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 3: Veterinary hygiene

June 2015

France

TABLE OF CONTENTS

1 STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1 PROCEDURE FOLLOWED

This Assessment Report has been established as a result of the evaluation of the active substance 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 3 (veterinary hygiene), 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 3.

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 3 was the 31st 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 21st of April 2008.

On the 14th of November 2013, 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 3, and should it be approved, to facilitate the authorisation of individual biocidal products in product-type 3 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

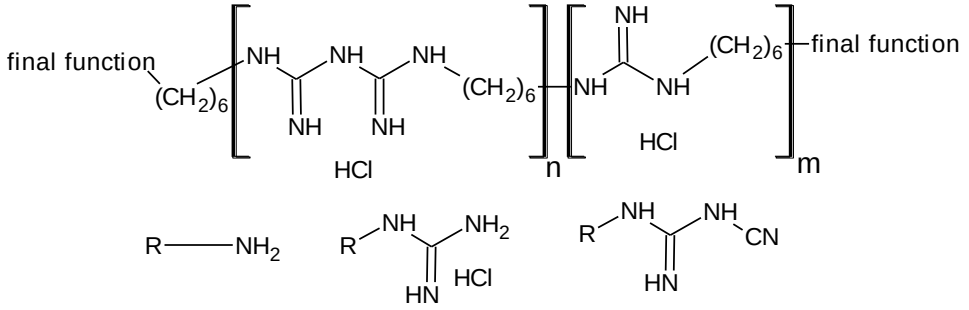
2.1.1 IDENTITY, PHYSICO-CHEMICAL PROPERTIES & METHODS OF ANALYSIS OF THE ACTIVE SUBSTANCE

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 function: amino	35% - 46%	39%
		Terminal function: guanidine	22% - 29%	25%
		Terminal 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.

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

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

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 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. Additional 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 characterisation 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 oxidizing 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 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 are 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

This Product Type 03 dossier for PHMB is provided to support the following use:

MG01: Disinfectants.

Product Type 03: Veterinary hygiene.

2.1.3.2 Function

Bactericide.

Virucidal and fungicidal activities initially claimed have been withdrawn during the evaluation of the dossier by the applicant.

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. It is concluded that 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 overlaying 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 intended uses of the VANTOCIL TG initially claimed by the applicant are (please refer also to Appendix II):

- Disinfection of animal housings:
  - Barrier disinfection (footbath for footwear);
  - Disinfection of housing (application by fogging);
- Small scale disinfection of veterinary establishments (floors, walls and work surface):
  - By mopping;
  - By wiping;
  - By spraying;
- Disinfection of teat-dips using teat-dipping cup.

The table below presents the efficacy data which support the efficacy of the active substance PHMB in the frame of active substance dossier. The data are generated from laboratory studies and should be consolidated at the product authorisation stage with tests on real products.

For the other uses presented by the applicant in the dossier (i.e. small scale disinfection techniques (wipes, mopping or trigger spray) or large scale disinfection techniques (fogging)), the efficacy data were insufficient.

For intended uses as dipping via footbath for footwear or teat-dip disinfection, the contact time used to fulfil the efficacy criteria of the efficacy standard methods (30 minutes) is not compatible with the field conditions regarding such uses (contact of few seconds with the product when footbath and teat-dip disinfection is considered). No risk assessment was therefore performed for these use patterns.

Table 2.1-4: Efficacy data which support the efficacy of PHMB

Scenario	**Application method**	**Product**	**In use concentration / contact time** (% w/w a.s. in the in-use solution)	**Activity**
Small equipment (livestock farming environment)	Dipping	VANTOCIL TG (20% w/w a.s.)	0.2 % Temperature 10 to 30°C, contact time of 30 minutes.	Bactericide Efficacy not demonstrated for mycobacteria and bacteria spores

As agreed at BPC Efficacy Working Group I 2015, innate activity of the active substance is also considered sufficiently demonstrated at that stage for surface application. The use dose of 0.2 % w/w a.s. (higher than the application rate claimed by the applicant) is used to assess the risk for the application by wiping with ready-to-use (RTU) wipes,

It has to be highlighted that the risk assessment for this use is done on the basis of a use dose that is not supported by any appropriate efficacy data. Therefore, the risk assessment does not reflect a realistic condition of use and has to be confirmed at product authorisation stage.

2.1.3.5 Resistance

The evaluation of the literature studies provided by the applicant does not show particular resistance of bacteria to PHMB. 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 scientific literature of:

- cross resistances
- modifications of the expression of genes as a mechanism of tolerance to subletal concentrations of PHMB

should be taken into account in the strategy of resistance management.

In particular, the concentration of 7,5 ppm of PHMB is shown to be subletal and thus susceptible to generate tolerance (E. coli A3-5-12).

Standard methods of measuring resistance brought about by biocide use are not available and should be developed for all type 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 a.s./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

The active substance is an antimicrobial agent which has a bactericidal effect. VANTOCIL TG containing 20% w/w a.s. in aqueous solution was proposed by the applicant as a representative biocidal product to illustrate the risk assessment of the active substance for the purpose of approval. The product is applied by professional users by dipping for small equipment disinfection, and for the small scale surface disinfection of veterinary areas with Ready to Use (RTU) wipes.

