
Tier 1 : Without PPE	1.54×10^{-4}	0.52	100	3377	5.20×10^{-3}	3
Task:	**Professional hand dishwashing – combined exposure (M&L + application phase)**					
Tier 1 : Without PPE	2.82×10^{-4}	0.52	100	1844	5.20×10^{-3}	5
Task:	**Professional– Total combined exposure (hand washing clothes + spot pre-treatment + hand dishwashing)**					
Tier 1 : Without PPE	2.54×10^{-3}	0.52	100	205	5.20×10^{-3}	49

Acceptable risk has been identified for hand washing laundry, hand dishwashing and spot treatment of clothes. since MOEs are lower than MOEref and associated %AELs are below 100% for systemic effects.

Acceptable risk related to systemic effects, has been identified for the different combined exposure considered.

- Risk assessment for local effects

The content of PHMB in the end use product is below classification limits of skin sensitisation. As the product is not classified for its sensitisation and irritations properties, the risk for dermal local effects is considered to be acceptable.

2.2.1.2.1.3.2 Household (HH), and industrial and institutional (I&I) uses – professional exposure

PHMB is claimed at a maximal concentration of 0.08 % in products used for surface cleaners.

The representative use for this kind of products is wiping or mopping hard surfaces such as floors.

The respective exposures are assessed using the surface disinfection models from the TNsG (models 1 and 3, TNsG (2002) pages 175 and 177, User guidance page 27). These models include exposure during diluting and mixing the surfactant in water and wiping surfaces using a rung cloth or a mop.

Table 2.2-10: Households and Industrial and Institutional uses professional primary exposure summary (Chronic exposure)

Tier	Dermal exposure	
PPE	Deposit on skin (hands)	Systemic dose
	%	mg a.s. / kg bw /day
Task:	**Professionals wiping surfaces with preserved product**	
Tier 1: Without PPE	0,08 %	1.51×10^{-3}
Tier 2: With gloves	0,08 %	5.19×10^{-4}

Risk characterisation for Household (HH), and industrial and institutional (I&I) uses

- Quantitative risk assessment for systemic effects

Table 2.2-11: Summary of risk assessment for professionals wiping surfaces with preserved product

	Total exposure (mg a.s./kg bw/d)	Relevant NOAEL (mg a.s./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.s./kg bw/d)	%AEL
Task:	**Professionals wiping surfaces with preserved product**					
Tier 1 : Without PPE	1.51×10^{-3}	0.52	100	343	5.20×10^{-3}	29
Tier 2: With gloves, coated coveralls	5.19×10^{-4}	0.52	100	1001	5.20×10^{-3}	10

An acceptable risk has been identified for professionals wiping surfaces without PPE, since MOE is higher than MOE_{ref} (100) and associated %AEL is below 100%, for the systemic effects.

- Quantitative risk assessment for local effects

The content of PHMB in the end use product is below classification limits of skin sensitisation. As the product is not classified for its sensitisation and irritations properties, the risk for dermal local effects is considered to be acceptable.

2.2.1.2.1.4 Overall assessment of the risk for the professional use of the active substance in biocidal product

Preserved product formulation

The risk for exposure during the manual mixing and loading of the biocidal product is acceptable in Tier 2 (with gloves and coverall) due to local and systemic effects.

Polymer emulsion uses (paper, textile and leather production):

The risk for the systemic and dermal effects is considered to be acceptable without PPE during mixing and loading and during post-application.

Liquid detergent

Acceptable risk has been identified for hand washing laundry, hand dishwashing and spot treatment of clothes without the wear of gloves.

Acceptable risk related to systemic effects, has been identified for the different combined considered tasks without PPE.

Wiping surface

Acceptable risk for the systemic and dermal effects has been identified for professionals wiping surface without PPE.

Local effects

PHMB has skin sensitisation potential. In rare situations where exposure to the a.s. may occur (accidental spills, etc.) plant workers must wear the appropriate personal protective equipment (PPE) to prevent over-exposure and to avoid any potential for skin/respiratory irritation or skin sensitisation.

If appropriate PPE is used while handling biocidal products during formulation, mixing/loading, and post application, the exposure concentration is not reduced but only the probability of occurrence. However, the exposure to concentrated products should be prevented.

Therefore, as the product is classified and labelled as sensitising, it should be handled with sufficient risk mitigation measures, including collective systems (e.g. automated dosing systems) additionally to PPE, in order to prevent any spillage on skin. In such conditions, considering furthermore that the intended users are operators trained to use chemicals, it may be assumed that dermal exposure would occur only in accidental circumstances.

Therefore, biocidal products containing up to 20% VANTOCIL TG can be used in dipping bath provided that appropriate risk mitigation measures are applied during the loading of the products and the cleaning of the dispensing pumps. Possible measures (not exhaustive list) are:

- The containers of the products are designed to prevent spillages during pouring,
- Automated systems preventing contacts with the product are used,
- Procedures are implemented to prevent contacts and spillages,
- Chemical-resistant coveralls, gloves, shoes and face-mask are worn,
- Use is restricted to operators informed of the hazards and formed for safe handling of the products.

Labels, MSDS and use instructions of the products shall inform the users of the hazards and of the protective measures. Written procedures and protective equipments shall be available at the places where the products are handled.

These RMMs are summarised in the tables below:

Table 2.2-12: Primary exposure –Mixing and loading during the formulation of preserved product

Hazard			Exposure							Risk
Hazard Category	Effects in terms of C&L	Additional relevant hazard information	PT	Who is exposed ?	Tasks, uses, processes	Potential exposure route	Frequency and duration of potential exposure	Potential degree of exposure	Relevant RMM&PPE	Conclusion on risk
Loading VANTOCIL TG during preserved product formulation										
Medium	Skin Sens 1B (H317)	-	6	Industrial and professional users	loading of the biocidal product (20% a.s.) during preserved product formulation	Skin	Daily	<u>Manual loading:</u> Small exposure to spills <u>Semi automated and fully automated loading systems:</u> Accidental exposure to spills during connection of container to the pumping system	**Organizational RMM** • Restriction of manual loading to only small quantities. High quantities should be restricted to semi-automated or automated processes. **Personal protective equipment** • Hand protection: Suitable chemical resistant safety gloves (EN 374) also with prolonged, direct contact (Recommended: Protective index 6, corresponding > 480 minutes of permeation time according to EN 374) Manufacturer's directions for use should be observed because of great diversity of types. • Body protection: Chemical protection clothes type 6 (eg EN 13034). Body protection must be chosen based on level of activity and exposure. **General safety and hygiene measures** Do not inhale gases/vapours/aerosols. Avoid contact with the skin, eyes and clothing. Handle in accordance with good industrial hygiene and safety practice. Wearing of closed work clothing is recommended. When using, do not eat, drink or smoke. Hands and/or face should be washed before breaks and at the end of the shift. At the end of the shift the skin should be cleaned and skin-care agents applied. Gloves must be inspected regularly and prior to each use. Replace if necessary (*e.g.*, pinhole leaks).	Acceptable: + Minimisation of manual phases; + Professionals using PPE; + Professionals following instructions for use; + Good standard of personal hygiene.

Hazard			Exposure							Risk
Hazard Category	**Effects in terms of C&L**	**Additional relevant hazard information**	**PT**	**Who is exposed ?**	**Tasks, uses, processes**	**Potential exposure route**	**Frequency and duration of potential exposure**	**Potential degree of exposure**	**Relevant RMM&PPE**	**Conclusion on risk**
Medium	STOT Rep 1 (H372)	-	6	Industrial and professional users	Loading of the biocidal product (20% a.s.) during preserved product formulation	Inhalation	Daily	No relevant exposure No inhalation exposure is expected due to the fact that the substance is not considered to be volatile. The mode of application does not concern aerosol spraying.	**No RPE is required due to the classification**	Acceptable

2.2.1.2.2 Primary exposure of non-professional users and risk characterisation

VANTOCIL TG is incorporated into liquid detergents at a maximum final a.s. concentration of 0.08%.

Exposure to PHMB may occur when people use liquid detergent products containing the active substance.

ConsExpo model was developed for non-professional users, the methods and most of the parameters are applicable for professional users. As no specific data and models can be found in TNsG, ConsExpo is the best available tool for this assessment, provided some parameters (from ConsExpo's Cleaning product factsheet, RIVM 2006) are modified as explained for each scenario according the Technical Meeting II 2008 agreements and the HEEG opinion.

Based on the use of PHMB in liquid detergents, non-professional exposure scenarios that were identified and considered in this section of the assessment are as follows:

- Hand washed laundry
- Pre-treatment of clothes
- Hand dishwashing
- Surface cleaning (household)

Detailed exposure assessments have been included in the Document IIB and the risk characterisations for the relevant end use applications are provided below for PHMB.

Relevant exposure paths

The most relevant paths of exposure to PHMB in the product for non professionals is the dermal route. The oral route and the inhalation are considered negligible. For non professional exposure, wearing PPE is not assumed.

2.2.1.2.2.1 Liquid detergents for spot pre-treatment, laundry and dishwashing

Table 2.2-13: Liquid detergents uses non professional primary exposure summary (Chronic exposure)

Tier	Dermal exposure	
PPE	Deposit on skin (hands)	Systemic dose
	mg/cm²	mg a.s. / kg bw /day
Task:	**Non-professional hand washing laundry/machine wash – Mixing and loading phase**	
Tier 1: Without PPE	0.08	1.52×10^{-6}
Task:	**Non-professional hand washing laundry – Application phase**	
Tier 1: Without PPE	0.0008	1.01×10^{-4}
Task:	**Non-professional hand washing laundry – combined exposure (mixing and loading phase + application phase)**	
Tier 1: Without PPE	Not relevant*	1.03×10^{-4}
Task:	**Non professional spot pre-treatment of clothes – application phase**	
Tier 1: Without PPE	0.08 %	1.21×10^{-5}
Task:	**Non professional hand dishwashing/machine wash – mixing and loading phase**	
Tier 1: Without PPE	0.08 %	6.22×10^{-6}
Task:	**Non professional hand dishwashing – application phase**	
Tier 1: Without PPE	0.000112 %	7.49×10^{-6}
Task:	**Non professional hand dishwashing – combined exposure (M&L + application phase)**	
Tier 1: Without PPE	Not relevant*	1.37×10^{-5}
Task:	**Non professional hand dishwashing – Total combined exposure (hand washing clothes + spot pre-treatment + hand dishwashing)**	
Tier 1: Without PPE	Not relevant*	1.28×10^{-4}

*As for local dermal effect it is the concentration of the PHMB during the event of contact that is relevant, combined exposure has only been assessed for systemic exposure.

Risk characterisation for liquid detergents

- Quantitative risk assessment for systemic effects

Table 2.2-14: Summary of risk assessment for non professional using liquid detergents

	Total exposure (mg a.s./kg bw/d)	Relevant NOAEL (mg a.s./kg bw/d)	MOE_{ref}	MOE	AEL (mg a.s./kg bw/d)	%AEL
Task:	**Non Professional hand washing laundry/machine wash– mixing and loading phase**					
Tier 1 : Without PPE	1.52×10^{-6}	0.52	100	342105	5.20×10^{-3}	<1
Task :	**Non Professional hand washing laundry – application phase**					
Tier 1: Without PPE	1.01×10^{-4}	0.52	100	5149	5.20×10^{-3}	2
Task :	**Non Professional hand washing laundry – combined exposure (mixing and loading phase + application phase)**					
Tier 1: Without PPE	1.03×10^{-4}	0.52	100	5072	5.20×10^{-3}	2
Task :	**Non Professional spot pre-treatment of clothes – application phase**					
Tier 1 : Without PPE	1.21×10^{-5}	0.52	100	42975	5.20×10^{-3}	<1
Task :	**Non Professional hand dishwashing/machine wash – mixing and loading phase**					
Tier 1 : Without PPE	6.22×10^{-6}	0.52	100	83601	5.20×10^{-3}	<1
Task :	**Non Professional hand dishwashing – application phase**					
Tier 1 : Without PPE	7.49×10^{-6}	0.52	100	69426	5.20×10^{-3}	<1
Task :	**Non Professional hand dishwashing – combined exposure (mixing and loading + application phase)**					
Tier 1 : Without PPE	1.37×10^{-5}	0.52	100	37929	5.20×10^{-3}	<1
Task :	**Non Professional– Total combined exposure (hand washing clothes + spot pre-treatment + hand dishwashing)**					
Tier 1 : Without PPE	5.99×10^{-5}	0.52	100	4052	5.20×10^{-3}	2

Acceptable risk has been identified for hand washing laundry hand dishwashing and spot treatment of clothes (loadings and applications), since MOEs are higher than MOE_{ref} and associated %AELs are below 100%, for systemic effects.

Acceptable risk related to systemic effects has been identified for the different combined tasks considered.

- Risk assessment for local effects

The content of PHMB in the end use product is below classification limits of skin sensitisation. As the product is not classified for its sensitisation and irritations properties, the risk for dermal local effects is considered to be acceptable.

2.2.1.2.2.2 Household (HH) uses

PHMB is used at a maximal concentration of 0.08% in products used for surface cleaners.

The representative use for this kind of products is wiping or mopping hard surfaces such as floors.

The exposure assessment was performed on one hand using the surface disinfection models from the TNsG (models 1 and 3, TNsG (2002) pages 175 and 177, User guidance page 27), and on another hand using ConsExpo 4.1 with default assumptions reported in the Cleaning products fact sheet (RIVM, 2007) for the application of "Floor, carpet and furniture products – Floor cleaning liquid". The assumptions do not differ significantly from those used with the TNsG models.

As exposure results obtained with ConsExpo are higher than thoses from default parameters of TNsG, and considering that ConsExpo is the model recommended by TNsG for consumer exposure estimation, the results from ConsExpo are used in the risk assessment.

Table 2.2-15: Households and Industrial and Institutional uses professional primary exposure summary (Chronic exposure)

Tier	Dermal exposure according ConsExpo 4.1	
PPE	Deposit on skin (hands)	Systemic dose
	mg/cm²	mg a.s. / kg bw /day
Task:	**Non-professionals mixing and loading phase**	
Tier 1: Without PPE	0,08 %	5.33×10^{-6}
Task:	**Non-professionals wiping surfaces with preserved product**	
Tier 1: Without PPE	0.004 %	5.07×10^{-4}
Task:	**Combined exposure: Mixing, loading and wiping phases**	
Tier 1: Without PPE	Not relevant*	5.12×10^{-4}

*As for local dermal effect it is the concentration of the PHMB during the event of contact that is relevant, combined exposure has only been assessed for systemic exposure.

Risk characterisation for Household (HH) uses

- Quantitative risk assessment for systemic effects

Table 2.2-16: Summary of risk assessment for non professional wiping surfaces with preserved product

	Total exposure (mg a.s./kg bw/d)	Relevant NOAEL (mg a.s./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.s./kg bw/d)	%AEL
Task:	**Non professionals wiping surfaces with preserved product– mixing and loading phase**					
Tier 1 : Without PPE	5.33×10^{-6}	0.52	100	97561	5.20×10^{-3}	<1
Task:	**Non professionals wiping surfaces with preserved product – application phase**					
Tier 1 : Without PPE	5.07×10^{-4}	0.52	100	1026	5.20×10^{-3}	10
Task:	**Non professionals wiping surfaces with preserved product – combined exposure (mixing and loading + application phase)**					
Tier 1 : Without PPE	5.12×10^{-4}	0.52	100	1015	5.20×10^{-3}	10

Acceptable risk has been identified for the non professionals wiping surfaces with preserved product, since MOE is higher than MOE_{ref} (100) and associated %AEL is below 100%, for the systemic effects during mixing/loading and application.

- Risk assessment for local effects

The content of PHMB in the end use product is below classification limits of skin sensitisation. As the product is not classified for its sensitisation and irritations properties, the risk for dermal local effects is considered to be acceptable.

2.2.1.2.2.3 Overall assessment of the risk for the non-professional uses of the active substance in biocidal products

Liquid detergent

Acceptable risk has been identified for hand washing laundry hand dishwashing and spot treatment of clothes without PPE.

Surface wiping

Acceptable risk has been identified for the non professionals wiping surfaces with preserved product without PPE.

2.2.1.2.3 Indirect exposure as a result of use (secondary exposure)

Relevant exposure paths

The relevant paths of indirect exposure to PHMB used as PT 6 in products are dermal and oral routes.

2.2.1.2.3.1 Preservatives for polymer emulsion used in paper, leather or textile additives

2.2.1.2.3.1.1 Dermal exposure of professionals from contact with processed leather

This scenario represents the exposure during handling of treated leather at any stage of the process.

It is considered that:

- all chemicals used during the whole process are protected with PHMB at a concentration of 0.06% w/w,
- 100% of PHMB in chemicals will migrates to the leather giving an a.s. concentration in leather of 0.031% w/w,
- 100% of migrated PHMB can transfer to the skin.

Table 2.2-17: Dermal exposure of professionals from contact with processed leather

Tier	Dermal exposure	
PPE	Deposit on skin (hands)	Systemic dose
	%	mg a.s. / kg bw /day
Task:	**Dermal exposure from contact with leather during process (handling of wet leather)**	
Tier 1: Without PPE	0.03%	2.76×10^{-2}
Tier 2: Gloves and impermeable coverall	0.03 %	1.51×10^{-3}

An equivalent scenario has been assessed with a concentration of 0.02% in polymer emulsion (lowest efficacious concentration demonstrated for polymer emulsions). Therefore, the concentration of PHMB in skin as a worst case is equivalent to 51.8% x 0.02% = 0.01%.

Table 2.2-18: Dermal exposure summary for professionals from contact with processed leather (chronic exposure)

	Tier 1	Tier 2: Gloves and impermeable coverall
Skin deposit concentration (%)	0.001%	0.001%
Dermal systemic dose (mg a.s./kg bw/d)	9.26×10^{-4}	5.07×10^{-4}

Risk characterisation for dermal exposure of professionals from contact with processed leather

- Quantitative risk assessment for systemic effects

Table 2.2-19: Summary of risk assessment for dermal exposure of professionals from contact with processed leather (chronic exposure)

	Total exposure (mg a.i/kg bw/d)	Relevant NOAEL (mg a.i./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.i./kg bw/d)	%AEL
Task:	**Dermal exposure of professionals from contact with processed leather – Chronic dermal exposure**					
Tier 1 : Without PPE	2.76×10^{-2}	0.52	100	19	5.20×10^{-3}	**531**
Tier 2: Gloves and impermeable coverall	1.51×10^{-3}	0.52	100	344	5.20×10^{-3}	29

Acceptable risk has been identified for the indirect exposure during contact with processed leather (professionals wearing gloves and impermeable coverall), since MOE is higher than MOE_{ref} (100) and associated %AEL is below 100%, for systemic effects.

Table 2.2-20: Summary of risk assessment for dermal exposure of professionals from contact with processed leather considering a concentration of 0.02% in polymer emulsion (chronic exposure, systemic effects)

	Total exposure (mg a.i/kg bw/d)	Relevant NOAEL (mg a.i./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.i./kg bw/d)	%AEL
Task:	**Dermal exposure of professionals from contact with processed leather – Chronic dermal exposure**					
Tier 1 : Without PPE	9.26×10^{-4}	0.52	100	56	5.20×10^{-3}	**178**
Tier 2: Gloves and impermeable coverall	5.07×10^{-4}	0.52	100	1026	5.20×10^{-3}	10

Acceptable risk has been identified for the indirect exposure during contact with processed leather (professionals wearing gloves and impermeable coverall), since MOE is higher than MOE_{ref} (100) and associated %AEL is below 100%, for systemic effects.

- Quantitative risk assessment for local effects

The content of PHMB in the end use product and in leather is below classification limits of skin sensitisation. As the product is not classified for its sensitisation and irritations properties, the risk for dermal local effects is considered to be acceptable.

2.2.1.2.3.1.2 Dermal exposure of general public from contact with leather/textile

The general public and professionals could be exposed during skin contact with leather or textile containing residues of PHMB. The worst case situation is the wear of leather or textile due to the large area of contact.

According to the OECD Guideline 2004 « Emission scenario document on textile finishing industry », the amount of additives used in manufacture of textile are lower than those used in manufacture of leather, it is considered that the contact leather is a worst case and covers contact with treated textile.

A reverse scenario is developed to assess the quantity of leather from which PHMB has to be extracted to have an unacceptable risk.