Primary exposure

The potential route of exposure to PHMB during mixing/loading of VANTOCIL TG, dipping of the equipment and wiping of the surfaces is the dermal route. Ingestion is

not considered to be a relevant route. Professional users only are considered for primary exposure.

Secondary exposure

Worker and general public are considered for secondary exposure.The potential route of exposure is the dermal route by touching treated materials, and dermal/oral by touching treated surface and hand-to-mouth contact. Ingestion of contaminated food of animal origin is also possible, considering a contamination of livestock in contact with treated materials.

Inhalation is not a relevant route because the active substance is non-volatile.

Table 2.2-2: Summary of main paths of human exposure

Exposure path	**Industrial use**	**Professional use**	**Non-Professional use**	**General public** (secondary exposure)	**Via the environment**
Inhalation	Not applicable	No	Not applicable	No	No
Dermal	Not applicable	Yes	Not applicable	Yes	No
Oral	Not applicable	No	Not applicable	Yes	No

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

2.2.1.2.1 Primary exposure

The process involves cleaning of equipments by **dipping** in a solution containing up to 0.2% w/w of active substance. The activities involved are:

- Manual mixing/loading of VANTOCIL TG when filling the dipping bath.
- Immersion/removal of treated equipment from the dipping bath.

A new scenario is assessed in this document: **surface wiping** using ready to use wipes for small scale disinfection of veterinary areas. This task was not considered in the first draft CAR, but is presented here in accordance with the decision taken at the BPC Efficacy Working Group I 2015.

It has to be highlighted that the risk assessment is done on the basis of a use dose that is not supported by any appropriate efficacy data. Therefore, the risk assessment does not reflect a realistic condition of use and has to be confirmed at product authorisation stage.

2.2.1.2.1.1 Professional exposure estimates and risk characterisation

2.2.1.2.1.1.1 Dipping: immersion/removal of small farming equipments from a dipping bath

⇨ Loading phase[5]

The loading scenario is defined as dispensing the product (containing up to 20% a.s.) into the dipping solution. It is done by professionals. For the exposure assessment, it is considered that the manual addition is the worst-case scenario, compared to an automated transfer.

⇨ Dipping phase[6]

This activity is typified by the use of an immersion bath for disinfection of equipment (small equipement in livestock farming environnement) in an agricultural environment. This task is done by professionals. It is assumed, as representative use, that specialised professionals dip 1 hour per day. During this task, users can be exposed to the dipping solution (containing up to 0.2% active substance).

⇨ Combined exposure

As the professional can conduct both mixing/loading and dipping tasks in the same work shift, the combined exposure is estimated as following.

Table 2.2-3: Exposure estimates for professional using biocidal products in diluting process

Tier	Dermal exposure	
PPE	Skin deposit concentration	Systemic dose
	% w/w a.s.	mg a.s./kg /d
Task – time frame :	**Mixing/Loading (worker) - daily**	
Tier 1: Without PPE	20	1.33×10^{-3}
Tier 2 : gloves and cotton coverall	20	1.72×10^{-4}
Task – time frame :	**Dipping (worker) - daily**	
Tier 1: Without PPE	0.2	1.63×10^{-2}
Tier 2 : gloves and cotton coverall	0.2	3.77×10^{-3}
Task – time frame :	**Total exposure on whole shift**	
Tier 1: Without PPE	-	1.76×10^{-2}
Mixing loading: Tier 1-without PPE Dipping: Tier2-Gloves and cotton coverall	-	5.09×10^{-3}
Mixing/Loading and dipping: Tier 2- Gloves and cotton coverall	-	3.94×10^{-3}

[5] EUROPOEM II database (Professional pouring formulation from a container into a fixed receiving vessel) gives indicative values expressed as mg of active substance per kg of poured active substance, reported in TNsG User guidance (2002) page 24.
[6] Dipping Model 1 (Professional dipping wooden articles in tanks and coating with fluid by pouring and scrubbing) gives indicative values expressed as mg of active substance per minute, reported in TNsG User guidance (2002) page 45 and TNsG version 2 (2007) page 167.

Risk characterisation for PHMB in Product Type 3 was performed for professional during a working day.

➔ **Risk characterisation for systemic effects**

The systemic exposure values were compared with the acute, medium-term and long-term AEL of PHMB. The results are presented in the following tables.

Table 2.2-4: Risk characterisation concerning systemic effects for combined exposure for professionals

	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
Mixing/Loading and dipping Tier 1 : Without PPE	1.76×10^{-2}	0.52	100	30	5.20×10^{-3}	**339**
Mixing/loading: Tier 1-without PPE Dipping: Tier2- Gloves and cotton coverall	5.09×10^{-3}	0.52	100	102	5.20×10^{-3}	98
Mixing/Loading and dipping: Tier 2- Gloves and cotton coverall	3.94×10^{-3}	0.52	100	132	5.20×10^{-3}	76

The risk characterisation for combined exposure during mixing, loading and dipping tasks is unacceptable in Tier 1, with a MOE (30) lower than the MOE_{ref} (100) and a %AEL (319) above 100%.