Table 2.2-21: Parameters for the exposure assessment of dermal secondary exposure with leather/textile

Parameters	Value	unit
AEL	0.0052	mg/kg
Body weight	60	kg
Dermal absorption	4%	
Transfer coefficient TNsG 2002 (Cotton, knitwear, plastic, wood-dried fluid-dry hand)	20%	
PHMB maximum concentration in leather	0.031%	w/w

Considering a conservative transfer coefficient of 100%, all of the PHMB contained in 126 g of leather have to be extracted to reach an unacceptable risk.

The estimation of what 126 g of leather represent is not easy to find. On the web site of French leather technical center it can be found that a treated skin for leather good is around 1.4-1.6 mm thickness and 1.1 -1.3 kg/m²[6].

So this 126 g of the same kind of leather would represent between 97-114 cm².

114 cm² is a very low surface of contact. It seems to be a realistic situation; therefore, the risk is considered to be unacceptable for general public wearing treated leather/textile with emulsion polymer containing PHMB.

An equivalent scenario has been assessed considering a concentration of 0.02% in polymer emulsion (lowest efficacious concentration demonstrated for polymer emulsions). Therefore, the concentration of PHMB in skin as a worst case is equivalent to 51.8% x 0.02% = 0.01%. Following the estimation presented above, all of the PHMB contained in 375 g of leather have to be extracted to reach an unacceptable risk. It would correspond to 288-341 cm².

It should be noted that this reversed scenario is worst case due to uncertainties on transfer factors from process liquid to leather then from leather to skin and the currently available data do not allow refinement. The refinement should be done at the product authorisation stage.

2.2.1.2.3.1.3 Dermal exposure of professionals from contact with paper (handling of dry paper)

This scenario assesses the exposure of workers from dry paper trough sampling and handling of the paper rolls. In the paper mill plant workers will be in contact with the paper in which PHMB can be present since the pulp is made with water treated with this emulsion of polymers.

Assuming that 100% of the additive used for paper production is the preserved polymer emulsion containing **0.06** % w/w a.s, the use of 25.8 kg of additive per ton of paper and assuming a paper density of 100 g/m², the final PHMB content may be up to **1.55×10^{-4} mg/cm² or 0.00155% w/w a.s.**.

The systemic dermal exposure to PHMB from the scenario described above are summarised below:

[6] http://www.ctc.fr/faq/questions.php3?theme=4; 07/10/2013

Table 2.2-22: Secondary dermal exposure estimates from handling dry paper

Tier	Dermal exposure	
PPE	Deposit on skin (hands)	Systemic dose
	%	mg a.s. / kg bw /day
Task:	**Dermal exposure from contact with paper (handling of dry paper)**	
Tier 1: Without PPE	0.06%	5.20×10^{-3}

Risk characterisation for indirect exposure to dry paper

- Quantitative risk assessment for systemic effects

Table 2.2-23: Summary of risk assessment for indirect exposure of dry paper (chronic exposure)

	Total exposure (mg a.i/kg bw/d)	Relevant NOAEL (mg a.i./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.i./kg bw/d)	%AEL
Task:	**Dermal exposure from contact with paper – Chronic dermal exposure**					
Tier 1 : Without PPE	5.20×10^{-3}	0.52	100	1200	5.20×10^{-3}	4

Acceptable risk has been identified for the indirect exposure during contact with paper, since MOE is higher than MOE_{ref} (100) and associated %AEL is below 100%, for systemic effects.

- Quantitative risk assessment for local effects

The content of PHMB in the end use product and in dry paper is below classification limits of skin sensitisation. As the product is not classified for its sensitisation and irritations properties, the risk for dermal local effects is considered to be acceptable.

2.2.1.2.3.1.4 Ingestion of paper by an infant

Indirect or secondary oral exposure may be possible for an infant or child who intentionally ingests paper manufactured in a process that uses PHMB. In order to determine which dose would not lead to systemic effects a reverse scenario was used:

The estimated of amount of active substance present in the paper after PHMB treatment is 1.55×10^{-4} mg/cm².

Table 2.2-24: Exposure Assumptions – Secondary Exposure from ingestion of paper by infant

Estimated of amount of active substance present in the paper after CMK treatment	1.55×10^{-4} mg/cm²
Oral absorption value	4 %
Infant body weight (TNsG, 2002)	10 kg
Child body weight (TNsG, 2002)	15 kg
Short-term systemic AEL	5.20×10^{-3} mg/kg bw/day

The reverse worst-case exposure scenario is calculated as follows:

Infant: 5.20×10^{-3} mg a.s./kg bw/d x 10 kg / [(1.55×10^{-4} mg a.s./cm² paper) x 4% absorp.] = **8390 cm².**

Child: 5.20×10^{-3} mg a.s./kg bw/d x 15 kg / [(1.55×10^{-4} mg a.s./cm² paper) x 4% absorp.] = **12580 cm².**

Then, it is considered as highly unrealistic that an unacceptable risk occurs concerning paper ingestion by infants and children.

2.2.1.2.3.2 Preservatives for detergents

2.2.1.2.3.2.1 Dermal exposure from washed dish

A reverse scenario of exposure has been established to calculate the maximum area of utensils that could be rubbed daily without risk of systemic effects. Assuming a scenario of 100% migration from the utensils onto the skin and assuming no rinse-off or drying step and a body weight of 60 kg, the maximum rubbed area without risk of systemic effects would be:

$Area_{max}$ = [AEL (mg/kg bw/day) x body weight (kg) /dermal absorption (%)] / [concentration of a.s. into product (%) x concentration of the product into washing solution (%) x of PHMB into final product x contamination value of HERA (mL/cm²)]
= [5.20×10^{-3} x 60/ 4%] / [0.08 % x 0.14% x 5.50×10^{-1}] = $1.27 \times 10^{+7}$ cm^2/d.
= $1.27 \times 10^{+3}$ m²/d

The situation where a person rubbes $1.27 \times 10^{+3}$ m² /d of utensils daily is unrealistic. Therefore, the risk for direct contact with residues on utensils is considered to be acceptable.

2.2.1.2.3.2.2 Dermal exposure from wearing clothes

Exposure to residual PHMB may be possible due to indirect or secondary exposure from clothes cleaned with detergents containing PHMB. Residues of components of laundry detergents may remain on textiles after washing and could come in contact with the skin via migration from textile to skin.

The estimated indirect dermal exposure for an adult with body weight 60 kg is:

Fraction of active substance in the textile: 3.68 mg a.s./kg
Systemic dose: **1.84 x 4% / 60 = 1.23 x 10^{-3}** mg a.s./kg bw/day

Based on the fact of an adult wears 1 kg of textile, it is considered that a child of 15kg wears 0.25 kg of textile.
The same calculations can be done for a child with body weight 15 kg.

Fraction of active substance in the textile: 3.68 mg a.s./kg
Systemic dose: **1.84 x 0.25 x 4% / 15 = 1.23 x 10^{-3}** mg a.s./kg bw/day

Risk characterisation for indirect exposure tof liquid detergents

- Quantitative risk assessment for systemic effects

Table 2.2-25: Summary of risk assessment for indirect exposure to liquid detergents (chronic exposure)

	Total exposure (mg a.s./kg bw/d)	Relevant NOAEL (mg a.s./kg bw/d)	MOE_{ref}	MOE	AEL (mg a.s./kg bw/d)	%AEL
Task:	**Adult/child in contact with textile cleaned with liquid detergent – Chronic dermal exposure**					
Tier 1 : Without PPE	3.96 x 10^{-5}	0.52	100	424	5.20 x 10^{-3}	24

Acceptable risk has been identified for the adults and children in contact with textile cleaned with liquid detergent, since MOE is higher than MOE_{ref} (100) and associated %AEL is below 100%, for systemic effects.

- Risk assessment for local effects

The content of PHMB in the end use product is below classification limits of skin sensitisation. As the product is not classified for its sensitisation and irritations properties, the risk for dermal local effects is considered to be acceptable.

2.2.1.2.3.2.3 Household (HH) uses

Indirect exposure following use of preserved surface cleaner occurs when an infant is crawling on a surface cleaned with treated product (oral and dermal exposure).

Table 2.2-26: Household (HH) uses indirect exposure summary (medium term exposure)

Tier	Dermal exposure	Oral exposure	Total exposure

PPE	Deposit on skin (hands)	Systemic dose	Systemic dose	Systemic dose
	%	mg a.s. / kg bw /day	mg a.s. / kg bw /day	mg a.s. / kg bw /day
Task:	**Infant crawling on surface cleaned with treated detergent- Chronic dermal exposure**			
Tier 1: Without PPE	1.20×10^{-4}	2.59×10^{-3}	2.88×10^{-4}	2.88×10^{-3}

Risk characterisation for indirect exposure for Household (HH) uses

- Quantitative risk assessment for systemic effects

Table 2.2-27: Summary of risk assessment for indirect exposure for an infant crawling on a surface cleaned with treated product

	Total exposure (mg a.s./kg bw/d)	Relevant NOAEL (mg a.s./kg bw/d)	MOE_{ref}	MOE	AEL (mg a.s./kg bw/d)	%AEL
Task:	**Infant crawling on surface cleaned with treated detergent-**					
Tier 1 : Without PPE	2.88×10^{-3}	0.52	100	181	5.20×10^{-3}	55

Acceptable risk has been identified for the indirect exposure of an infant crawling on a surface cleaned with preserved product, since MOE higher than MOE_{ref} (100) and associated %AEL is below 100%, for the systemic effects.

- Risk assessment for local effects

The content of PHMB in the end use product is below classification limits of skin sensitisation. As the product is not classified for its sensitisation and irritations properties, the risk for dermal local effects is considered to be acceptable.

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2.2.1.2.3.3 Indirect exposure via food

Incidence on consumer safety following the consumption of contaminated products was assessed, considering that consumers can be exposed to residues left on vessels and surfaces cleaned with preserved products and to residues which can migrate from wrapping material into the food.

No specific hydrolysis studies were provided. Based on physical-chemical properties of PHMB, the decomposition of the PHMB in normal circumstances of use is not expected and only PHMB is considered as a residue for the risk assessment.

No experimental data/studies were provided. Consequently, the daily exposure to PHMB was assessed with worst case scenarios, using default values from the

European guidelines documents[7] and additional proposed values/calculation concerning PT6 currently under discussion for harmonization (DRAWG 2012).

Three categories of scenarios were considered as a worst case and for cumulative risk assessment:

- Scenario 1 : dishwashing
- Scenario 2 : surface treatment
- Scenario 3 : packaging/wrapping material

Without additional information and as a general and worst case approach, a residue transfer of 100% was considered from the preserved product to the vessels, surface, wrapping material and finally contaminated food.

Because of the highly chelating properties of PHMB with organic matters and surfaces such as plastic, steel, ceramic and glass, no rinsing step with clear water could be considered effective and relevant since no information to demonstrate its efficiency were given.

For scenarios 1 and 2, both the validated concentration of 0.04% w/w a.s. and the maximal claimed concentration of 0.08% w/w a.s. were considered. As a general approach, it was considered that the preserved product is diluted before use. A default value of 0.14% was considered to cover the most common conditions of use for detergents used for dishwashing and a dilution of 1/20 of the pure biocidal product in water was considered for surface detergents.

For scenario 3, both the validated concentration of 0.02% w/w a.s. and the maximal claimed concentration of 0.06% w/w a.s. were considered.It has been considered that the amount of polymer emulsions used as additives in paper is 25.8 kg/ton of paper. Thus, since the lowest concentration of PHMB in the polymer emulsions is 0.02%, its relative concentration in wrapping material would be 25.8 kg/ton x 0.02% = 5.16 mg a.s./kg of wrapping material. This value was considered as the worst case concentration of PHMB which would be transferred in wrapping material. Furthermore, according to the DRAWG opinion on identifying worst case uses for PT6 biocidal products in order to minimize the number of uses to be assessed for dietary risk, it is assumed that the potential contamination of feed by residues arising from packaging paper are covered by the wrapping material scenario on foods.

Following these considerations, secondary exposure via ingesting food placed on vessels, surfaces or wrapped material previously contaminated by a product containing PHMB as PT06 was assessed.

Cumulated dishwashing, surface and wrapping material scenarios shows that the exposure to PHMB without any rinsing step would be relevant, but below the defined ADI or ARfD of 0.13mg/kg bw/day (i.e. 7.2% of the ADI or ARfD for a child and 1.4 % for an adult if using the validated concentration of PHMB, 16.4% of the ADI or ARfD for a child and 3.3% for an adult if using the maximal concentration of PHMB claimed by the applicant).

These scenarios are considered as covering the non-professional as well as the professional PT6 uses of PHMB. Consequently, the risk for the consumer following

[7] Dietary Risk Assessment Working Group (DRAWG): «Guidance on estimating transfer of biocidal active substances into food » and «Guidance on estimating livestock exposure to biocidal active substances »

transfer into the food of products containing PHMB as PT06 is considered as acceptable.

2.2.1.2.3.4 Indirect exposure: conclusion

Leather/textile:

Acceptable risk has been identified for the indirect exposure during contact with processed leather for professionals wearing gloves and impermeable coverall.

The risk is considered to be unacceptable for general public wearing treated leather/textile with emulsion polymer containing PHMB.

It should be noted that this reversed scenario is worst case due to uncertainties on transfer factors from process liquid to leather then from leather to skin and the currently available data do not allow refinement. The refinement should be done at the product authorisation stage.

Paper:

The dermal contact with dry paper is considered to be acceptable for professionals and general public.

It is considered as highly unrealistic that an unacceptable risk can occur when paper is ingested by infants and children.

Liquid detergent:

Dermal exposure from washing dish: the situation where a person rubbes 1.27 x 10^3 m² /d of utensils daily is unrealistic. Therefore, the risk for direct contact with residues on utensils is considered to be acceptable.

Dermal exposure from wearing clothes: acceptable risk has been identified for the adults and children in contact with textile cleaned with liquid detergent

Household:

Acceptable risk has been identified for the indirect local exposure of an infant crawling on a surface cleaned with preserved product

Indirect exposure via food:

The risk for the consumer following transfer into the food of products containing PHMB as PT06 is considered acceptable.

2.2.1.3 Overall conclusion for human health

Table 2.2-28: Overall conlusion of the risk assessment for human health

	Primary exposure	Secondary exposure	Secondary exposure via food
Product formulation (Professionals)	Acceptable with gloves and coverall	NR	NR
Polymer emulsion uses (Professionals) – paper/leather / textile	Acceptable	**Professionals:** Acceptable with gloves and coverall. **General public:** - Textile/leather **Unacceptable** for dermal contact with leather - Paper Acceptable (ingestion paper by infant and dermal contact with paper)	Acceptable
Liquid detergent (Professionals and non-professionals)	Laundry washing and dishwashing detergent spot-treatment of clothes: Acceptable for professionals and non professionals without PPE	Acceptable	
Household detergent	Acceptable for professionals and non professionals without PPE	Acceptable	

2.2.2 SUMMARY OF ENVIRONMENTAL RISK ASSESSMENTS

2.2.2.1 Fate and distribution in the environment

2.2.2.1.1 Abiotic degradation

2.2.2.1.1.1 Hydrolysis as a function of pH

Hydrolysis study following the OECD guideline 111 was performed. Less than 10% hydrolysis was found after 5 days at 50°C for all pHs (4, 7, 9) tested. Consequently, PHMB is considered to be hydrolytically stable.

2.2.2.1.1.2 Photolysis in water

According to OECD guideline 316, direct photolysis can be an important dissipation pathway for some chemical pollutants that exhibit significant light absorption above the 290 nm cut-off of solar irradiation at the earth's surface. As PHMB absorption spectra maximum was not found in visible wavelength, PHMB could be considered as not photodegradable.

2.2.2.1.1.3 Photolysis in air

PHMB degrades quickly in the atmosphere by reaction with OH radicals with a highest DT_{50} of 1.351 hours (24H day, 5 . 10^5 OH/cm^3). Nonetheless, considering that PHMB is not volatile, potential photodegradation of PHMB is negligible.

Therefore, the abiotic degradation processes will have a minimal influence on the fate and behaviour of PHMB in the environment.

2.2.2.1.2 Biodegradation

2.2.2.1.2.1 Ready biodegradation

A ready biodegradation test is performed on the active substance according to OECD guideline 301B. After 99 days, 3.8% of PHMB is mineralized. Thus this substance is considered as non readily biodegradable.

2.2.2.1.2.2 STP compartment

A simulation test according to OECD 303A guideline is conducted to investigate PHMB degradation in conditions imitating a domestic sewage treatment plant. During the 144 days-period, less than 1% of PHMB is mineralized. 18% of the

applied radioactivity is measured in the aqueous effluent, and the residual 82% is sorbed onto the sludge biomass.

PHMB is very slightly mineralized. The water discharge observed is caused only by a modification of PHMB distribution related to its property of adsorption leading to an accumulation of this active substance in activated sludge.

2.2.2.1.2.3 Aquatic compartment

In seawater, a study performed with OECD 306 guideline demonstrated that after 56 days, at concentrations of 1 and 0.1 mg a.s..L^{-1}, 2.6% and 10.1% CO_2 mineralisation was observed respectively. For the highest concentration, some evidence of toxicity was noticed and could explain the lower level of mineralization.

2.2.2.1.2.4 Water/sediment system

A simulation test according to OECD 308 guideline was conducted to investigate PHMB degradation in condition imitating aquatic system. The route and rate of [14C]-PHMB biotransformation was investigated under aerobic condition in two flooded sediment systems (loam and loamy sand) over a period of 101 days. PHMB rapidly dissipated from the water phase, partitioning into the sediment phase where it remained tightly bound for the duration of the study. Less than 3% of PHMB was mineralized to CO_2 after a period of 101 days.

Removal from the water phase has a half-life between 1 to 2.3 days. No half-life from the sediment phase and the whole system were available. In both loam and loamy sand sediments, the main amount (from 77% to 97%) of PHMB in the sediment is fixed in the humin fraction (NER).

2.2.2.1.2.5 Soil

Soil biodegradation was investigated in two reliable studies designed to assess the aerobic degradation in soil.

The first of these studies was conducted according to OECD 304A. Less than 5% mineralization of PHMB is observed during the 64 day study and approximately 90% of applied ^{14}C-PHMB remained bound to soil. No information on primary degradation of the polymers was provided.

The second study assesses the rate and route of degradation in soil according to the OECD guideline 307. Biodegradation of ^{14}C-PHMB was investigated in four different soils (loamy sand, silty clay loam, clay loam and sandy loam) under aerobic conditions over a period of 123 days. PHMB was highly adsorbed to four different soils, with <5% being mineralized to $^{14}CO_2$. The amount of PHMB in non extractable residues was >70%. Therefore, it was not possible to identify any breakdown product, nor to calculate degradation kinetics.

As a conclusion, PHMB was found to be non biodegradable and slight rates of mineralization were found in water/sediment system and soil. Moreover, in the aquatic and terrestrial simulation studies, it seems that more than 90% of PHMB

is bound with NER while in the sewage treatment plant more than 80% of PHMB is PHMB forms NER. Therefore, PHMB is adsorbed very quickly and very strongly to organic matter, which induces a very limited bioavailability for biodegradation processes.

2.2.2.1.3 Distribution

Several studies on adsorption/desorption properties according to OECD guidelines 121 and 106 show that PHMB adsorbs rapidly and strongly on any kind of sediments, sewage sludge or soils. PHMB remains practically immobile after adsorption. The Koc values are ranged from 151415 to 428713. The arithmetic mean value of K_{oc} of 276670 is used for the risk assessment.

2.2.2.1.4 Accumulation

The low Kow and the high molecular weight indicate the substance is unlikely to bioaccumulate.

2.2.2.2 Effects assessment on environmental organisms (active substance)

2.2.2.2.1 Aquatic organisms

Acute toxicity data are available for fish and algae. An acute key study with *Daphnia magna* (conducted prior to guideline publications but using a test protocol similar to OECD 202) was submitted. eCA considered this study as invalid due to important waiving and because the validity criteria were not fulfilled. This data gap was accepted by eCA since a chronic study was submitted.

Chronic toxicity data are available for the three trophic levels (fish, algae and invertebrates).The most sensitive endpoint is the NOEC/EC10 value of 7.43 $\mu g.L^{-1}$ of a.s. based on growth rate parameter and on measured concentration from growth inhibition test performed on green algae *Selenastrum capricornutum*.

Hence, the $PNEC_{surface\ water}$ is estimated to be 0.743 $\mu g.L^{-1}$ of a.s. since a safety factor of 10 according to the TGD should be applied to the lowest endpoint for aquatic environment when acute and chronic data for three trophic levels are available.

2.2.2.2.2 Inhibition of aquatic microbial activity

The most sensitive NOEC is the one related to the inhibition of nitrification of activated sludge microorganisms, which gives a NOEC of 12 $mg.L^{-1}$ of a.s.. By applying an assessment factor of 1 according to the TGD part II, table 17, the $PNEC_{microorganisms}$ is estimated to be 12 $mg.L^{-1}$ of a.s.

2.2.2.2.3 Sediment dwelling organisms

No effects were observed at any concentration in a relevant study performed with sediment dwelling organisms. Therefore, the NOEC, based on mean measured concentrations, derived from this 28-day spiked sediment study is equal to 196 $mg.kg^{-1}$ wwt sediment of a.s. on *Chironomus riparius*.

With only one long-term test available, an assessment factor of 100 is applied according to the table 19 of the TGD part II to derive the $PNEC_{sediment}$. Therefore, the $PNEC_{sediment}$ for a.s. is 1.96 $mg.kg^{-1}$ wwt.

However, it should be noted that during the exposure period, the organisms were fed with a fish food suspension. About feeding of the organism during the test, the standard guideline OECD218 mentioned that [§31, p.7]:

"*When testing strongly adsorbing substances (e.g. with log Kow > 5), or substances covalently binding to sediment, the amount of food necessary to ensure survival and natural growth of the organisms may be added to the formulated sediment before the stabilisation period.*". As a consequence the feeding method applied for the test does not follow the standard guideline, considering the high adsorption properties of the PHMB.Therefore, the results from this study should actually be taken with caution.

As a consequence, it was decided at the Working Group-I-2015 that $PNEC_{sediment}$ should also be calculated via EPM with an additional factor of 10 taking the high adsorption properties of PHMB (TGD part II), and the lowest value should be used for the risk assessment.

The PNECsediment was calculated based on equilibrium partitioning by applying the equation 70 of the TGD, part II. Therefore the $PNEC_{sediment(EPM)}$ for a.s. is 446.94 µg a.s./kg wwt. This value will be used in the risk assessment for sediment compartment.

2.2.2.2.4 Terrestrial compartment

No adverse effect was observed in the study carried out on microorganisms, plants and earthworms. Therefore, in all studies the relevant endpoint is considered as the highest test concentration.The standardized EC50 derived from the acute toxicity on earthworms gives the lowest value of 358.2 mg a.s..kg^{-1} wet weight. This value is used to determine the $PNEC_{soil}$.

For the determination of the assessment factor, as no effects were seen in any of the studies, the issue on the most sensitive species as specified in the MOTA v.5 might not be as relevant. Based on the lack of effects in the studies, it was agreed at WG-I-2015 that an AF of 100 should be sufficient to derive the PNECsoil. .

Consequently, the $PNEC_{soil}$ for PHMB is 3.58 mg a.s. kg^{-1} wet weight.

2.2.2.3 Summary of PNEC values

The table below summarises the PNEC value retained for risk assessment:

Table 2.2-29: PNEC values for active substance PHMB used for the risk assessment part

$PNEC_{water}$	0.743 µg.L^{-1} of a.s.
$PNEC_{sediment}$	446.94 µg.kg^{-1} wwt sediment of a.s.
$PNEC_{soil}$	3.58 mg.kg^{-1} wwt soil of a.s.
$PNEC_{microorganisms}$	12 mg.L^{-1} of a.s.

2.2.2.4 Environmental effect assessment (product)

No additional data on the environment effects of the biocidal products were submitted. The risk assessment is based on the effect of the active substance PHMB.

2.2.2.5 PBT, Endocrine Disrupting (ED) and POP assessment

According to the annex XIII of the REACH regulation EC/1907/2006, substances are classified as PBT when they fulfill the criteria for all three inherent properties Persistent (P), Bioaccumulable (B), Toxic (T), and/or vPvB when they fulfill the criteria the two inherent properties very Persistent (vP), very Bioaccumulable (vB).

2.2.2.5.1 Persistence criteria

According to the annex XIII of the REACH regulation, criteria for substance to be persistent (and very persistent) are fulfilled when:

- $T_{1/2}$ in marine water > 60 days (60 days for vP criterion) or,
- $T_{1/2}$ in fresh or estuarine water > 40 days (60 days for vP criterion) or,
- $T_{1/2}$ in marine sediment > 180 days or,
- $T_{1/2}$ in freshwater sediment > 120 days (180 days for vP criterion).

According to study results on biodegradability of active substance PHMB in STP, water/sediment, and soil compartment (*c.f.* section 2.2.2.1.2), **PHMB fulfills the P and vP criteria**:

- for soil compartment, DT50/DT90 are greater than 1 year, not extractable residues are > 90% in all tested soils, and mineralization is <5% over the 123 days of incubation .
- for surface water, DT50 in whole system is greater than 6 months at 20°C, non-extractable > 90%, and mineralisation is <3% after 101 days.

2.2.2.5.2 Bioaccumulation criteria

According to the annex XIII of the REACH regulation, criteria for substance to be bioaccumulable are fulfilled when the bioconcentration factor (BCF) exceeds a

value of 2000 L/kg. Moreover, a substance is considered to potentially fulfill the B criteria when log K_{ow} exceeds a value of 4.5.

The applicant has proposed an estimation of the intrinsic potential for bioconcentration using the octanol/water partition coefficient and the models given in the Technical Guidance Document For Risk Assessment Of New And Existing Substances (Chapter 3 p. 126). This linear relation is valid only for a Kow ranging between 2 and 6 or higher than 6 and could not be used for PHMB. Nevertheless, the low Kow, the high molecular weight (PHMB >700 g/mol) may indicate the substance is unlikely to bioaccumulate. However, PHMB contains also polymers with short chain of carbons which could penetrate into organisms.

Therefore, Applicant reviewed available data and proposed qualitative explanations based on theoretical consideration. Applicant explained that a quantitative prediction of the solubility of low molecular weight oligomers (*i.e.* the dimer) was not considered possible given the available data. However, given the relationship between water solubility and Kow then a lower solubility would lead to a higher Kow and thus a higher BCF. Plus, the smallest oligomers, such as dimers, would be expected to have higher water solubility than larger oligomers. It can therefore expect the dimer to have a lower Kow and thus a lower BCF. Based on this theoretical consideration, there is no concern over the bioaccumulation potential of low MW oligomers. This view is supported by the measured Kow value (Kow = 0.005; log Kow = -2.29) which reflects the value for a mixture of oligomers. This measured Kow is extremely low and makes it extremely improbable that the Kow for any low molecular weight oligomers would even approach the generally accepted trigger limit of 4.5.

Based on the Kow, the BCF for aquatic organism and for terrestrial organisms is estimated to be 0.002 and 0.0013 L/kg, respectively.

Considering the low logKow (-2.29), the BCF for aquatic organism (0.002) and for terrestrial organisms (0.0013), PHMB is not considered to fulfill the B criterion.

2.2.2.5.3 Toxicity criteria

According to the annex XIII of the REACH regulation, the toxicity criterion is fulfilled when the chronic NOEC for aquatic organism is less than 0.01 mg/L or when the substance meets the criteria for classification as carcinogenic (1A or 1B), germ cell mutagenic (1A or 1B) or toxic for reproduction (1A, 1B or 2).

Based on ecotoxicity on the most sensitive species *Selenastrum capricornutum* (*i.e.* NOEC/EC10 = 0.00743 mg/L of a.s.), active substance **PHMB is considered to fulfill T criteria**.

Therefore, PHMB is not considered to fulfill the PBT nor vPvB criterion. Anyhow, as PHMB fulfill the criteria of vP and T, **PHMB should be considered as a candidate for substitution, according to the article 10 of the Biocides Regulation EU/528/2012.**

2.2.2.5.4 ED properties

PHMB is not known to represent and Endocrine Disruptor with regard to the environment. Considering the mode of action of the substance, observed effects on reproduction on fish and daphnia is not expected to be linked to an ED-mode of action.

2.2.2.5.5 POP assessment

According to the screening criteria described in the Annex D of the Stockolm convention, PHMB is not a POP.

2.2.2.6 Environmental exposure assessment

2.2.2.6.1 Definition of the stages of life cycle

PHMB is added as preservatives for products during storage, before products are used. After this 'Product Formulation' stage, the preserved products may be left on the shelf in the containers for a long period of time. This is effectively the 'Use' stage for PHMB since it acts as a biocide in the product containers prior to these being opened and used. The use of products containing preservatives could be seen as the disposal phase of PHMB since it is no longer required to prevent organisms growing in the container of preserved product. However it is clear that this "disposal phase" for PHMB will involve the potential for significant environmental exposure.

Therefore in this assessment the life cycle phases of the ultimate product are those that are considered:

- The "re-formulation" of PHMB into those products has been termed "**Formulation**";
- The use of preserved products has been termed "Use".

The term "disposal" is used to denote the disposal of the spent or unused fluid which may also contain PHMB.

2.2.2.6.2 Presentation of the uses for evaluation

The major fields of PHMB uses, considering the representative product VANTOCIL TG ca. 20% PHMB w/w, evaluated for approval as preservatives for products during storage (PT06) are summarised in Table 2.2-30. According to the general information provided above, an environmental exposure assessment has been conducted for the "Formulation" and "Use" stages of the preserved product.

Table 2.2-30. PHMB Major end-uses (uses of the preserved products).

MG/PT	Field of use envisaged	Minimal concentration at which the active substance PHMB will be used
Washing and cleaning fluids, human hygienic products		
PT06.1	**Detergents –** Used to control the growth of bacteria in the products such as liquid fabric softeners, dishwashing detergents, liquid laundry detergents, liquid soaps and hand cleaners, and the surfactants used to formulate such products.	0.04% w/w a.s.
Additives used in paper, textile and leather production		
PT06.3	**Pulp and paper additives –** Used to control the growth of bacteria in water-soluble and water-dispersed pulp and paper additives in storage containers before use.	0.02% w/w a.s.
PT06.4	**Textile additives –** Used to control the growth of bacteria in water-soluble and water-dispersed textile additives in storage containers before use.	0.02% w/w a.s.
PT06.5	**Leather additives –** Used to control the growth of bacteria in water-soluble and water-dispersed leather additives in storage containers before use.	0.02% w/w a.s.

When possible and relevant, both scenarios based on tonnage and consumption data should be applied for the formuation and use phases of preserved products.

In all cases, the STP is the primary compartment of exposure for the proposed uses. As a result of this, there will be a potential for exposure of STP and both the aquatic (surface water and sediment) and the terrestrial (soil and groundwater) compartments, the latter as a result of contaminated sewage sludge spreading on land. Since the emissions to the STP have been determined, equations from the TGD were used to calculate the predicted environmental exposure concentrations in the relevant environmental compartments.

2.2.2.6.3 Exposure assessment by Tonnage

The tonnage values were given by the applicant as confidential data. It should be noted that the applicant provided a specific tonnage value only for sub-type PT06.1 (preservation of detergents). For the other intended sub-types, tonnage values were not specified. As a consequence, emissions of PHMB during formulation and use based on tonnage were estimated only for sub-type PT06.1 (preservation of detergents).

For the use phase of detergents, emissions from amateur and professional applications have been calculated, and added for the assessment of the risk for the environment as these uses will results in cumulative emissions to the STP.

Moreover, in order to carry out an assessment including the total intended tonnage for PT6, a scenario considering the 'dispersive use' of all PHMB amounts was conducted.

2.2.2.6.4 Exposure assessment by Consumption rate

A more targeted assessment based on consumption parameters was undertaken for the uses of PHMB mentioned in Table 2.2-30. For preservatives for products during storage, an ECB Environmental Emission Scenario Document (ESD)[8] is available to address the "use" stage of preserved products. Due to the wide-ranging uses of preservatives for products during storage, this document is only a framework document and it refers to other ESDs where the use pattern of the product requiring in-can preservation is better described (Table 2.2-31).

Table 2.2-31. Specific emission scenario document applied for environmental risk assessment of PHMB uses as preservatives for products during storage (PT06).

Field of use	Specific ESD
PT06.1 – Detergents	• **For professional uses:** *Supplement to the methodology for risk evaluation of biocides: Environmental Emission Scenarios for Product Type 2: Private and public health area disinfectants and other biocidal products (sanitary and medical sector)* - RIVM. March 2001. • **For amateur uses**: *Environmental Emission Scenarios for biocides used as human hygiene biocidal products (Product type 1)* -European Commission DG ENV/RIVM. January 2004.
PT06.3 – Pulp and paper additives	• OECD (2006): *Emission scenario document on non-integrated paper mills*. • Tissier C, Migné V (2001) *ESD for biocides used in paper coating and finishing (Product type 6, 7 & 9)*. • EC (2001): Integrated Pollution Prevention and Control (IPPC), *Reference Document on Best Available Techniques in the Pulp and Paper Industry*.
PT06.4 – Textile additives	• OECD (2004). OECD series on emission scenario documents – number 7 – *Emission scenario document on textile finishing industry*. ENV/JM/MONO(2004)12. • EC (2003): Integrated Pollution Prevention and Control (IPPC), *Reference Document on Best Available Techniques in Textiles Industry*.
PT06.5 – Leather additives	• OECD (2004). *Emission scenario document on Leather Processing*. • EC (2003): Integrated Pollution Prevention and Control (IPPC), *Reference Document on Best Available Techniques for the Tanning of Hides and skins*.

2.2.2.7 Risk characterisation for the environment

To carry out a quantitative risk assessment for the environment when PHMB is used as a preservative for products during storage, the PEC values were compared to the respective PNEC values for the different compartments, resulting

[8] European Commission, ESD for Biocides used as In-can Preservatives (Product type 6). January 2004.

in PEC/PNEC ratios. These ratios are presented below, for each of the uses mentioned in Table 2.2-30 and for the cumulative risk assessment. Detailed PEC/PNEC ratios from the tonnage approach are presented in the confidential doc IIC of the Competant Authority Report.

2.2.2.7.1 PHMB as preservative in detergent (PT6.1)

The use phase of PHMB in detergents (PT6.1) has been evaluated both for the professional uses and amateur uses. Afterwards, emissions estimated from the amateur uses and the professional uses of detergents have been cumulated for the risk assessment. Calculations based on consumption approach are applied considering market shares of 1 and 0.5.

Table 2.2-32. Risk assessment for the use of PHMB as preservative in detergents

Compartment / PEC/PNEC*	STP	Surface water	Sediment	Soil	Groundwater, $\mu g.L^{-1}$*
Tonnage approach					
Formulation	<1	<1	**>1**	<1	<0.1
In-use (professional)	<1	<1	**>1**	<1	<0.1
In-use (amateur)	<1	<1	<1	<1	<0.1
In-use (professional and amateur)	<1	<1	**>1**	<1	<0.1
Consumption approach					
Professional use					
Market share: 1	4.32E-04	0.49	**4.93**	0.27	< 0.1
Market share: 0.5	2.16E-04	0.25	**2.47**	0.14	< 0.1
Amateur uses (human hygiene products, washing and cleaning products)					
Market share: 1	1.48E-03	**1.69**	**16.88**	0.93	< 0.1
Market share: 0.5	7.40E-04	0.84	**8.44**	0.47	< 0.1
Aggregated uses					
Market share: 1	1.91E-03	**2.18**	**21.86**	**1.21**	< 0.1
Market share: 0.5	9.58E-04	**1.09**	**10.91**	0.60	< 0.1

* According to groundwater concentrations modelized by FOCUS PEARL 4.4.4 and compared to the maximum permissible concentration set for drinking water by the Directive 98/83/EC of 0.1 µg/L.

As shown in Table 2.2-32, the risk assessment for the environment of the PHMB use as preservative in detergent indicates:

- Through the tonnage approach, unacceptable risk for the sediment compartment for the formulation phase, the professional use and the total use (professional and amateur) of detergents ;

- Through the consumption approach and considering a market share of 0.5, unacceptable risk for the sediment compartment for professional and amateur uses.
- Through the consumption approach and considering a market share of 0.5, unacceptable risk for the freshwater and the sediment compartments for aggregated uses.

In conclusion, the formulation and the uses of detergents preserved by PHMB as PT6.1 are cause for concern in relation to the contamination of the environment according to the scenario of PHMB releases through tonnage and consumption approaches.

2.2.2.7.2 PHMB as preservative in pulp and paper additives (PT6.3)

The use phase of PHMB as preservative in pulp and paper additives (PT6.3) has been evaluated for three types of paper production: newsprint, printing and writing paper, and tissue paper. Afterwards, emissions have been cumulated for the risk assessment, considering a mill producing all the types of paper (Table 2.2-33). Calculations based on consumption approach are applied considering market shares of 1 and 0.5.

Table 2.2-33. Risk assessment for the use of PHMB as preservative in pulp and paper additives

Compartment / PEC/PNEC*	STP	Surface water	Sediment	Soil	Groundwater, $\mu g.L^{-1}$*
Tonnage approach					
Formulation	Not determined in absence of specific tonnage value				
In-use					
Consumption approach					
Newsprint					
Market share: 1	1.06E-03	**1.21**	**12.14**	0.67	< 0.1
Market share: 0.5	5.32E-04	0.61	**6.07**	0.34	< 0.1
Printing and writing paper					
Market share: 1	1.03E-03	**1.18**	**11.75**	0.65	< 0.1
Market share: 0.5	5.15E-04	0.59	**5.88**	0.33	< 0.1
Tissue paper					
Market share: 1	9.47E-04	**1.08**	**10.81**	0.60	< 0.1
Market share: 0.5	4.74E-04	0.54	**5.40**	0.30	< 0.1
Mill producing all type of paper					
Market share: 1	3.04E-03	**3.47**	**34.71**	**1.92**	< 0.1

Market share: 0.5	1.52E-03	**1.74**	**17.35**	0.96	< 0.1

* According to groundwater concentrations modelized by FOCUS PEARL 4.4.4 and compared to the maximum permissible concentration set for drinking water by the Directive 98/83/EC of 0.1 µg/L.

As shown in Table 2.2-33, and considering results for a market share of 0.5 in order to be in accordance with the MOTA, PEC/PNEC ratios indicate that:

- For use of VANTOCIL TG as PT6.3 in additives for newsprint production, the predicted PHMB emission levels will give rise to adverse effects to organisms present in the sediment.
- For use of VANTOCIL TG as PT6.3 in additives for printing and writing paper, the predicted PHMB emission levels will give rise to adverse effects to organisms present in the sediment.
- For use of VANTOCIL TG as PT6.3 in additives for tissue paper production, the predicted PHMB emission levels will give rise to adverse effects to organisms present in the sediment.
- For all uses of VANTOCIL TG as PT6.3, the predicted PHMB emission levels will give rise to no adverse effects in organisms present in the terrestrial compartment and to the STP. With regard to predicted PHMB concentrations in groundwater, these exceed the 0.1 µg/L limit set by the EU Groundwater Directive only for both market shares.
- For aggregated uses of VANTOCIL TG as PT6.3 (i.e. considering a mill producing all the types of paper), the predicted PHMB emission levels will give rise to adverse effects to organisms present in the surface water and the sediment.

In conclusion, the uses of VANTOCIL TG as PT6.3 according to scenarios of PHMB releases are cause for concern in relation to the contamination of the sediment compartment considering the emission for each type of paper.

2.2.2.7.3 PHMB as preservative in Textile additives (PT6.4)

The use phase of PHMB as preservative in textile additives (PT6.4) has been evaluated for the following paper treatment: pretreatment, exhaust process, padding process, printing and coating process. Afterwards, emissions have been cumulated for the risk assessment, considering the whole textile production process (Table 2.2-34). Calculations based on consumption approach are applied considering market shares of 1 and 0.5.

Table 2.2-34. Risk assessment for the use of PHMB as preservative in textile additives

Compartment / PEC/PNEC*	STP	Surface water	Sediment	Soil	Groundwater, $\mu g.L^{-1}$*
Tonnage approach					
Formulation	Not determined in absence of specific tonnage value				
In-use					
Consumption approach					
Pre-treatment	2.34E-03	**2.67**	**26.70**	**1.48**	< 0.1
Exhaust process	1.17E-04	0.13	**1.34**	0.07	< 0.1
Padding, printing, and coating processes	2.19E-03	**2.50**	**25.04**	**1.39**	< 0.1
Whole textile production					
Market share: 1	4.65E-03	**5.31**	**53.08**	**2.94**	< 0.1
Market share: 0.5	2.33E-03	**2.65**	**26.54**	**1.47**	< 0.1

* According to groundwater concentrations modelized by FOCUS PEARL 4.4.4 and compared to the maximum permissible concentration set for drinking water by the Directive 98/83/EC of 0.1 µg/L

As shown in Table 2.2-34, the applied scenarios of PHMB releases for the use of VANTOCIL TG as PT6.4 show:

- PEC/PNEC ratios > 1 for the freshwater for uses in additives for textile pre-treatment, padding, printing, and coating processes; PEC/PNEC ratios < 1 for the freshwater for uses in additives for textile exhaust process; PEC/PNEC ratios > 1 for the freshwater when considering uses for the whole textile production at both market shares.
- PEC/PNEC ratios > 1 for the sediment compartment for all types of use.
- PEC/PNEC ratios < 1 for STP for all types of use.
- PEC/PNEC ratios < 1 for the terrestrial compartment only for use in additives for textile exhaust process. For all other types of use, PEC/PNEC ratios > 1 for the terrestrial compartment.
- With regard to predicted PHMB concentrations in groundwater, these do not exceed the 0.1 µg/L limit set by the EU Groundwater Directive for all type of uses.

In conclusion, the uses of VANTOCIL TG as PT6.4 according to scenarios of PHMB releases are cause for concern in relation to the contamination of the aquatic compartment (including sediment) for all types of use, and for contamination of terrestrial compartment for all types of use, except for use in additives for textile exhaust process. The uses of VANTOCIL TG as PT6.4 according to scenarios of PHMB releases are cause for no concern in relation for contamination of groundwater for all types of use.

As a consequence, the uses of products preserved by PHMB as PT6.4 are cause for concern in relation to the contamination of the environment according to the scenario of releases of PHMB through a consumption approach.

2.2.2.7.4 PHMB as preservative in leather additives (PT6.5)

The use phase of PHMB as preservative in leather additives (PT6.5) has been evaluated for the different types of skin in the sequence of the process steps. Afterwards, emissions have been cumulated for the risk assessment, considering the whole leather production process (Table 2.2-35).

Table 2.2-35. Risk assessment for the use of PHMB as preservative in leather additives

Compartment / PEC/PNEC*	STP	Surface water	Sediment	Soil	Groundwater, $\mu g.L^{-1}$*
Tonnage approach					
Formulation	Not determined in absence of specific tonnage value				
In-use					
Consumption approach					
Raw hide treatment	1.42E-03	**1.62**	**16.18**	0.90	< 0.1
Pelt treatment	5.06E-04	0.58	**5.78**	0.32	< 0.1
Shaved treatment	3.11E-03	**3.55**	**35.50**	**1.97**	< 0.1
Crust leather treatment	6.75E-05	0.08	0.77	0.04	< 0.1
Whole leather production process					
Market share: 1	5.10E-03	**5.82**	**58.22**	**3.23**	< 0.1
Market share: 0.5	2.55E-03	**2.91**	**29.11**	**1.61**	< 0.1

* According to groundwater concentrations modelized by FOCUS PEARL 4.4.4 and compared to the maximum permissible concentration set for drinking water by the Directive 98/83/EC of 0.1 µg/L

As shown in Table 2.2-35, the applied scenarios of PHMB releases for the use of VANTOCIL TG as PT6.5 show:

- PEC/PNEC ratios > 1 for the water column of aquatic environment for all types of use, except uses in additives for the pelt-, and crust leather-treatment.
- PEC/PNEC ratios > 1 for the sediment of freshwater environment for all types of use, except uses in additives for crust leather-treatment.
- PEC/PNEC ratios < 1 for STP for all types of use.
- PEC/PNEC ratios < 1 for the terrestrial compartment for all types of use, except use in additives for shaved treatment; PEC/PNEC ratios > 1 for the

terrestrial compartment for both market shares when all releases are aggregated (*i.e.* releases from a whole tannery). With regard to predicted PHMB concentrations in groundwater, these do not exceed the 0.1 µg/L limit set by the EU Groundwater Directive for all type of uses.

In conclusion, the uses of VANTOCIL TG as PT6.5 according to scenarios of PHMB releases are cause for no concern in relation to the contamination of aquatic (including sediment) and terrestrial compartments, only if PHMB is used in additives for crust leather treatment, corresponding to the skin type at the finishing process.

2.2.2.7.5 Cumulative assessment on the total tonnage value

Table 2.2-36. Risk assessment for the use of PHMB as preservative

Compartment / PEC/PNEC*	STP	Surface water	Sediment	Soil	Groundwater, $\mu g.L^{-1}$*
Tonnage approach					
In-use	<1	<1	**>1**	<1	< 0.1

* According to groundwater concentrations modelized by FOCUS PEARL 4.4.4 and compared to the maximum permissible concentration set for drinking water by the Directive 98/83/EC of 0.1 µg/L.

As shown in Table 2.2-36, unacceptable risks are predicted for the sediment compartment, when a general dispersive scenario is applied to the total provided tonnage.

In conclusion, the dispersive uses of products preserved by PHMB as PT6 is cause for concern in relation to the contamination of the environment according to the scenario of releases of PHMB.

2.2.2.8 Overall conclusion of the environmental risk assessment

Considering that:

- VANTOCIL TG, containing 20% w/w of PHMB, is used as a preservative (PT06) for detergents (PT06.1), pulp and paper treatment additives (PT06.3), textile treatment additives (PT06.4), and leather treatment additives (PT06.5);
- The concentration of VANTOCIL TG is in order to obtain a concentration in water-based products to be preserved before use of 0.04% w/w of PHMB for detergents, and 0.02% w/w of PHMB for pulp and paper-, textile- and leather-additives;
- VANTOCIL TG used as PT06 will ultimately be discharged to drain and will enter a municipal sewage treatment plant (STP);
- In accordance with the realistic case scenarios, based on a consumption approach:

- The risk assessment for the preservations of detergents (PT06.1) is considered **unacceptable** for the aquatic compartment (including sediment) both for professional and amateur uses;
- The risk assessment for the preservation of pulp and paper treatment additives (PT06.3) is considered **unacceptable** for the aquatic compartment (including sediment);
- The risk assessment for the preservation of textile treatment additives (PT06.4) is considered **unacceptable** for the aquatic compartment (including sediment) for all types of use, and for the terrestrial compartment except for the use in additives for textile exhaust process;
- The risk assessment for leather processing fluids (PT06.5) is considered **acceptable** for the aquatic compartment (including sediment) and for terrestrial compartment only if PHMB is used in additives for crust leather treatment, corresponding to the skin type at the finishing process.

In accordance with the scenarios based on tonnage approach, the risk assessment (*c.f.* confidential document II-C) leads to:

- Unacceptable risks for the sediment compartment for detergent preservation (PT06.1) for the formulation phase, the professional use and the total use (professional and amateur) of detergents.
- Unacceptable risks for the sediment compartment when a wide dispersive use scenario is applied considering the global tonnage for PHMB used as PT06.

In conclusion, the uses of PHMB as PT06, according to the use scenarios for in-can preservation of detergents (PT06.1), pulp and paper treatment additives (PT06.3), textile treatment additives (PT06.4) are cause for concern for the environment; the use scenarios for in-can preservation for leather treatment additives (PT06.5), are cause for no concern for the environment only if PHMB is used in additives for crust leather treatment, corresponding to the skin type at the finishing process.

The wide dispersive tonnage approach based on the total tonnage used for PT06 leads to unacceptable risks for the sediment.

2.3 OVERALL CONCLUSIONS OF THE RISK ASSESSMENT

The outcome of the assessment for PHMB (1600; 1.8) in product-type 6, presented in the Table below, is specified in the BPC opinion following discussions at the 11th meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA web-site.

Substitution/exclusion criteria:

There is no evidence of endocrine effects of PHMB. The substance cannot be considered as carcinogenic, mutagenic and toxic for the reproduction (CMR). PHMB is considered as Toxic for the environment, and very Persistent (vP, T of PBT) and is therefore candidate for substitution.

Scenario	Human Health		Environment					
	Primary exposure	Secondary exposure (pro/non-pro)	STP	Aquatic compartment	Terrestrial compartment	Groundwater	Air	Secondary poisoning
Preservatives for liquid detergents – Bacteria: 0.04% w/w a.s. to 0.08% w/w a.s.								
Formulation by professionals	Acceptable (1)	NR	Acceptable (2)	**Unacceptable (2)**	Acceptable (2)	Acceptable (2)	NR	NR
Uses by professionals	**Laundry washing, dishwashing and spot-treatment of clothes:** Acceptable	Acceptable	Acceptable (2),(3)	**Unacceptable (2),(3)**	Acceptable (2),(3)	Acceptable (2),(3)	NR	NR
Uses by non-professionals	**Laundry washing, dishwashing, spot-treatment of clothes:** Acceptable	Acceptable	Acceptable (2),(3)	**Unacceptable (2),(3)**	Acceptable (2),(3)	Acceptable (2),(3)		
Preservatives for pulp and paper additives – Bacteria: 0.02% w/w a.s. to 0.06% w/w a.s.								
Formulation by	Acceptable (1)	NR	ND	ND	ND	ND	NR	NR

professionals								
Uses by professionals	Acceptable	Acceptable	Acceptable (3)	**Unacceptable (3)**	Acceptable (3)	Acceptable (3)	NR	NR
Preservatives for textile additives – Bacteria: 0.02% w/w a.s. to 0.06% w/w a.s.								
Formulation by professionals	Acceptable (1)	NR	ND	ND	ND	ND	NR	NR
Uses by professionals	Acceptable	ND	Acceptable (3)	**Unacceptable (3)**	Acceptable (3), (4)	Acceptable (3)	NR	NR
Preservatives for leather additives – Bacteria: 0.02% w/w a.s. to 0.06% w/w a.s.								
Formulation by professionals	Acceptable (1)	NR	ND	ND	ND	ND	NR	NR
Uses by professionals	Acceptable	**Unacceptable**	Acceptable (3)	Acceptable (3),(5)	Acceptable (3),(5)	Acceptable (3)	NR	NR
Dispersive uses of products preserved by PHMB as PT6 (*i.e.* cumulative assessment on the total tonnage value)	NR	NR	Acceptable (2)	**Unacceptable (2)**	Acceptable (2)	Acceptable (2)	NR	NR

NR: Not Relevant
ND: Not Determined (in absence of scenario or specific tonnage value provided by the applicant)

Conditions:

(1) With gloves and coverall during mixing and loading.
(2) Based on tonnage approach.
(3) Based on consumption approach.
(4) Only for uses in textile exhaust process.
(5) Only if used in crust leather, corresponding to the skin type at the finishing process.

3 APPENDICES

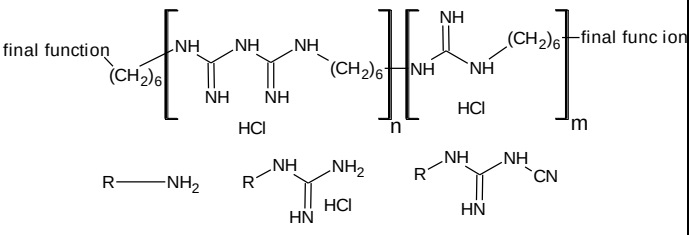
APPENDIX I: LIST OF ENDPOINTS

Chapter 1: Identity, Physical and Chemical Properties, Details of Uses, Further Information, and Proposed Classification and Labelling

Active substance (ISO Common Name)	PHMB (1600; 1.8) i.e. polyhexamethylene biguanide with a mean number-average molecular weight (Mn) of 1600 and a mean polydispersity (PDI) of 1.8Polyhexamethylene biguanide (PHMB)
Function (e.g. fungicide)	Bactericide.
Rapporteur Member State	France

Identity (Annex IIA, point II.)

Chemical name (IUPAC)	CoPoly(bisiminoimidocarbonyl,hexamethylene hydrochloride),(iminoimidocarbonyl, hexame-thylène hydrochloride) or Co poly(5-imino-7-imino-4,6,8-triazaundecamethylene hydrochloride) (5-imino-4,6-diazanonamethylenehydrochloride)
Chemical name (CA)	• Guanidine, N,N''-1,6-hexanediylbis[N'-cyano-, polymer with 1,6-hexanediamine, hydrochloride • N,N''-1,6-Hexanediylbis(N'-cyanoguanidine) polymer with 1,6-hexanediamine, hydrochloride • Poly(iminocarbonimidoyliminocarbonimidoylimino-1,6-hexanediyl
CAS No	27083-27-8
EC No	Not Applicable: the substance is a polymer.
Other substance No.	Not relevant.
Minimum purity of the active substance as manufactured (g/kg or g/l)	The active substance as manufactured (TK) is a 20 % w/w aqueous solution of PHMB plus impurities (total solid) PHMB in dried material ≥ 95.6%
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	HMD ≤ 4.3 g/kg
Molecular formula	Terminal function- $(CH_2)_6$- $[C_8H_{18}N_5Cl]_n$ $[C_7H_{16}N_3Cl]_m$ - terminal function Possible terminal functions:

	NH_2 (amine) $C_2H_3N_4$ (cyanoguanide) CH_5N_3Cl (guanidine) range / average m+n: 2-40 / 11 n /(m+n) [biguanide %]: 90.8 - 91.9% / 91.3 % m /(m+n) [guanide %]: 8.1 - 9.2 % / 8.6 % Terminal function: amino: 35% - 46% / 39% guanidine: 22% - 29% / 25% cyanoguanide: 31 - 39% / 35%
Molecular mass	Number average molecular weight (Mn) = 1610 Mass average molecular weight (Mw)= 2986.
Structural formula	

Physical and chemical properties (Annex IIA, point III)

Melting point (state purity)	Glass transition temperature = 90.2-91°C
Boiling point (state purity)	TK : 100.2°C TC: Decomposition before boiling
Temperature of decomposition	205 to 210°C
Appearance (state purity)	TK : Very pale yellow, Mobile liquid, odourless TC Dusty white solid
Relative density (state purity)	TK : 1.04 at 20°C TC : 1.20 at 20°C
Surface tension	The active substance is not expected to be surface active based on structural consideration.
Vapour pressure (in Pa, state temperature)	dried PHMB is considered as not volatile
Henry's law constant (Pa m^3 mol^{-1})	Henry's law is not applicable for PHMB. PHMB has only slight possibility to pass from water to air.
Solubility in water (g/l or mg/l, state temperature)	426 g/L at 25°C (41% w/w)
Solubility in organic solvents (in g/l or mg/l, state temperature)	Methanol: 41% w/w at 25°C

(Annex IIIA, point III.1)	Ethanol: 4.99 g/L (0.5% w/w) Acetone: 2.7 x10-3 g/L Dichloromethane: 2.0 x10-4 g/L Toluene: 2.0 x 10-4 g/L Ethyl acetate: 1.0 x10-4 g/L n-Hexane: 1.0 x10-4 g/L Acetonitrile: 8.0 x10-4 g/L
Stability in organic solvents used in biocidal products including relevant breakdown products (IIIA, point III.2)	No organic solvent in BP.
Partition coefficient (log P_{OW}) (state temperature)	Log Pow = -2.3 at 25ºC ; pH 7.4
Hydrolytic stability (DT_{50}) (state pH and temperature) (point VII.7.6.2.1)	Not calculated: insignificant hydrolysis (<10%) at all pHs after 5 days at 50°C.
Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG)	1.2 ± 0.5 x 10^{-1} g equiv/L at 25°C
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Spectrum wavelength maximum: - Distilled water: 236 nm - 0.1M aqueous HCl: 205 nm - 0.1M aqueous NaOH: 234nm
Photostability (DT_{50}) (aqueous, sunlight, state pH) (point VII.7.6.2.2)	Not calculated: Under artificial and natural sunlight, PHMB was not photodegraded in laboratory grade water.
Quantum yield of direct photo-transformation in water at S > 290 nm (point VII.7.6.2.2)	Not relevant. See above.
Flammability	TC: Not Flammable. TC: No ignition below 400°C
Explosive properties	Not Explosive.

Classification and proposed labelling (Annex IIA, point IX.)

with regard to physical/chemical data	**Harmonised classification (TC)**: None **Proposed classification of PHMB 20 % in water (TK) and VANTOCIL TG**: None
with regard to toxicological data	**Harmonised classification (TC):** Acute Tox 4; H302: Harmful if swallowed. Skin Sens. 1B; H317: May cause an allergic skin reaction. Eye Dam. 1; H318: Causes serious eye damage. Carc. 2; H351: Suspected of causing cancer. STOT RE 1; H372 (respiratory tract) (Inhalation): Causes damage to organs through prolonged or repeated exposure by inhalation.

	Proposed classification of PHMB 20 % in water (TK) and VANTOCIL TG: Acute Tox 4; H332: Harmful if inhaled. Skin Sens. 1B; H317: May cause an allergic skin reaction. Carc. 2; H351: Suspected of causing cancer. STOT RE 1; H372 (respiratory tract) (Inhalation): Causes damage to organs through prolonged or repeated exposure by inhalation.
with regard to fate and behaviour data	**Harmonised classification (TC):** None **Proposed classification of PHMB 20 % in water (TK) and VANTOCIL TG:** None
with regard to ecotoxicological data	**Harmonised classification (TC):** Aquatic Acute 1; H400 (M-factor = 10): Very toxic to aquatic life. Aquatic Chronic 1; H410 (M-factor = 10): Very toxic to aquatic life with long lasting effects. **Proposed classification of PHMB 20 % in water (TK) and VANTOCIL TG**: Aquatic Acute 1; H400: Very toxic to aquatic life. Aquatic Chronic 1; H410: Very toxic to aquatic life with long lasting effects.

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method) (Annex IIA, point 4.1)	Gravimetric Analysis: An aliquot of the test substance of known weight is determined gravimetrically after freeze drying until it reaches a constant weight.
Impurities in technical active substance (principle of method) (Annex IIA, point 4.1)	Inorganic salts monitored by determining % w/w sulphated ash. Residual starting materials monitored by gas chromatography with flame ionisation detection and HPLC with UV detection. Impurities/related substances, monitored by using size exclusion chromatography (SEC) with UV detection. Water monitored using Karl Fischer titration.

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	Not technically feasible for an enforcement method
Air (principle of method and LOQ) (Annex IIA, point 4.2)	Occurrence of PHMB in air is not probable. No method required
Surface water water (principle of method and LOQ) (Annex IIA,	Not technically feasible for an enforcement method

point 4.2)	
Drinking water (principle of method and LOQ) (Annex IIA, point 4.2)	Method required
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	Method required
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Method not available Methods will be required when MRLs will be set
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals (Annex IIA, VI.6.2)

Rate and extent of oral absorption:	4% = closest estimate (oral absorption of PHMB ranges approximately from 0.3 to 8%).
Rate and extent of dermal absorption:	4% corresponding to oral absorption, based on default value proposed in the EFSA guidance on dermal absorption.
Distribution:	Uniformly distributed. Target organs: liver and kidneys
Potential for accumulation:	No evidence for bioaccumulation.
Rate and extent of excretion:	Most excreted (>90%) in the faeces.
Toxicologically significant metabolite	-

Acute toxicity (Annex IIA, VI.6.1)

Rat LD_{50} oral	The oral LD_{50} of the 20 % aqueous solution is from 2.5 g (Vantocil P)/kg to > 5g /kg of PHMB 20 % w/w in rat
Rat LD_{50} dermal	The dermal LD_{50} of the 20 % aqueous solution is > 2000 mg/kg of PHMB 20 % w/w in rabbit.
Rat LC_{50} inhalation	No available acute data. Based on RAC opinion: Xn; R20 is warranted.
Skin irritation	Slight to moderate irritant on rabbit. Slight irritant to human skin. But does not meet the criteria for classification.
Eye irritation	20% PHMB in aqueous solution is a moderate irritant but does not meet the criteria for classification

Skin sensitization (test method used and result)	Moderate to strong potency sensitizer based on animal data. Human studies indicate that PHMB is a skin sensitizer in humans, although with a rare frequency of sensitisation in the current conditions of consumer uses. It meets the classification criteria for an R43, may cause sensitisation by skin contact or Skin Sens. 1B H317 because of low incidences from human data.

Repeated dose toxicity (Annex IIA, VI. 6.3, 6.4, and 6.5)

Species/ target / critical effect	Rat/liver and kidney/slight effects to parameters of clinical chemistry, decrease in weight gain, minor histopathological change to the liver and kidneys. Acute, mid and long-term exposure: NOAEL = 13 mg/kg/d (Rat - developmental study)
Lowest relevant inhalation NOAEC	Acute, mid and long-term exposure: Rat – 28 day exposure – 0.024 mg/m^3

Genotoxicity (Annex IIA, VI.6.6)	Not genotoxic *in vitro* or *in vivo.*

Carcinogenicity (Annex IIA, VI.6.7)

Species/type of tumour	PHMB increases the incidence of benign and malign vascular tumours in female rats by oral route and in male and female mice by oral and dermal route. The tumours are induced mainly in the liver, which is one of the target organ of PHMB and the increase is clearly seen at doses above the MTD. However, it is also observed more equivocally at doses below MTD (mouse oral study at mid-dose and rat oral study at high dose). These increases are not considered incidental when considering the clear induction of vascular tumours at higher doses and they are considered biologically significant and attributed to treatment. A classification as carcinogenic category 3; R40 is warranted.
lowest dose with tumours	Rat – via diet - NOAEL for carcinogenicity can be established at 36 mg/kg bw/d in males and 45 mg/kg bw/d in females.

Reproductive toxicity (Annex IIA, VI.6.8)

Species/ Reproduction target / critical effect	Rat – lower bodyweights in F0 and F1 animals during the premating period.
Lowest relevant reproductive NOAEL	F0 – 600 ppm (70 – 77 mg/kg bw/d) F1 – 600 ppm (70 – 77 mg/kg bw/d) F2 – 2000 ppm (239 - 258 mg/kg bw/d)
Species/Developmental target / critical	Rabbit – no developmental effects related to

effect	treatment. Rat – increase in extra ribs at maternal toxic doses.
Lowest relevant developmental NOAEL	Rabbit: Parental: 20 mg/kg/d Developmental: 20 mg/kg/d Rat: Parental: 13 mg/kg/d Developmental: 54 mg/kg/d

Neurotoxicity (Annex IIIA, VI.1)

Species/ target/critical effect	Not applicable since no specific studies have been conducted for this endpoint.
Lowest relevant neurotoxicity NOAEL	N/A

Other toxicological studies (Annex IIIA, VI/XI)

Neurotoxicity	See section on neurotoxicity.
Toxic effects on livestock and pets	Not relevant, low exposure.
Studies related to the exposure of the a.s. to humans	Studies related to human exposure of the a. s. are not required on the basis of the results of the human health exposure and risk assessments.
Food and feeding stuffs	Expected contact with food/feed. Exposure estimates based on "worst" case and cumulative assumptions with dishwashing, surface cleaning and packaging scenarios, regarding magnitude of residues, transfer to food and consumption do not indicate a concern for human health
Other tests related to exposure of the a.s. to human considered to be necessary	Further studies are not necessary for the purpose of a comprehensive evaluation of the a. s.
Tests to assess toxic effects from metabolites of treated plants	Not relevant because PHMB-based products are not used on plants.
Mechanistic studies	No studies are available with data to define the mechanism of action for the toxicity.
Further human health related studies	Not required.

Medical data (Annex IIA, VI.6.9)

Medical surveillance data on manufacturing plant personnel	No evidence of adverse effects on workers of manufacturing plants.
Direct observations, e.g. clinical cases, poisoning incidents	No data available.
Health records, both from industry and any other sources	From the data available, no evidence of adverse health effects of PHMB.
Epidemiological studies on the general	No data available.

population	
Diagnosis of poisoning including specific signs of poisoning and clinical tests	***Skin*:** Exposure may cause redness and swelling. ***Eye:*** ***20% PHMB in aqueous solution:*** Exposure may cause eye irritation –redness and swelling. ***Inhalation*:** irritation of the respiratory tract may occur. Exposure may cause coughing. ***Ingestion*:** may cause irritation of the gastrointestinal tract with nausea vomiting or diarrhoea.
Sensitization/allergenicity observations	PHMB is a skin sensitizer in humans, although with a rare frequency of sensitisation in the current conditions of consumer uses.
Specific treatment in case of an accident or poisoning: first aid measures and medical treatment	***Skin*:** Remove contaminated clothing. Wash immediately with water followed by soap and water. Obtain medical attention. Patient may experience an eczematous rash to compound should they have been sensitized by prior exposure. This rash would be expected to respond to removal from exposure and treatment with cortico-steroids. Contaminated clothing should be laundered before re-issue. ***Eye*:** ***20% PHMB in aqueous solution:*** Irrigate with eyewash solution or clean water, holding the eyelids apart, for at least 15 minutes. Obtain medical attention as a precaution. ***Inhalation*:** Remove patient from exposure. Obtain medical attention if ill effects occur. ***Ingestion*:** Provided the patient is conscious, wash out mouth with water and give 200-300 ml (half a pint) of water to drink. Do not induce vomiting. Obtain medical attention.
Prognosis following poisoning	The prognosis is excellent if First Aid is administered promptly. Skin: Prompt cleansing should minimize irritation to the skin. Patient may be experience sensitization to compound should future exposure occur. Eye: Prompt irrigation should minimize irritation of the eye. Inhalation: Prompt removal from exposure should minimize irritation to the respiratory tract. Ingestion: Prompt treatment should minimize irritation of the gastrointestinal tract.

Summary (Annex IIA, VI.6.10)

Systemic effects		
	AEL	**MOE_{ref}**
acute, medium and long-term	5.2 µg a.s./kg bw/d	100
	ADI - ARfD	**MOE_{ref}**
Chronic and acute	0.13 mg a.s./kg bw/d	100
Local effects by inhalation		
	AEC	**MOE_{ref}**
acute	0.96 µg/m^3	25
medium-term	0.32 µg/m^3	75
long-term	0.16 µg/m^3	150

Acceptable exposure scenarios (including method of calculation)

Professional users	**Formulation of product to be preserved** (detergent and polymer emulsion): The risk is considered to be acceptable for professionals with gloves and coverall. **Preservatives for polymer emulsion used in paper/textile leather production:** The risk is considered to be acceptable without PPE. **Preservatives for detergents:** Liquid detergent (wash laundry, pre-treatment of clothes and dishwashing): the risk is considered to be acceptable without PPE. Acceptable risk for the systemic and dermal effects has been identified for professionals wiping surface without gloves and coverall.
Non-professional users	**Preservatives for detergents:** Liquid detergent (wash laundry, pre-treatment of clothes and dishwashing): the risk is considered to be acceptable without PPE. **Household uses (wiping surface):** The risk is considered to be acceptable without PPE.
Indirect exposure as a result of use	**Paper:** The dermal contact with dry paper is considered to be acceptable for professionals and general public. It is considered as highly unrealistic that an unacceptable risk occurred concerning paper ingestion by infants and children.

	Leather textile: Acceptable risk has been identified for the indirect exposure during contact with processed leather for professionals wearing gloves and impermeable coverall. The risk is considered to be unacceptable for general public wearing treated leather/textile with emulsion polymer containing PHMB. It should be noted that this reversed scenario is worst case due to uncertainties on transfer factors from process liquid to leather then from leather to skin and the currently available data do not allow refinement. The refinement should be done at the product step. **Liquid detergent:** Dermal exposure from washing dish: The situation where a person rubbes 3.27 x 10^{+3} m^2 /d of utensils daily is unrealistic. Therefore, the risk for direct contact with residues on utensils is considered to be acceptable. Dermal exposure from wearing clothes : Acceptable risk has been identified for the adults and children in contact with textile cleaned with liquid detergent **Household:** Acceptable risk has been identified for the indirect local exposure of an infant crawling on a surface cleaned with preserved product **Food and feeding stuffs** Expected contact with food/feed. Exposure estimates based on "worst" case and cumulative assumptions with dishwashing, surface cleaning and packaging scenarios, regarding magnitude of residues, transfer to food and consumption do not indicate a concern for human health. Concerning the secondary and cumulative exposure via ingestion of food placed on vessels, surfaces and wrapping material previously contaminated by a product containing PHMB as PT06, without considering any rinsing step, the fraction of ADI or ARfD is below 100% for adult and child. The risk for the consumer following transfer into the food of products containing PHMB as PT06 is considered acceptable.

[1)] Technical Notes for Guidance – Human Exposure to Biocidal Products – Guidance on Exposure Estimation (June 2002)

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water (Annex point IIA, VII.7.6; Annex point IIIA, XII.2.1, 2.2)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH	50°C, pH 4, 7 and 9: hydrolytically stable

and temperature)	(<10% hydrolysis seen after 5 days). No metabolites identified.
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	PHMB absorption spectra maximum was not found in visible wavelength. PHMB is considered as not photodegradable
Readily biodegradable (yes/no)	No.
Inherent biodegradability	No.
Biodegradation in seawater	Up to 10.1% mineralisation after 56 days.
Anaerobic water/sediment study: DT_{50} total systems (nonsterile) DT_{90} total systems (nonsterile)	No $DT_{50\ total\ system}$ determined
Non-extractable residues	According to a water/sediment degradation study on PHMB, > 90% of non-extractable residues in sediment after 101 days.
Distribution in water / sediment systems (active substance)	According to a water/sediment degradation study on PHMB: - Water = 0.3% after 101 days (DT_{50} for removal from the water phase are 1 to 2.3 days); - Sediment > 90% after 101 days; - Mineralisation <3% after 101 days.
Distribution in water / sediment systems (metabolites)	**It was not possible to investigate the identity of degradation products due to the sorptive nature of PHMB.**

Route and rate of degradation in soil (Annex point IIIA, VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

Mineralisation (aerobic)	Less than 5% mineralisation after 123 days.
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50}lab (25ºC, aerobic)- not calculated as <5% mineralisation observed.
Field studies (state location, range or median with number of measurements)	No direct soil exposure expected. Therefore, there is no requirement for terrestrial testing and submission of a field soil dissipation and accumulation study is not required.
Anaerobic degradation	Further studies not required as exposure to anaerobic conditions is not likely where the active substance is to be used.
Soil photolysis	Not required because the degradation of

	PHMB in soil is primarily microbially mediated.
Non-extractable residues	According to a soil degradation study on PHMB, > 90% of non-extractable residues in soil after 123 days.
Relevant metabolites - name and/or code, % of applied a.s. (range and maximum)	It was not possible to investigate the identity of degradation products due to the sorptive nature of PHMB.
Soil accumulation and plateau concentration	Not required. According to the TNsG this study is required only where the biocide is directly applied or emitted to soil. From the Risk assessment at Doc IIB, Chapter 3 and Doc IIC Chapter 2, there is no direct soil exposure.

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	Kd (adsorption distribution coefficient): 3172-7614 L/kg (arithmetic mean value of 6177 L/kg) Kom: 88032-244036 L/kg (arithmetic mean value of 160344 L/kg) Koc: 151415-428713 L/kg (arithmetic mean value of 276670 L/kg) Adsorption is independent of pH.
K_{OC}	276670 L/kg (log K_{OC} = 5.44)

Fate and behaviour in air (Annex point IIIA, VII.3, VII.5)

Direct photolysis in air	Not required.
Quantum yield of direct photolysis	Not determined.
Photo-oxidative degradation in air	DT_{50} 1.351 – 6.37 hours (24H day, 5 x 10^5 OH/cm^3) derived by the Atkinson method of calculation.
Volatilisation	PHMB is not volatile.

Monitoring data, if available (Annex VI, para. 44)

Soil (indicate location and type of study)	No monitoring data has been reported.
Surface water (indicate location and type of study)	No monitoring data has been reported.
Ground water (indicate location and type of study)	No monitoring data has been reported.
Air (indicate location and type of study)	No monitoring data has been reported.

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group) for PHMB
(Annex IIA, VII. 7.1 - 7.4, Annex IIIA, XII. 2.2 and XII 2.4)

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss	96 h (flow through system)	Mortality	LC_{50}: 26 µg PHMB.l^{-1} (mc) NOEC: 9.8 µg PHMB.l^{-1} (mc)
Oncorhynchus mykiss	28 days (flow through system)	Growth	NOEC = 10 µg PHMB.l^{-1} (mc)
Invertebrates			
Daphnia magna	21 days (semi static system)	Growth and reproduction	NOEC: 8.4 µg PHMB.l^{-1} (mc)
Algae			
Selenastrum capricornutum	72 h (static system)	Rate	ErC_{50} = 15 µg.l^{-1} (mc) NOEC = 7.43 µg.l^{-1} (mc)
Microorganisms			
Activated sludge	4 h	Nitrification inhibition	NOEC: 12 mg PHMB.l^{-1} (mc)
Active anaerobic sludge	48 h	Inhibition of CO_2 and CH_4 production	NOEC: 20 mg PHMB.g^{-1} MLTS (mc)

(mc: measured concentration)

Effects on earthworms or other soil non-target organisms
(Annex IIIA, XIII.3.2)

Acute toxicity to earthworm (Annex IIIA, point XIII.3.2)	Mortality after a 14-days exposure: LC_{50}: > 882 mg PHMB.kg^{-1} wet weight soil NOEC = 882 mg PHMB.kg^{-1} wet weight soil After standardization at 3.4% of organic matter: LC_{50_std}: > 358.2 mg PHMB.kg^{-1} wet weight soil $NOEC_{std}$ = 358.2 mg PHMB.kg^{-1} wet weight soil
Reproductive toxicity to other soil non-target macro-organisms, long-term test	Not required.

with terrestrial plants (Annex IIIA, point XIII.3.2)	

Effects on soil micro-organisms
(Annex IIA, VII.7.4)

Nitrogen transformation	Inhibition after a 14-days exposure: LC_{50}: > 882 mg PHMB.kg^{-1} wet weight soil NOEC = 882 mg PHMB.kg^{-1} wet weight soil After normalization at 3.4% of organic matter: LC_{50_std}: > 1609.01 mg PHMB.kg^{-1} wet weight soil $NOEC_{std}$ = 1609.01 mg PHMB.kg^{-1} wet weight soil
Carbon mineralisation	Not required

Effects on sediment dwelling organisms
(Annex IIIA, XIII.3.4)

Toxicity to *Chironomus riparius*	Emergence of adult midges over to a 28-day period in spiked sediment: EC_{50} > 196 mg PHMB.kg^{-1} wet weight sediment (measured concentration) NOEC = 196 mg PHMB. kg^{-1} wet weight sediment (measured concentration)

Effects on plants
(Annex IIIA, XIII.3.4)

Toxicity to plants (*Avena sativa, Brassica oleracea, Phaseolus aureus*)	Seedling emergence after a 28-days exposure: EC_{50}: > 1000 mg PHMB.kg^{-1} wet weight soil NOEC: 1000 mg PHMB.kg^{-1} wet weight soil After normalization at 3.4% of organic matter: LC_{50_std}: > 772.73 mg PHMB.kg^{-1} wet weight soil $NOEC_{std}$ = 772.73 mg PHMB.kg^{-1} wet weight soil

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	Data submitted in Doc IIIA, Section 6 (Mammalian Toxicity) adequately describes the toxicity to mammals. Additional data/testing on mammals is not appropriate and would be against the spirit of EU legislation on minimising animal testing.

Acute toxicity to birds (Annex IIIA, point XIII.1.1)	Not required
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	Not required
Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	Not required.

Effects on honeybees (Annex IIIA, point XIII.3.1)

Acute oral toxicity	Not required.
Acute contact toxicity	Not required.

Effects on other beneficial arthropods (Annex IIIA, point XIII.3.1)

Acute oral toxicity	Not required.
Acute contact toxicity	Not required.
Acute toxicity to other beneficial arthropods	Not required.

Bio-concentration (Annex IIA, point 7.5)

Bio-concentration factor (BCF)	$BCF_{aquatic\ organism}$ calculated from log Kow = 0.002; $BCF_{terrestrial\ organism}$ calculated from log Kow = 0.0013; therefore no bioaccumulation expected.
Depuration time (DT_{50}) / (DT_{90})	Not applicable as no bioaccumulation expected.
Level of metabolites (%) in organisms accounting for > 10 % of residues	Not applicable as no bioaccumulation expected.

Chapter 6: Other End Points

Not applicable, no other end points.

APPENDIX II: LIST OF INTENDED USES

LIST OF INTENDED USES FOR WHICH A RISK ASSESSMENT WAS PERFORMED

Object and/or situation	Product name	Organisms controlled	Formulation		Application			Applied amount per treatment	Remarks
			Type	Conc [% PHMB]	Method	Number	Interval		
Preservatives for detergents.	VANTOCIL TG	Bacteria	SL*	20 % w/w	Manual or semi-automated dosing	1	One application. by incorporation at the time of manufacture	0.04% w/v active substance (400 ppm) 0.01 % up to 0.08% w/w a.s. claimed by the applicant	Industrial use only The activity has been demonstrated on a fabric conditioner.
Preservatives for fluids used in paper production, textile and leather production.	VANTOCIL IB	Bacteria	SL*	20 % w/w	Manual or semi-automated dosing	1	One application. by incorporation at the time of manufacture	0.02 % w/v active substance (200 ppm) 0.01 % up to 0.06% w/w a.s. claimed by the applicant	Industrial use only The activity has been demonstrated on a latex emulsion

Note *: SL (Soluble concentrate): A liquid homogenous preparation to be applied as a true solution of the active substance after dilution with water.

LIST OF OTHER INTENTED USES CLAIMED BY THE APPLICANT

Object and/or situation	**Product name**	**Formulation** Conc [% a.s.]	**Application method**	**Claimed applied amount per treatment**	**Remarks**
Detergent (wet wipes liquor*)*	VANTOCIL TG	20%	Manual or semi-automated dosing	0.01 to 0.08 % w/w a.s.	Data which support the efficacy are not sufficient
Timber products preservatives	VANTOCIL TG	20%	Manual or semi-automated dosing	0.05 to 0.10 % w/w a.s.	Data which support the efficacy are not sufficient
Glues and adhesives (polymer emulsions)	VANTOCIL TG	20%	Manual or semi-automated dosing	0.01 to 0.03 % w/w a.s.	Data which support the efficacy are not sufficient
Glues and adhesives (wall paper paste)	VANTOCIL TG	20%	Manual or semi-automated dosing	0.02 to 0.06 % w/w a.s.	Data which support the efficacy are not sufficient

APPENDIX III: LIST OF STANDARD ABBREVIATIONS

List of standard terms and abbreviations (adapted from: (i) Guidelines and criteria for the preparation of PPP dossiers[9]; (ii) TNsG on Data Requirements[10]).

Stand. term / Abbreviation	Explanation
A	ampere
ACh	acetylcholine
AChE	acetylcholinesterase
ADI	acceptable daily intake
ADME	administration distribution metabolism and excretion
ADP	adenosine diphosphate
AE	acid equivalent
AF	assessment factor
AFID	alkali flame-ionisation detector or detection
A/G	albumin/globulin ratio
a.i.	active ingredient
ALT	alanine aminotransferase (SGPT)
Ann.	Annex
AEC	acceptable concentration level
AEL	acceptable exposure level
AMD	automatic multiple development
ANOVA	analysis of variance
AP	alkaline phosphatase
approx	approximate
ARfD	acute reference dose
a.s.	active substance (TC)
AST	aspartate aminotransferase (SGOT)
ASV	air saturation value
ATP	adenosine triphosphate
BAF	bioaccumulation factor
BCF	bioconcentration factor
bfa	body fluid assay
BOD	biological oxygen demand
bp	boiling point
BPD	Biocidal Products Directive
BSAF	biota-sediment accumulation factor
BSP	bromosulfophthalein
Bt	*Bacillus thuringiensis*
Bti	*Bacillus thuringiensis israelensis*
Btk	*Bacillus thuringiensis kurstaki*
Btt	*Bacillus thuringiensis tenebrionis*
BUN	blood urea nitrogen
bw	body weight
c	centi- (x 10^{-2})
°C	degrees Celsius (centigrade)
CA	controlled atmosphere
CAD	computer aided design
CADDY	computer aided dossier and data supply (an electronic dossier interchange and archiving format)
cd	candela
CDA	controlled drop(let) application
cDNA	complementary DANN
CEC	cation exchange capacity
cf	confer, compare to
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CL	confidence limits
cm	centimetre
CNS	central nervous system
COD	chemical oxygen demand
CPK	creatinine phosphatase
cv	coefficient of variation
Cv	ceiling value

[9] 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

[10] European Chemicals Bureau, ECB (1996) Technical Guidance Documents in support of the Commission Directive 93/67/EEC on risk assessment for new notified substances and the Commission Regulation (EC) 1488/94 for existing substances

Stand. term / Abbreviation	Explanation
d	day(s)
DCA	Dichloroacetaldehyde
DDVP	Dimethyl Dichloro Vinyl Phosphate
DIS	draft international standard *(ISO)*
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
dna	designated national authority
DO	dissolved oxygen
DOC	dissolved organic carbon
dpi	days post inoculation
DRP	detailed review paper *(OECD)*
$DT_{50(lab)}$	period required for 50 percent dissipation (under laboratory conditions) (define method of estimation)
$DT_{90(field)}$	period required for 90 percent dissipation (under field conditions) (define method of estimation)
dw	dry weight
ε	decadic molar extinction coefficient
EC_{50}	median effective concentration
ECD	electron capture detector
ED_{50}	median effective dose
EINECS	European inventory of existing commercial substances
ELINCS	European list of notified chemical substances
ELISA	enzyme linked immunosorbent assay
e-mail	electronic mail
EMDI	estimated maximum daily intake
EN	European norm
EPMA	electron probe micro-analysis
ERL	extraneous residue limit
ESPE46/51	evaluation system for pesticides
EUSES	European Union system for the evaluation of substances
F	field
F_0	parental generation
F_1	filial generation, first
F_2	filial generation, second

Stand. term / Abbreviation	Explanation
FBS	full base set
FELS	fish early-life stage
FIA	fluorescence immuno-assay
FID	flame ionisation detector
F_{mol}	fractional equivalent of the metabolite´s molecular weight compared to the active substance
FOB	functional observation battery
f_{oc}	organic carbon factor (compartment dependent)
fp	freezing point
FPD	flame photometric detector
FPLC	fast protein liquid chromatography
g	gram(s)
GC	gas chromatography
GC-EC	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionisation detector
GC-MS	gas chromatography-mass spectrometry
GC-MSD	gas chromatography with mass-selective detection
GEP	good experimental practice
GFP	good field practice
GGT	gamma glutamyl transferase
GI	gastro-intestinal
GIT	gastro-intestinal tract
GL	guideline level
GLC	gas liquid chromatography
GLP	good laboratory practice
GM	geometric mean
GMO	genetically modified organism
GMM	genetically modified micro-organism
GPC	gel-permeation chromatography
GPMT	guinea pig maximisation test
GPS	global positioning system
GSH	glutathione
GV	granulosevirus
h	hour(s)

Stand. term / Abbreviation	Explanation
H	Henry's Law constant (calculated as a unitless value)
ha	hectare(s)
Hb	haemoglobin
HC5	concentration which will be harmless to at least 95 % of the species present with a given level of confidence (usually 95 %)
HCG	human chorionic gonadotropin
Hct	haematocrit
HDT	highest dose tested
hL	hectolitre
HEED	high energy electron diffraction
HID	helium ionisation detector
HPAEC	high performance anion exchange chromatography
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography - mass spectrometry
HPPLC	high pressure planar liquid chromatography
HPTLC	high performance thin layer chromatography
HRGC	high resolution gas chromatography
H_S	Shannon-Weaver index
Ht	haematocrit
HUSS	human and use safety standard
I	indoor
I_{50}	inhibitory dose, 50%
IC_{50}	median immobilisation concentration or median inhibitory concentration 1
ICM	integrated crop management
ID	ionisation detector
IEDI	international estimated daily intake
IGR	insect growth regulator
im	intramuscular
inh	inhalation
INT	2-p-iodophenyl-3-p-nitrophenyl-5-phenyltetrazoliumchloride testing method

Stand. term / Abbreviation	Explanation
ip	intraperitoneal
IPM	integrated pest management
IR	infrared
IRAC	Insecticide resistance action committee
ISBN	international standard book number
ISSN	international standard serial number
IUCLID	International Uniform Chemical Information Database
iv	intravenous
IVF	*in vitro* fertilisation
k *(in combination)*	kilo
k	rate constant for biodegradation
K	Kelvin
Ka	acid dissociation constant
Kb	base dissociation constant
K_{ads}	adsorption constant
K_{des}	apparent desorption coefficient
kg	kilogram
K_H	Henry´s Law constant (in atmosphere per cubic metre per mole)
K_{oc}	organic carbon adsorption coefficient
K_{om}	organic matter adsorption coefficient
K_{ow}	octanol-water partition coefficient
Kp	solid-water partition coefficient
kPa	kilopascal(s)
l, L	litre
LAN	local area network
LASER	light amplification by stimulated emission of radiation
LBC	loosely bound capacity
LC	liquid chromatography
LC-MS	liquid chromatography- mass spectrometry
LC_{50}	lethal concentration, median
LCA	life cycle analysis
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase

Stand. term / Abbreviation	Explanation
ln	natural logarithm
LOAEC	lowest observable adverse effect concentration
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOEC	lowest observable effect concentration
LOEL	lowest observable effect level
log	logarithm to the base 10
LOQ	limit of quantification (determination)
LPLC	low pressure liquid chromatography
LSC	liquid scintillation counting or counter
LSD	least squared denominator multiple range test
LSS	liquid scintillation spectrometry
LT	lethal threshold
m	metre
M	molar
µm	micrometre (micron)
MAC	maximum allowable concentration
MAK	maximum allowable concentration
MC	moisture content
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
MDL	method detection limit
MFO	mixed function oxidase
µg	microgram
mg	milligram
MHC	moisture holding capacity
MIC	minimum inhibitory concentration
min	minute(s)
MKC	minimum killing concentration
mL	millilitre
MLT	median lethal time
MLD	minimum lethal dose
mm	millimetre
MMAD	mass median aerodynamic diameter

Stand. term / Abbreviation	Explanation
mo	month(s)
MOE	margin of exposure
mol	mole(s)
mp	melting point
MRE	maximum residue expected
MRL	maximum residue level or limit
mRNA	messenger ribonucleic acid
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MT	material test
MW	molecular weight
n.a.	not applicable
n-	normal (defining isomeric configuration)
n	number of observations
NAEL	no adverse effect level
nd	not detected
NEDI	national estimated daily intake
NEL	no effect level
NERL	no effect residue level
ng	nanogram
nm	nanometre
NMR	nuclear magnetic resonance
no, n°	number
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEL	no observed effect level
NOIS	notice of intent to suspend
NPD	nitrogen-phosphorus detector or detection
NPV	nuclear polyhedrosis virus
NR	not reported
NTE	neurotoxic target esterase
OC	organic carbon content

Stand. term / Abbreviation	Explanation
OCR	optical character recognition
ODP	ozone-depleting potential
ODS	ozone-depleting substances
OH	hydroxide
OJ	Official Journal
OM	organic matter content
OP	Organophosphate
Pa	pascal
PAD	pulsed amperometric detection
2-PAM	2-pralidoxime
pc	paper chromatography
PC	personal computer
PCV	haematocrit (packed corpuscular volume)
PDI	polydispersity
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PED	plasma-emissions-detector
pH	pH-value
PHED	pesticide handler's exposure data
PIC	prior informed consent
pic	phage inhibitory capacity
PIXE	proton induced X-ray emission
pKa	negative logarithm (to the base 10) of the acid dissociation constant
pKb	negative logarithm (to the base 10) of the base dissociation constant
PND	post natal day
PNEC	predicted no effect concentration (compartment to be added as subscript)
po	by mouth
POP	persistent organic pollutants
ppb	parts per billion (10^{-9})

Stand. term / Abbreviation	Explanation
PPE	personal protective equipment
ppm	parts per million (10^{-6})
PPP	plant protection product
ppq	parts per quadrillion (10^{-24})
ppt	parts per trillion (10^{-12})
PSP	phenolsulfophthalein
PrT	prothrombin time
PRL	practical residue limit
PT	product type
PT(CEN)	project team CEN
PTT	partial thromboplastin time
QA	quality assurance
QAU	quality assurance unit
(Q)SAR	quantitative structure-activity relationship
r	correlation coefficient
r^2	coefficient of determination
RA	risk assessment
RBC	red blood cell
REI	restricted entry interval
RENI	Registry Nomenclature Information System
Rf	retardation factor
RfD	reference dose
RH	relative humidity
RL_{50}	median residual lifetime
RNA	ribonucleic acid
RP	reversed phase
rpm	revolutions per minute
rRNA	ribosomal ribonucleic acid
RRT	relative retention time
RSD	relative standard deviation
RTU	ready-to-use
s	second
S	solubility
SAC	strong adsorption capacity
SAP	serum alkaline phosphatase
SAR	structure/activity relationship

Stand. term / Abbreviation	Explanation
SBLC	shallow bed liquid chromatography
sc	subcutaneous
sce	sister chromatid exchange
SCAS	semi-continous activated sludge
SCTER	smallest chronic toxicity exposure ratio (TER)
SD	standard deviation
se	standard error
SEM	standard error of the mean
SEP	standard evaluation procedure
SF	safety factor
SFC	supercritical fluid chromatography
SFE	supercritical fluid extraction
SIMS	secondary ion mass spectroscopy
S/L	short term to long term ratio
SMEs	small and medium sized enterprises
SOP	standard operating procedures
sp	species (only after a generic name)
SPE	solid phase extraction
SPF	specific pathogen free
spp	subspecies
SSD	sulphur specific detector
SSMS	spark source mass spectrometry
STEL	short term exposure limit
STER	smallest toxicity exposure ratio (TER)
STMR	supervised trials median residue
STP	sewage treatment plant
t	tonne(s) (metric ton)
$t_{½}$	half-life (define method of estimation)
T_3	tri-iodothyroxine
T_4	thyroxine
T_{25}	tumorigenic dose that causes tumours in 25 % of the test animals
TADI	temporary acceptable daily intake
TBC	tightly bound capacity
TC	technical material according to GIFAP monograph n°2 nomentanclature
TCD	thermal conductivity detector

Stand. term / Abbreviation	Explanation
TG	technical guideline, technical group
TGD	Technical guidance document
TID	thermionic detector, alkali flame detector
TDR	time domain reflectrometry
TER	toxicity exposure ratio
TER_I	toxicity exposure ratio for initial exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
tert	tertiary (in a chemical name)
TEP	typical end-use product
TGGE	temperature gradient gel electrophoresis
TIFF	tag image file format
TK	TK: technical concentrate according to GIFAP monograph n°2 nomentanclature
TLC	thin layer chromatography
TIm	median tolerance limit
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TMRC	theoretical maximum residue contribution
TMRL	temporary maximum residue limit
TNsG	technical notes for guidance
TOC	total organic carbon
Tremcard	transport emergency card
tRNA	transfer ribonucleic acid
TSH	thyroid stimulating hormone (thyrotropin)
TTC	2,3,5-triphenylterazoliumchloride testing method
TWA	time weighted average
UDS	unscheduled DNA synthesis
UF	uncertainty factor (safety factor)
ULV	ultra low volume
UR	unit risk
UV	ultraviolet

Stand. term / Abbreviation	Explanation
UVC	unknown or variable composition, complex reaction products
UVCB	undefined or variable composition, complex reaction products in biological material
v/v	volume ratio (volume per volume)
vis	visible
WBC	white blood cell
wk	week
wt	weight
w/v	weight per volume
ww	wet weight
w/w	weight per weight
XRFA	X-ray fluorescence analysis
yr	year
<	less than
≤	less than or equal to
>	greater than
≥	greater than or equal to

APPENDIX IV: SUMMARY OF THE RESULTS OF THE PUBLIC CONSULTATION

Refer to separate document.

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

Evaluation of active substances

List of References - Part A

Polyhexamethylene biguanide
(Mn = 1600; PDI =1.8)

(PHMB)

Applicant: Lonza

Product-types 1, 2, 3, 4, 6, 9, 11

DRAFT FINAL CAR

May 2015

eCA: FRANCE

This document is a list of all the studies submitted by the Applicant to support the PT1, 2, 3, 4, 6, 9, 11 dossiers. Claims of data protection are proposal from the Applicant.

Studies indicated as "Relied on" are validated studies from which endpoints were established. This corresponds to the list of protected studies.

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_2 (PT1, 3, 4, 6, 11 only)	McGeechan P	2008	Evaluation of the Bactericidal Efficacy of Solid PHMB (EN1276:1997) Arch UK Biocides Microbiology Laboratory, Blackley, Manchester, UK Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-2-05	Other	No
A3_3	Sudworth J	2002	DS6222: Physico-Chemical Data- Project 1270585 Analytical Science Group, Blackley, Manchester, UK Project 1270585 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-3-01	KS	Yes (PT1,2.3.6,9.1 1)
A3_3	Field B.P.	1991	VANTOCIL P: Measurement of selected physical/chemical properties Analytical Science Group, Blackley, Manchester, UK Project 0176 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-3-02	KS	Yes (PT1.2.3.6,9.1 1)
A3_3	Blake J	2003	Product Chemistry and Phys/chemical characteristics study for EPA, Grangemouth solid PHMB. (By analysis of chemical structure and not by experimentation) Analytical Science Group, Blackley, Manchester, UK Project 1273537 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-2-03	KS	Yes (PT1.2.3.6.9.1 1)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_3	Macnab J.I	2002	Determination of the vapour pressure of poly(hexamethylene)biguanide Syngenta Technology and Projects Process Hazards Section, Huddersfield, UK PC/274 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-3-03	KS	No
A3_3	Bowhill L.	2007	PHMB: Determination of n-Octanol:Water Partition Coefficient InterTek Analytical Science Group, Blackley, Manchester, UK Study 1304881 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-3-04	KS	Yes (PT1.2.3.6,9.1 1)
A3_3	Gillings E, Brown D and Reynolds L F.	1983	The determination of the Octanol-Water Partition Coefficient of Vantocil IB Brixham Environmental Laboratory, Brixham, UK BLS/B/0207 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-3-05	IUCLID	No
A3_3	Schofield D.J	2007	Vantocil 100: Physical Chemical Testing. InterTek Analytical Science Group, Blackley, Manchester, UK Study 1307428 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-3-06	KS	Yes (PT1.2.3.6,9.1 1)
A3_3	Bannon C	2008	Viscosity of VANTOCIL TG Arch Chemicals Inc., Cheshire, USA 112-07B10PHMB Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-3-07	KS	Yes (PT1.2.3.6,9.1 1)
A3_3	Chang S.	2008	Determination of the vapour pressure of Polyhexamethylene Biguanide (PHMB) Arch Chemicals Inc., Cheshire, USA Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-3-08	KS	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_3	Bannon C	2008	Melting point of Solid PHMB Arch Chemicals Inc., Cheshire, USA 122-08B10PHMB Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-3-09	KS	No
A3_4	Pickup M.	2002	The extraction and detection of poly(hexamethylenebiguanide) from environmental matrices. Analytical Science Group, Blackley, Manchester, UK Pickup M J Unpublished ; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-4-01	KS	No
A3_4	DeMatteo V A	2008	Validation of the method for determining solution strength for VANTOCIL TG Arch Chemicals Inc, Cheshire, USA 119-08B10PHMB Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-4-02	KS	No
A3_4	Ritter, J.C	2008	INTERIM REPORT: Preliminary Method for the Analysis of PHMB in Drinking Water by Electrochemical Detection with Sample Pre concentration Arch Chemicals Inc, Cheshire, USA Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-4-03	Other	No
A3_4	Taylor, D.B	2009	Analysis of PHMB in Water by Linear Sweep Stripping Voltammetry, Method Validation. Arch Chemicals Inc, Cheshire, USA Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-4-04	KS	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
PHMB PT02 B3_5 (PT6 only)	McGeechan P.	2006	Evaluation of the Bacterisostatic and Fungistatic efficacy of VANTOCIL IB. Arch UK Biocides Microbiology Group, Manchester, UK. Report no.004. Not GLP, Unpublished	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I.	PHMB PT02 dossier: ARCH B3-5-04		Yes (PT6)
PT02 IIIB5.10.14	Crane E.	2010	Validation Protocol for Quantitative Suspension Testing for Arch Biocides. MGS Laboratories Ltd., Egham, UK. CVP-2009-014-05 Unpublished, Non-GLP	Arch Chemicals Inc	Yes: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH B3-5-14	KS	Yes (PT2.3.4.9.11)
PT02 IIIB5.10.15	Crane E.	2010	Validation Protocol for Quantitative Suspension Testing for Arch Biocides. MGS Laboratories Ltd., Egham, UK. CVP-2009-014-05 Unpublished, Non-GLP	Arch Chemicals Inc	Yes: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH B3-5-14	KS	Yes (PT2.4.11)
PT02 IIIB5.10.16	Crane E.	2010	Validation Protocol for Quantitative Suspension Testing for Arch Biocides. MGS Laboratories Ltd., Egham, UK. CVP-2009-014-05 Unpublished, Non-GLP	Arch Chemicals Inc	Yes: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH B3-5-14	KS	Yes (PT2,4)
A3_5_02 (B3-5 PT02)	Crane E.	2010	Validation Protocol for Quantitative Suspension Testing for Arch Biocides. MGS Laboratories Ltd., Egham, UK. CVP-2009-014-05 Unpublished, Non-GLP	Arch Chemicals Inc	Yes: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH B3-5-16	KS	Yes (PT3.9)
A3_5	McGeechan P.	2006	PHMB: Mode of Action Arch UK Biocides, Manchester, UK ARCH PHMB 019. Unpublished; not GLP	Arch Chemicals Inc	No	ARCH A3-5-01	Other	Yes (PT1.2.3.11)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_5	Moore L E.	2004	Evaluation of the risks associated with long term use of cationic antimicrobials Univeristy of Manchester, Manchester, UK ARCH PHMB 020. Unpublished; not GLP	Arch Chemicals Inc	No	ARCH A3-5-02	Other	Yes (PT1.2.3.11)
A3_5	Livermoore D.	2001	MICs of Avecia compounds PUBLIC HEALTH LABORATORY SERVICE CENTRAL PUBLIC HEALTH LABORATORY Antibiotic Resistance Monitoring and Reference Laboratory PHLSCentral Public Health Laboratory 61 Colindale Avenue, London NW9 5HT ARCH PHMB 021. Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-03	Other	Yes (PT1.2.3.11)
A3_5	Gilbert P., Moore L.E.	2005	Cationic antiseptics: diversity of action under a common epithet Univeristy of Manchester, Manchester, UK Journal of Applied Microbiology 2005, 99, 703-715 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-04	Other	Yes (PT1.2.3.4.9.11)
A3_5	Moore L.E. *et al.*	2008	In vitro study of the effect of cationic biocides on bacterial population dynamics and susceptibility Univeristy of Manchester, Manchester, UK Applied and Environmental Microbiology 2008 p. 4825-4834 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-05	Other	Yes (PT1.2.3.4.9.11)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_5	Tambe S.M. *et al.*	2001	In vitro evaluation of the risk of developing bacterial resistance to antiseptics and antibiotics used in medical devices Columbia University, New York, USA Journal of Antimicrobial Chemotherapy 2001 47, 589-598 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-06	Other	Yes (PT1.2.3.4.9.11)
A3_5	Turner N.A. *et al.*	2000	Emergence of resistance to biocides during differentiation of *Acanthamoeba castellanii* Cardiff University, Cardiff, UK Journal of Antimicrobial Chemotherapy 2000 46, 27-34 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-07	Other	Yes (PT1.2.3.5.9.11)
A3_5	Gilbert P.	No date given	Polyhexamethylene biguanide and infection control Univeristy of Manchester, Manchester, UK www.kendallamd.com Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-08	Other	Yes (PT1.2.3.4.9.11)
A3_5	Fraud S. *et al.*	2008	MexCD-OprJ Multidrug Efflux System of Pseudomonas aeruginosa: Involvement in Chlorhexidine Resistance and Induction by Membrane-Damaging Agents Dependent upon the AlgU Stress Response Sigma Factor Queen's University, Ontario, Canada Antimicrobial Agents and Chemo, Dec 2008, Vol 52, No. 12, p4478-4482 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-09	Other	Yes (PT1.2.3.4.9.11)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_5	Lakkis C. *et al.*	2001	Resistance of Pseudomonas aeruginosa Isolates to Hydrogel Contact Disinfection Correlates with Cytotoxicity University of Melbourne, Victoria, Australia Journa l of Clinical Microbiology, Apr 2001, Vol 39, No. 4, p1477-1486 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-10	Other	Yes (PT1.2.3.4.9.11)
A3_5	Geraldo I.M. *et al.*	2008	Rapid antibacterial activity of 2 novel hand soaps: evaluation of the risk of development of bacterial resistance to the antibacterial agents University of Melbourne, Victoria, Australia Infect Control Hosp Epidemiol. 2008 Aug; 29 (8): 736-41 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-11	Other	Yes (PT1.2.3.4.9.11)
A3_5	Allen M.J. *et al.*	2006	The response of Escherichia coli to exposure to the biocide polyhexamethylene biguanide Cardiff University, Cardiff, UK Microbiology. 2006 Apr; 152 (Pt4): 989-1000 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-12	Other	Yes (PT1.2.3.4.9.11)
A3_5	Khunkitti W. *et al.*	1998	Biguanide-induced changes in Acanthamoeba castellanii: an electron microscopic study University of Wales Cardiff, Cardiff, UK J Appl Microbiol. 1998 Jan; 84 (1): 53-62 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-13	Other	Yes (PT1.2.3.4.9.11)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_5	Turner N.A. *et al.*	2004	Resistance, biguanide sorption and biguanide-induced pentose leakage during encystment of Acanthamoeba castellanii New York University School of Medicine, New York, USA J Appl Microbiol. 2004; 96 (6): 1287-95 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-14	Other	Yes (PT1.2.3.4.9.1 1)
A3_5	Pérez-Santonja J.J. *et al.*	2003	Persistently culture positive Acanthamoeba keratitis: in vivo resistance and in vitro sensitivity Moorfields Eye Hospital, London, UK Ophthalmology. 2003 Aug; 110 (8): 1593-600 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-15	Other	Yes (PT1.2.3.4.9.1 1)
A3_5	Lloyd D. *et al.*	2001	Encystation in Acanthamoeba castellanii: development of biocide resistance Cardiff University, Cardiff, UK J Eukaryot Microbiol. 2001 Jan-Feb; 48 (1): 11-6 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-16	Other	Yes (PT1.2.3.4.9.1 1)
A3_5	Murdoch D. *et al.*	1998	Acanthamoeba keratitis in New Zealand, including two cases with in vivo resistance to polyhexamethylene biguanide Auckland Hospital, Auckland, New Zealand Aust NZJ Opthalmol. 1998 Aug; 26 (3): 231-6 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-17	Other	Yes (PT1.2.3.4.9.1 1)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_5	Noble J.A. *et al.*	2002	Phagocytosis affects biguanide sensitivity of Acanthamoeba spp. Georgia State University, Atlanta, USA Antimicrobial Agents and Chemotherapy (2002) 46 (7), 2069-2076 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-18	Other	Yes (PT1.2.3.4.9.11)
A3_5	Jones M.V. *et al.*	1989	Resistance of Pseudomonas aeruginosa to amphoteric and quaternary ammonium biocides Unilever Research, Bedford, UK Microbios (1989) 58 (234), 49-61 Published; not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-5-19	Other	Yes (PT1.2.3.4.9.11)
A3_6.1	Anon.	1966	Antibacterial 9073: Toxicological report. Central Toxicological Laboratory, Macclesfield, UK CTL/T/558 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-03	IUCLID	No
A3_6.1	[redacted]	2003	Acute oral toxicity in the rat – up and down procedure. [redacted] Project number: 780/273 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-02	KS	No
A3_6.1	[redacted]	2003	Acute dermal toxicity (limit test) in the rat. [redacted] Project number: 780/274 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-04	KS	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.1	[redacted]	2003	Acute dermal irritation in the rabbit . [redacted] Project number: 780/275 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-10	KS	No
A3_6.1	[redacted]	2003	Acute eye irritation in the rabbit. [redacted] Project number: 780/276 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-12	KS	No
A3_6.1	[redacted]	1993	Polyhexamethylene Biguanide PHMB: Skin sensitisation in the guinea pig of a 20% aqueous solution. [redacted] CTL/P/3889. Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-16	KS	Yes (PT1.2.3.6.9.11)
A3_6.1	Jackson SJ	1979	Vantocil P: Acute Oral and Dermal Toxicity. Central Toxicological Laboratory, Macclesfield, UK CTL/T/1361. Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-01	KS	Yes (PT1.2.3.6.9.11)
A3_6.1	[redacted]	1980	Vantocil P: Skin irritation in the rabbit. [redacted] CTL/T/1409 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-08	KS	Yes (PT1.2.3.6.9.11)
A3_6.1	Jackson SJ	1979	Vantocil P: Skin corrosivity study . Central Toxicological Laboratory, Macclesfield, UK CTL/T/1362 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-09	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.1	[redacted]	1980	Vantocil IB: Skin sensitisation studies in the guinea pig [redacted] CTL/T/1423 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-17	IUCLID	No
A3_6.1	Jackson SJ	1983	Vantocil IB and Chlorhexidine Gluconate: Potential for cross-reactivity in a skin sensitisation study Central Toxicological Laboratory, Macclesfield, UK CTL/T/1953 Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-19	IUCLID	No
A3_6.1	[redacted]	1983	Vantocil IB: The effect of variation in induction concentration on skin sensitisation in the guinea pig. [redacted] CTL/T/1952 Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-18	IUCLID	No
A3_6.1	Kinch D.A.	1969	The irritant properties of Vantocil IB. Central Toxicological Laboratory, Macclesfield, UK HO/IH/T/704A. Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-13	IUCLID	No
A3_6.1	Kinch D.A.	1969	Further Studies on the irritant effects of Vantocil IB. Central Toxicological Laboratory, Macclesfield, UK HO/IH/T/704B. Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-14	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.1	[redacted]	1981	Vantocil IB: Eye irritation to the rabbit. [redacted] CTL/T/1727. Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-11	KS	Yes (PT1.2.3.6.9.11)
A3_6.1	[redacted]	1993	Baquacil 20% PHMB and Sodium Dichloroisocyanurate: Comparative assessment of sensory irritation potential in the mouse. [redacted] CTL/L/5346 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-06	KS	No
A3_6.1	Proteau J.	1979	Baquacil SB: Eye irritation French study. Association Pour L'aide Aux Recherches interessant La Medecine Du Travail D8/11 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-15	IUCLID	No
A3_6.1	Stevens M.A.	1969	Skin toxicity of Polyhexamethylene biguanide (PHB) solution: Vantocil IB: 20% PHB in water (Antibacterial 9073: 25% PHMB in water) Central Toxicological Laboratory, Macclesfield, UK TR 684 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-05	IUCLID	No
A3_6.1	Wnorowski G.	2003	Acute Inhalation Toxicity Feasibility Assessment. Product Safety Laboratories, East Brunswick, New Jersey. OPPTS 870.1300 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-61-07	Other	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.12	Smith I	1981	Human sensitisation testing of VANTOCIL IB. Ian Smith Consultancy. Project Number 0018; CTL/C/1109. Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-612-01	KS	No
A3_6.12	Hink G, Ison A	1989	Photoreaction patch test using natural sunlight. Hill Top Research, Ohio. Report ref. 76-165-72; CTL/C/2163 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-612-02	KS	Yes (PT1.2.3.6.9.11)
A3_6.12	Schnuch A, Geier J, Brasch J etal.	2000	Polyhexamethylene biguanide: A relevant contact allergen? Contact Dermatitis 42:302-3 03 Published; Not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-612-03	IUCLID	No
A3_6.12	Schnuch A, et al	2007	The biocide polyhexamethylene biguanide remains an uncommon contact allergen. Recent multicentre surveillance data. Contact Dermatitis 2007: 56: 235–239 Published; Not GLP	Published	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-612-04	IUCLID	No
A3_6.12	Geimer P	2007	PHMB: Arch Medical Surveillance Programme Statement from Arch Medical Director dated 23 April 2007 UnPublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-612-05	Other	No
A3_6.14	Sueki H	2001	Polyhexamethylene Biguanide, Cosmocil CQ: Skin Irritation Study in Humans. Dept of Biochemical Toxicology Showa University, Japan. Report APJ-1. Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-614-01	KS	Yes (PT1.2.3.6.9.11)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.2	[redacted]	1975	Characterisation of the Urinary Polymer-related Material from Rats given Poly[biguanide-1,5-diylhexamethylene hydrochloride] [redacted] Makromol. Chem. 177, 2591-2605 Published; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-62-02	IUCLID	No
A3_6.2	Clowes HM	1996	PHMB: In Vitro Absorption through Human Epidermis. Central Toxicological Laboratory, Macclesfield, UK CTL/P/5120. Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-62-03	KS	Yes (PT1.2.3.6.9.11)
A3_6.2	Clowes HM	1998	PHMB: In Vitro absorption from a 20% solution through human epidermis at spa temperature. Central Toxicological Laboratory, Macclesfield, UK CTL/P/5916. Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-62-04	KS	Yes (PT1.2.3.6.9.11)
A3_6.2	Clowes HM	1995	PHMB: In Vitro Absorption from a 0.5% solution through bovine teat and udder skin . Central Toxicological Laboratory, Macclesfield, UK CTL/P/5683 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-62-06	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.2	Clowes HM	1997	Development of a method to measure in vitro absorption of chemicals through bovine udder and teat skin. Central Toxicological Laboratory, Macclesfield, UK CTL/L/7823 Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-62-07	Other	No
A3_6.2	Dugard PH, Mawdsley SJ	1982	14C-Polyhexamethylene Biguanide (PHMB): Absorption through human epidermis and rat skin in vitro. Central Toxicological Laboratory, Macclesfield, UK CTL/R/579 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-62-05	IUCLID	Yes (PT1.2.3.6.9.1 1)
A3_6.2	[redacted]	1976	Studies of Vantocil C14 in Rat and Human Skin. [redacted] D8/35 Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-62-08	IUCLID	No
A3_6.2	[redacted]	1976	Whole Body Autoradiography of Mice Treated with Vantocil C14. [redacted] Report No 1976_03_03 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-62-09	IUCLID	No
A3_6.2	[redacted]	1995	Bioavailability following dietary administration in the rat. [redacted] CTL/P/4595 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-62-01	KS	Yes (PT1.2.3.6.9.1 1)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.2	[redacted]	1995	PHMB: Absorption, Distribution, Metabolism and Excretion following Single Oral Dosing (20 mg/kg) in the Rat. [redacted] Report No. CTL/P/4537. Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-62-10	KS	Yes (PT1.2.3.6.9.11)
A3_6.3	Banham PJ, Marsh DJ	1992	Polyhexamethylene Biguanide: Analysis in dosing solutions. Central Toxicological Laboratory, Macclesfield, UK CTL/I/157 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-15	IUCLID	No
A3_6.3	Carney IF	1976	Vantocil IB: Subacute inhalation toxicity. Central Toxicological Laboratory, Macclesfield, UK CTL/T/983 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-06	IUCLID	Yes (PT1.2.3.6.9.11)
A3_6.3	[redacted]	1972	Vantocil IB: Subacute dermal toxicity study in the rabbit. [redacted] CTL/P/22 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-04	IUCLID	No
A3_6.3	[redacted]	1992	PHMB Polyhexamethylene Biguanide: 28 day drinking water study in the mouse. [redacted] CTL/L/4429 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-02	KS	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.3	[redacted]	1992	PHMB: Polyhexamethylene Biguanide: An investigation of its palatability to the mouse in drinking water. [redacted] CTL/L/4843 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-13	IUCLID	No
A3_6.3	[redacted]	1992	PHMB Polyhexamethylene Biguanide: 28 day drinking water study in the rat. [redacted] CTL/L/4428 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-01	KS	No
A3_6.3	[redacted]	1993	PHMB: 21 day dermal toxicity study in the rat. [redacted] CTL/P/4200 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-03	KS	Yes (PT1.2.3.6.9.1 1)
A3_6.3	Marsh D.L.	1993	PHMB: Gravimetric and homogeneity data to support dietary toxicity studies. Central Toxicological Laboratory, Macclesfield, UK CTL/T/2842 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-12	Other	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.3	[redacted]	2006	POLYHEXAMETHYLENE BIGUANIDE: 28 DAY INHALATION STUDY IN RATS WITH RECOVERY [redacted] CTL/MR0219/REGULATORY/REVISION - 001 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-05	KS	Yes (PT1.2.3.6.9.11)
A3_6.3	[redacted]	2006	POLYHEXAMETHYLENE BIGUANIDE: 5 DAY PRELIMINARY INHALATION STUDY IN THE RAT [redacted] MR0218-TEC Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-16	IUCLID	No
A3_6.3	[redacted]	2006	POLYHEXAMETHYLENE BIGUANIDE: 5 DAY PRELIMINARY INHALATION STUDY IN THE RAT. [redacted] MR0220-TEC Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-17	IUCLID	No
A3_6.3	[redacted]	1993	6-Week Dietary Toxicity in the Dog [redacted] CTL/L/5227 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-10	KS	Yes (PT1.2.3.6.9.11)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.3	[redacted]	1992	Polyhexamethylene Biguanide: Maximum tolerated dose study in the dog. [redacted] CTL/L/4870 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-14	IUCLID	No
A3_6.4	[redacted]	1966	Antibacterial 9073: Ninety-day oral toxicity of antibacterial 9073- Albino rats [redacted] CTL/R/199 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-08	IUCLID	No
A3_6.4	[redacted]	1966	Antibacterial 9073: Ninety-day oral toxicity of antibacterial 9073- beagle dogs [redacted] CTL/R/202 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-11	IUCLID	No
A3_6.4	[redacted]	1993	Polyhexamethylene Biguanide PHMB: 90 day oncogenicity sighting study in the mouse. [redacted] CTL/T/2825 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-09	KS	No
A3_6.4	[redacted]	1993	Polyhexamethylene Biguanide PHMB: 90 day oncogenic sighting study in the rat. [redacted] CTL/T/2824. Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-63-07	KS	Yes (PT1.2.3.6.9.1 1)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.5	[redacted]	1977	Baquacil SB: 2-Year Feeding Study in Rats. [redacted] CTL/P/333. Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-65-01	KS	No
A3_6.5	[redacted]	1996	Polyhexamethylene Biguanide: Two Year Feeding Study in Rats. Pathology Working Group Peer Review of Proliferative Vascular Lesions in Male & Female Rats. [redacted] CTL/C/3172. Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-65-03	KS	Yes (PT1.2.3.6.9.11)
A3_6.5	[redacted]	1977	Baquacil SB: Life-Time Feeding Study in the Mouse. [redacted] CTL/P/332. Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-65-06	KS	No
A3_6.5	[redacted]	1996	Polyhexamethylene Biguanide: Two Year Feeding Study in Rats. [redacted] CTL/P/4663. Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-65-02	KS	Yes (PT1.2.3.6.9.11)
A3_6.5	[redacted]	1993	Polyhexamethylene Biguanide: 2 year drinking water study in the rat. TERMINATED early in week 39 [redacted] CTL/T/2830. Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-65-04	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.5	[redacted]	1995	Polyhexamethylene Biguanide: 1 year dietary toxicity study in the dog. [redacted] CTL/P/4488 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-65-07	KS	Yes (PT1.2.3.6.9.11)
A3_6.5	Mosinger M.	1973	Prolonged Oral Intake of Vantocil IB Centre D'Explorations et de Recherches Medicales D3/2 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-65-05	IUCLID	No
A3_6.6	[redacted]	1981	Vantocil P: Mutation assays using P388 mouse lymphoma cells. [redacted] CTL/P/622 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-66-06	KS	No
A3_6.6	Callander R D	1989	Vantocil IB: An evaluation in the Salmonella mutation assay. Central Toxicological Laboratory, Macclesfield, UK CTL/P/2406 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-66-01	KS	Yes (PT1.2.3.6.9.11)
A3_6.6	Hastwell RM & McGregor DB.	1979	Testing for mutagenic activity in Salmonella typhimurium Inveresk Research International, Edinburgh, Scotland. IRI 411156 (CTL/C/1720) Unpublished, Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-66-03	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.6	Howard CA.	1989	Vantocil IB: An evaluation in the in vitro cytogenetic assay in human lymphocytes. Central Toxicological Laboratory, Macclesfield, UK CTL/P/2582 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-66-04	KS	Yes (PT1.2.3.6.9.11)
A3_6.6	[redacted]	1989	Vantocil IB: An evaluation in the mouse micronucleus test. [redacted] CTL/P/2436 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-66-07	KS	Yes (PT1.2.3.6.9.11)
A3_6.6	Richardson CR, Anderson D.	1981	Vantocil P: Cytogenetic study in human lymphocytes in vitro. Central Toxicological Laboratory, Macclesfield, UK CTL/P/613 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-66-05	KS	Yes (PT1.2.3.6.9.11)
A3_6.6	Trueman RW	1980	An examination of 'Vantocil' IB for potential carcinogenicity using two in vitro assays. Central Toxicological Laboratory, Macclesfield, UK CTL/P/492	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-66-02	IUCLID	No
A3_6.6	[redacted]	1989	Vantocil IB: Assessment for the induction of unscheduled DNA synthesis in rat hepatocytes in vivo. [redacted] CTL/P/2603 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-66-08	KS	Yes (PT1.2.3.6.9.11)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.7	[redacted]	2002	Historical control data for occurrence of hemangiosarcoma (angiosarcoma) in C57BL/10J/CD-1 Alpk Mice. Supplemental info for CTL/P/4649. [redacted] AP-1 Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-67-04	Other	No
A3_6.7	[redacted]	2002	Historical control data for occurrence of hemangiosarcoma (angiosarcoma) in Alpk:ApfSD Wistar Rats (re: CTL/P/4663, CTL/C/3172). [redacted] AP-5 Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-67-05	Other	No
A3_6.7	[redacted]	1996	Polyhexamethylene Biguanide: Two Year Feeding Study in Rats. Pathology Working Group Peer Review of Proliferative Vascular Lesions in Male & Female Rats. [redacted] CTL/C/3172 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-65-03	KS	Yes (PT1.2.3.6.9.11)
A3_6.7	[redacted]	1977	Baquacil SB: 80-week skin painting study in the mouse. [redacted] CTL/P/331 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-67-01	KS	Yes (PT1.2.3.6.9.11)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.7	[redacted]	2002	Polyhexamethylene Biguanide (PHMB): Two year Oncogenic Study in Mice. Statistical analysis of the result from the Pathology Working Group peer review of Vascular lesions in male and female mice. Supplemental info for CTL/P/4649. [redacted] AP-7 Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-67-06	Other	No
A3_6.7	[redacted]	1996	Polyhexamethylene Biguanide: Two Year Feeding Study in Rats. [redacted] CTL/P/4663 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-65-02	KS	Yes (PT1.2.3.6.9.11)
A3_6.7	[redacted]	2002	PHMB 2-year oncogenic study in mice. PWG peer review of vascular proliferative lesions in male and female mice. [redacted] EPL Project No 698-001 (= CTL PM0937) Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-67-03	KS	Yes (PT1.2.3.6.9.11)
A3_6.7	[redacted]	1996	Polyhexamethylene Biguanide: Two year Oncogenic Study in Mice. [redacted] CTL/P/4649 Unpublished, GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-67-02	KS	Yes (PT1.2.3.6.9.11)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.7	[redacted]	2008	Studies to Elucidate the Potential Involvement of the Kupffer Cell in PHMB Mouse Liver Hemangiosarcomas [redacted] 15 Dec 2008 Unpublished, not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-67-07	KS	Yes (PT1.2.3.6.9.11)
A3_6.7	Mann P.C, Berry C and Greaves P	2009	Scientific Advisory Panel Review Of Polyhexamethylene Biguanide (Phmb): Carcinogenicity Studies, Pathology Working Groups, Regulatory Responses And Mode-Of-Action Studies Experimental Pathology Laboratories, Inc. P.O. Box 169, Sterling, VA 20167-0169 EPL STUDY NO. 880-001 5 August 2009 Unpublished, not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-67-08	KS	No
A3_6.8	[redacted]	1976	Teratology Evaluation of IL-780 in Rabbits [redacted] FDRL 5022 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-68-04	IUCLID	No
A3_6.8	[redacted]	1992	PHMB: Dose range finding study in the rabbit. [redacted] CTL/l/5052 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-68-03	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.8	[redacted]	1993	Polyhexamethylene Biguanide PHMB: Dose range finding study in the pregnant rabbit. [redacted] CTL/T/2821 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-68-02	KS	No
A3_6.8	[redacted]	1993	PHMB:Developmental toxicity study in the rabbit. [redacted] CTL/P/3997 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-68-01	KS	Yes (PT1.2.3.6.9.11)
A3_6.8	Evans DP	1981	Re-evaluation of skeletal variants incorporating historical data. Central Toxicological Laboratory, Macclesfield, UK re: Report CTL/P/335 ReEvaluation Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-68-08	IUCLID	No
A3_6.8	[redacted]	1981	Baquacil SB : Mouse Teratology Study (CTL/P/335): Historical control data & clarification of start date. [redacted] re: Report CTL/P/335 Historical Control Data Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-68-09	Other	No
A3_6.8	[redacted]	1976	Baquacil SB: A teratology study in the rat by dietary administration. [redacted] CTL/P/262 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-68-05	KS	Yes (PT1.2.3.6.9.11)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_6.8	[redacted]	1977	Baquacil SB: Teratogenicity study in the mouse. [redacted] CTL/P/335 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-68-07	IUCLID	No
A3_6.8	[redacted]	1995	Polyhexamethylene Biguanide: Multigeneration study in the rat. [redacted] CTL/P/4455 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-68-10	KS	Yes (PT1.2.3.6.9.11)
A3_6.8	[redacted]	1977	20% PHMB: Three generation reproduction study in the rat CTL/C/2161 Reformatted for EPA 5 July 1990. [redacted] Report No. NV-5- L57, Project number 458-119. Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-68-11	IUCLID	No
A3_6.8	[redacted]	1988	The Post-natal Fate of Supernumary Ribs in Rat Teratogenicity Studies. [redacted]Tox 8 (2) 91-94. Published; GLP unknown	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-68-06	IUCLID	No
A3_7.1.	Brown D., Dowell D.G.	1975	Vantocil IB and sewage treatment Brixham Environmental Laboratory, Brixham, UK BL/B/1649 Unpublished; NOT GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-10	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.1.	Brown D., Gillings E.	1983	The determination of the partition of Vantocil IB between a river sediment and water Brixham Environmental Laboratory, Brixham, UK BLS/B/0208 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-14	IUCLID	No
A3_7.1.	[redacted]	1980	Vantocil IB: Effect of soil on acute toxicity to rainbow trout. [redacted] BLS/B/0044 Unpublished; not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-19	IUCLID	No
A3_7.1.	Evans K.P., Beaumont G.L., Williams D.G.	1995	PHMB Hydrolysis study for EPA Registration: Project 302, Guideline ref. 161-1 (1995) ASG, Blackley, Manchester, UK Project 302 Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-03	IUCLID	No
A3_7.1.	Gilbert J L	1997	PHMB: Determination of COD Brixham Environmental Laboratory, Brixham, UK BLS 2378 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-01	IUCLID	No
A3_7.1.	Gilbert JL, Long KWJ, Roberts GC	1995	PHMB: Anaerobic biodegradability Brixham Environmental Laboratory, Brixham, UK BL5342/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-12	KS	Yes (PT2.9)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.1.	Gilbert JL, Roberts GC, Woods CB	1993	PHMB: Activated sludge sorption and desorption Brixham Environmental Laboratory, Brixham, UK BL5385/B Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-15	KS	Yes (PT2.9)
A3_7.1.	Habeeb. S.B.	2010	PHMB: Aerobic Transformation in Two Aquatic Sediment Systems ABC Laboratories Inc., Missouri, USA 65393 Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-22		Yes (PT2.9)
A3_7.1.	Jones B.K.	1976	Vantocil IB: microbial degradation studies Central Toxicological Laboratory, Macclesfield, UK CTL/P/289 Unpublished; NOT GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-11	IUCLID	No
A3_7.1.	Leahey J.P., Griggs R.E., Hughes H.E.	1975	Baquacil: Preliminary study of the photodegradation in water. ICI Plant Protection Ltd TMJ 1163B Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-05	KS	Yes (PT2.9)
A3_7.1.	Long K.W.J.	1995	PHMB: Aerobic biodegradation in water (adapted microorganisms). Brixham Environmental Laboratory, Brixham, UK BL1878/B Unpublished; not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-07	IUCLID	No
A3_7.1.	Long K.W.J., Roberts G.C.	1994	PHMB: Aerobic biodegradation in water Brixham Environmental Laboratory, Brixham, UK BL5172/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-06	KS	Yes (PT2.9)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.1.	O'Malley et al	2006	Biodegradability of end-groups of the biocide polyhexamethylene biguanide (PHMB) assessed using model compounds J Ind Microbiol Biotechnol (2006) 33: 677–684 Published; not GLP	Published	NO	ARCH A3-71-17	IUCLID	Yes (PT2.9)
A3_7.1.	O'Malley et al	2007	Microbial degradation of the biocide polyhexamethylene biguanide: isolation and characterization of enrichment consortia and determination of degradation by measurement of stable isotope incorporation into DNA. Journal of Applied Microbiology ISSN 1364-5072 Published; not GLP	Published	NO	ARCH A3-71-18	IUCLID	Yes (PT2.9)
A3_7.1.	Oteyza T	2007	PHMB: Toxicity to the green alga Selenastrum capricornutum in the presence of treated sewage effluent. Brixham Environmental Laboratory, Brixham, UK BLS/3377/B Unpublished; not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-20	IUCLID	No
A3_7.1.	Penwell A.J., Roberts G.C., Daniel M.	2003	PHMB: Biodegradation by the ligninolytic fungus *Phanerochaete chrysosporium* (2003) Brixham Environmental Laboratory, Brixham, UK BL6915/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-13	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.1.	Penwell AJ, MacLean SA, Palmer S, Roberts GC	2005	PHMB: Aerobic sewage treatment simulation and chronic toxicity of treated effluent to Daphnia magna Brixham Environmental Laboratory, Brixham, UK BL7802/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-09	KS	No
A3_7.1.	Penwell AJ, MacLean SA, Roberts GC	2005	PHMB: Biodegradability in sea water Brixham Environmental Laboratory, Brixham, UK BL7804/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-08	KS	Yes (PT2.9)
A3_7.1.	Peurou F., Roberts G.C.	2004	PHMB: Effect of sediment on the acute toxicity to Daphnia magna Brixham Environmental Laboratory, Brixham, UK BL7117/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-16	KS	Yes (PT2.9)
A3_7.1.	Sarff P.	2010	PHMB: Estimation of the Adsorption Coefficient (K_{oc}) on Soil and/or Sewage Sludge Using High Performance Liquid Chromatography (HPLC) ABC Laboratories Inc., Missouri, USA 65395 Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-21		Yes (PT1.2.3.6.9.11)
A3_7.1.	Sudworth J.	2006	PHMB: Hydrolysis as a function of pH InterTek ASG, Blackley, Manchester, UK Project 1302832 Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-02	KS	Yes (PT1.2.3.6.9.11)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.1.	Turner W.R., Ramaswamy H.N.	1979	Baquacil: Hydrolysis/photodegradation study Source: ICI General Analysis Group, Analytical and Physical Chemistry Section Ref: R5 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-71-04	IUCLID	No
A3_7.2	Gilbert JL, Gillings EG, Roberts GC	1995	PHMB: Aerobic biodegradation in soil Brixham Environmental Laboratory, Brixham, UK BL5311/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-72-01	KS	Yes (PT1.2.3.6.9.1 1)
A3_7.2	Habeeb. S.B.	2010	PHMB: Determination of Adsorption – Desorption Using the Batch Equilibrium Method ABC Laboratories Inc., Missouri, USA 65392 Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-72-05		Yes (PT1.2.3.6.9.1 1)
A3_7.2	Habeeb. S.B.	2010	PHMB: Aerobic Transformation in Four Soils ABC Laboratories Inc., Missouri, USA 65394 Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-72-06		Yes (PT1.2.3.6.9.1 1)
A3_7.2	Hill I.R, Willis J.H	1975	BAQUACIL: Preliminary laboratory studies of the degradation of C14-BAQUACIL in soil Jealott's Hill Research Station, Bracknell, Berkshire, UK TMJ 1165 Unpublished; not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-72-03	IUCLID	No
A3_7.2	Jones-Hughes TL, Penwell A J, Roberts GC	2005	PHMB: Biodegradation in sludge amended soil Brixham Environmental Laboratory, Brixham, UK BL7132/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-72-02	KS	Yes (PT1.2.3.6.9.1 1)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.2	Riley D., Stevens J.E.	1975	Baquacil: Adsorption and leaching in soil. ICI Plant Protection. Report AR 2586A Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-72-04	KS	Yes (PT2.9)
A3_7.3	Ritter, J.C	2006	Estimation of Photochemical Degradation of Polyhexamethylene Biguanide (PHMB) Using the Atkinson Calculation Method Central Analytical Department, Chesire USA CASR-03-2006 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-73-01	KS	Yes (PT1.2.3.6.9.11)
A3_7.4	Brown D	1985	Toxicity to Brown shrimp (Crangon crangon) of Vantocil IB Brixham Environmental Laboratory, Brixham, UK BL/B/2630 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-13	IUCLID	No
A3_7.4	Brown D	1981	Effect of Vantocil on the reproduction of Daphnia magna Brixham Environmental Laboratory, Brixham, UK BLS/B/0042 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-27	IUCLID	No
A3_7.4	[redacted]	1981	Determination of the acute toxicity of Vantocil P to Rainbow Trout (Salmo gairdneri) [redacted] BL/B/2081 Unpublished; Not GLP but QA'd	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-02	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.4	Brown D.	1981	Toxicity to the green alga (Scenedesmus quadricauda) of Vantocil IB (1981) summary only Brixham Environmental Laboratory, Brixham, UK BLS/B/0043 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-19	IUCLID	No
A3_7.4	[redacted]	1980	Vantocil P: Acute tox to rainbow trout [redacted] Plaice BL/B/2031 Unpublished; Not GLP but QA'd	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-03	IUCLID	No
A3_7.4	[redacted]	1977	Acute toxicity of Vantocil IB, mix No 1857, to Bluegill (Lepomis macrochirus) and the water flea (Daphnia magna) [redacted] CTL/C/3039 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-10	IUCLID	No
A3_7.4	[redacted]	1988	Vantocil IB: Acute tox to rainbow trout [redacted] BLS/B/0532 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-04	IUCLID	No
A3_7.4	Gilbert JL, Roberts GC	2002	PHMB: Toxicity to the sediment dwelling larvae Chironomus riparius Brixham Environmental Laboratory, Brixham, UK BL7135/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-28	KS	Yes (PT1.2.3.6.9.1 1)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.4	Gillings E.	1995	PHMB: Prelim. Investigation of the effects of pH on sorption to glass. Brixham Environmental Laboratory, Brixham, UK BLS1937/B Unpublished; not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-30	IUCLID	No
A3_7.4	[redacted]	1975	Determination of the acute toxicity to Rainbow Trout of Vantocil IB in freshwater. [redacted] BL/B/1631 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-05	IUCLID	No
A3_7.4	Hutchinson T.H.	1993	Vantocil IB: Acute Toxicity to marine polychaete Platynereis dumerilii Brixham Environmental Laboratory, Brixham, UK BL4953/B Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-15	IUCLID	No
A3_7.4	Hutchinson T.H., Jha A.N	1993	Vantocil IB: Effects on fertilisation in marine polychaete Platynereis dumerilii. Brixham Environmental Laboratory, Brixham, UK BL5003/B Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-16	IUCLID	No
A3_7.4	Hutchinson T.H., Jha A.N	1993	Vantocil IB: Effects on embryo development in a polychaete. Brixham Environmental Laboratory, Brixham, UK BL5004/B Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-17	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.4	[redacted]	1991	Vantocil IB: Effects on survival and growth of sheepshead minnow (Cyprinodon variegatus) larvae [redacted] BL4351/B Unpublished; Not ? GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-25	IUCLID	No
A3_7.4	Maddock B.G.	1983	Vantocil IB: Toxicity to brown shrimp Brixham Environmental Laboratory, Brixham, UK BLS/B/0211 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-14	IUCLID	No
A3_7.4	Maddock BG	1983	Toxicity to Plaice (Pleuronectes platessa) of Vantocil IB Brixham Environmental Laboratory, Brixham, UK BLS/B/0210 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-07	IUCLID	No
A3_7.4	Mather J.I.	1988	VANTOCIL IB: Bacterial Growth inhibition (P.putida) Brixham Environmental Laboratory, Brixham, UK BLS/B/0558 Unpublished; not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-23	IUCLID	No
A3_7.4	Pearson CR	1981	Acute toxicity of Vantocil IB to Daphnia magna (1981) summary only Brixham Environmental Laboratory, Brixham, UK BLS/B/0041 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-11	KS	Yes (PT2.9)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.4	Penwell A.J.	2006	PHMB: Chronic toxicity to Daphnia magna Brixham Environmental Laboratory, Brixham, UK BL8365/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-26	KS	Yes (PT1.2.3.6.9.1 1)
A3_7.4	Penwell A.J., Roberts G.C.	2000	VANTOCIL IB: Inhibition of anaerobic gas production from sewage sludge Brixham Environmental Laboratory, Brixham, UK BL6914/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-20	KS	Yes (PT1.2.3.6.9.1 1)
A3_7.4	Penwell A.J., Smyth D.V.	2006	PHMB: Toxicity to the green alga Selenastrum capricornutum Brixham Environmental Laboratory, Brixham, UK BL8161/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-18	KS	Yes (PT1.2.3.6.9.1 1)
A3_7.4	[redacted]	1996	PHMB: Acute toxicity to rainbow trout (Oncorhynchus mykiss) [redacted] BL5506/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-01	KS	Yes (PT1.2.3.6.9.1 1)
A3_7.4	[redacted]	2004	PHMB: Summary of rangefinding data in Rainbow trout static and flowthrough test systems. [redacted] BL/B/2976 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-06	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.4	Penwell AJ, Roberts GC	2000	VANTOCIL IB: Inhibition of nitrification of activated sludge microorganisms Brixham Environmental Laboratory, Brixham, UK BL6913/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-21	KS	Yes (PT1.2.3.6.9.11)
A3_7.4	Penwell AJ, Roberts GC	2000	VANTOCIL IB: Effect on the respiration rate of activated sludge Brixham Environmental Laboratory, Brixham, UK BL6678/B OECD 209 Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-22	IUCLID	No
A3_7.4	[redacted]	2001	PHMB: Effects on growth of juvenile rainbow trout (Oncorhynchus mykiss) [redacted] BL7096/B Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-24	KS	Yes (PT1.2.3.6.9.11)
A3_7.4	Roberts GC	2004	[14C] PHMB: Evaluation of Sorption to Various Storage Vessels. Brixham Environmental Laboratory, Brixham, UK BLS3110/B Unpublished; not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-31	IUCLID	No
A3_7.4	[redacted]	1993	Study X022/B, Vantocil IB: acute toxicity to Bluegill sunfish (Lepomis macrochirus) [redacted] BL4778/B Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-09	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.4	[redacted]	1981	Acute toxicity of Vantocil P to Bluegill (Lepomis macrochirus) [redacted] BW-81-3-847 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-08	IUCLID	No
A3_7.4	Stewart K.M., Thompson R.S.	1991	Vantocil IB: Acute toxicity to mysid shrimp (Mysidopsis bahia) summary only Brixham Environmental Laboratory, Brixham, UK BL4365/B	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-12	IUCLID	No
A3_7.4	Thompson RS	1983	The effect of Vantocil P on the growth of Lemna minor (Duckweed) Brixham Environmental Laboratory, Brixham, UK BLS/B/0225 Unpublished; Not GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-74-29	IUCLID	No
A3_7.5	[redacted]	1979	Baquacil Mix #5889. Acute Oral LD50 - Mallard Duck. MRID No: 27491 + Phase 3 Summary of MRID 27491. Guideline reference 71-1: Acute dietary LD50 test for waterfowl. [redacted] Project No 123-131 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-75-09	KS	Yes (PT1.2.3.6.9.1 1)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.5	[redacted]	1979	Baquacil Mix #5889. Eight day dietary LC50 Bobwhite Quail MRID No: 41382 + Phase 3 Summary of MRID 41382. Guideline reference 71-2: Acute dietary LC50 test for upland game birds [redacted] Project No 123-129 Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-75-10	IUCLID	No
A3_7.5	[redacted]	1979	Baquacil Mix #5889. Eight day dietary LC50 Mallard Duck. Final report. MRID No: 27492 [redacted] Project No 123-130 Unpublished; Not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-75-11	IUCLID	No
A3_7.5	Gilbert JL, Roberts GC	2002	PHMB: Acute toxicity to the earthworm Eisenia foetida Brixham Environmental Laboratory, Brixham, UK BL7134/B Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-75-02	KS	Yes (PT1.2.3.6.9.11)
A3_7.5	Penwell AJ, Roberts GC	2003	PHMB: Effect on nitrogen transformation by soil microorganisms Brixham Environmental Laboratory, Brixham, UK BL7133/B OECD 216 Unpublished; GLP	Arch Chemicals Inc	YES Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-75-01	KS	Yes (PT2.9)
A3_7.5	Penwell AJ, Roberts GC	2002	PHMB: Effect on seedling emergence and growth Brixham Environmental Laboratory, Brixham, UK BL7131/B Unpublished; GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-75-05	KS	Yes (PT1.2.3.6.9.11)

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.5	Stanley R.D.	1983	The effect of Vantocil P on the Earthworm (Lumbricus terrestris) Brixham Environmental Laboratory, Brixham, UK BLS/B/0224 Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-75-03	IUCLID	No
A3_7.5	Stanley R.D.	1983	The effect of Vantocil P on the germination and growth of Lepidium sativum (Cress) seeds Brixham Environmental Laboratory, Brixham, UK BLS/B/0222 Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-75-06	IUCLID	No
A3_7.5	Stanley R.D.	1983	The effect of Vantocil P on the germination and growth of Avena sativa (Oat) seeds Brixham Environmental Laboratory, Brixham, UK BLS/B/0223 Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-75-07	IUCLID	No
A3_7.5	Stanley R.D., Tapp J.F.	1981	The effects of Synperonic NP8, Vantocil P, and Chlordane on Lumbiricus Terrestris and Allolobophora Caliginsoa. Brixham Environmental Laboratory, Brixham, UK BL/A/2111 Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-75-04	IUCLID	No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
A3_7.5	Stanley R.D., Tapp J.F.	1981	The Effects of Synperonic NP8, Vantocil P, and Potassium Chlorate on the growth of Avena Satura. . Brixham Environmental Laboratory, Brixham, UK BL/A/2136 Unpublished; not GLP	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I	ARCH A3-75-08	IUCLID	No

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

Evaluation of active substances

List of References – Part B

Polyhexamethylene biguanide

(Mn = 1600; PDI =1.8)

(PHMB)

Applicant: Lonza

Product-type 6

Preservatives for products during storage

FINAL CAR

June 2015

eCA: FRANCE

This document is a list of all the studies submitted by the Applicant to support the PT06 dossier. Claims of data protection are proposal from the Applicant.

Studies indicated as "Relied on" are validated studies from which endpoints were established. This corresponds to the list of protected studies.

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
TP6 B5-10.1	McGeechan P.	2006	Evaluation of the preservative Efficacy of VANTOCIL TG. In a Fabric Conditioner. Arch UK Biocides Ltd, Microbiology Group, Manchester, UK. Report no. 030. Unpublished, Not GLP.	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I.	ARCH B3-5-01	KS	Yes
TP6 B5-10.2	McGeechan P.	2006	Evaluation of the preservative Efficacy of VANTOCIL TG. In Wet Wipe Lotions. Arch UK Biocides Ltd, Microbiology Group, Manchester, UK. Report no. 031. Unpublished, Not GLP.	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I.	ARCH B3-5-02		No
TP6 B5-10.3	Mitchell K	2004	Wet State Preservation Testing of PVA Adhesive Sample. Arch UK Biocides Ltd, Microbiology Group, Manchester, UK. Report no. 4573.37. Unpublished, Not GLP.	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I.	ARCH B3-5-03		No
TP6 B5-10.4	Mainey C	2005	Wet state preservation testing of wall paper adhesive. Arch UK Biocides Ltd, Microbiology Group, Manchester, UK. Report no. 4917.37. Unpublished, Not GLP.	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I.	ARCH B3-5-04		No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
TP6 B5-10.5	Mitchell K	2004	Wet State Preservation Testing of Latex Sample. Arch UK Biocides Ltd, Microbiology Group, Manchester, UK. Report no. 4573.39 Unpublished, Not GLP.	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I.	ARCH B3-5-05	KS	Yes
TP6 B5-10.6	Hull M. R	1999	The effect of adding Vantocil IBb and Zeneca Proxel alone and in combination on bacterial growth in used wood treatment product. Hickson Timber Products Limited, Technical Centre, Castleford. Report no. W12/127. Unpublished, Not GLP.	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I.	ARCH B3-5-06		No
TP6 B5-10.6	Hull M. R	2011	Report W12/127: Addendum – Clarification of Test Method ARCH TIMBER PROTECTION, Castleford, UK. Report no. W12/127 addendum Unpublished, Not GLP.	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I.	ARCH B3-5-06 addendum		No
TP6 B5-10.7	Shaw C. H	2007	Evaluation of the Efficacy of Vantocil TG as a Preservative for Cut Flower Nutrient Solutions. Arch UK Biocides Ltd, Microbiology Group, Manchester, UK. Report no. A1606162. Unpublished, Not GLP.	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I.	ARCH B3-5-07		No

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
TP6 B5-10.8	Shaw C. H	2007	Evaluation of the Efficacy of Vantocil TG as a Preservative for Cut Flower Nutrient Solutions. Arch UK Biocides Ltd, Microbiology Group, Manchester, UK. Report no. A1606160. Unpublished, Not GLP.	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I.	ARCH B3-5-08		No