The risk characterisation for combined exposure is acceptable during a mixing and loading phase without PPE (personal protective equipment) and a dipping phase with gloves and cotton coverall, with a MOE (102) higher than the MOE_{ref} (100) and a %AEL (98) below 100%.

➔ **Risk characterisation for local effects**

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

Personal protective equipment (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.

In addition, 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 formulations (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.

2.2.1.2.1.1.2 Wiping surfaces using ready to use wipes for small scale disinfection of veterinary areas

The applicant did not provide details about the size of the wipes and did not specify what was meant by "small scale disinfection".

Wipe can be used for cleaning all washable surfaces. The primary exposure consists to the handling of wipe containing 0.2% liquor of PHMB.

No specific model was presented in the available Technical Notes for guidance (TNsG[7]) for ready to use wipes.

The most relevant model for wiping with ready to use wipe is the "all purpose cleaners-wet tissues: application" model according to Cleaning Products Fact Sheet to assess the risks for the consumer (RIVM report 320104003/2006, page 63). It is mentioned that 0.047 gram (value of 75th percentile) remained on the surface of the inner hand area, which is about 1.4 % of total liquid fraction of tissues when firmly touching wet tissue.

As no data on the quantity of liquid in the tissues is provided by applicant, the transfer value from ConsExpo, 0.047 g of product, will be used.

A reverse scenario was performed to determine the maximum number of wipes that can be used per day with an acceptable risk.

Table 2.2-5: Estimation of maximum number of wipes can be used per day with an acceptable risk

	Tier 1 Without PPE
Dermal systemic dose for one wipe (mg a.s./kg bw/wipe)	6.27×10^{-5}
Maximum number of wipes per day	82

➔ **Risk characterisation for systemic effects**

According to ConsExpo, the time of cleaning estimated for one wipe is 2 minutes. Based on this hypothesis, we need 2.7 hours per day to use 82 wipes. For a professional of veterinary environment, this situation is considered to be unrealistic.

[7] Technical Notes for Guidance – Human Exposure to biocidal products. June 2007. http://echa.europa.eu/documents/10162/16960215/bpd_guid_tnsg-human-exposure-2007_en.pdf.

Due to the high maximum number of wipes can be used per day, the risk for systemic effects is acceptable for professionals wiping with ready to use wipes for small scale disinfection of veterinary areas.

➔ **Risk characterisation for local dermal effects**

The concentration of wipe liquor is below the concentration limit of irritation and sensitisation classification. Therefore, the risk for local effects is considered to be acceptable.

It has to be highlighted that the risk assessment is done on the basis of a use dose that is not supported by any appropriate efficacy data. Therefore, the risk assessment does not reflect a realistic condition of use and has to be confirmed at product authorisation stage.

2.2.1.2.1.1.3 Conclusion for professional users

The risks linked to the use of PHMB based products during the scenarios of mixing/loading and dipping, with the wear of PPE (gloves and cotton coverall), and during the scenario of wiping surface with ready to use wipes, by professionals, are considered acceptable.

Concerning the local dermal effects during the loading of 20% PHMB product, the product should be handled by professionals only and PPE have to be worn, in order to consider the risk as accidental and managed.

2.2.1.2.1.2 Non-professionals exposure

Non-professional or consumer direct exposure to treatment fluids containing PHMB used in the agriculture for PT03 applications is not relevant since these biocidal products are sold for professional use only.

2.2.1.2.2 Secondary exposure as a result of use

Secondary exposure to the active substance can occur via dermal contact with residues on equipments. Hand to mouth contact is also envisaged. Additionally, treated materials can be in contact with feed and livestock. Secondary exposure after ingestion of PHMB transferred from treated small husbandry equipments and from surface to livestock, and incidence on consumer safety following the consumption of contaminated products of animal origin, were assessed.

2.2.1.2.2.1 Exposure by dermal contact with residues on equipements

Starting from AEL, a reverse scenario of exposure has been established. It has allowed calculating the maximum area of equipments that could be rubbed daily without risk of systemic effects.

In TNsG transfer coefficient of dry residues for smooth object are quite high even with dry hand (60%). So it was assumed in case of wet hand or that the treated objects are wet a transfer of 100%. Assuming a scenario of 100% migration from the dipped equipements 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 (%)] /contamination of equipement by active substance (mg a.s. /cm^2) =

[5.2 x 10^{-3} x 60/4%] /1.1 x 10^{-3} = 7.1 x 10^{+3} cm^2/d.

$Area_{max}$ = 0.7 m^2/d

The situation where a person rubs 0.7 m^2 of equipements daily is realist. Therefore, the risk for direct contact with residues on equipments is considered to be unacceptable.

Acceptable risk for direct contact with residues on equipment must be demonstrated at product authorisation stage. This may include data to refine the assumptions rinsing and transfer coefficients.

2.2.1.2.2.2 Exposure by dermal and oral contact with residues on disinfected surfaces

Indirect exposure following use of surface disinfectant occurs when an infant is crawling on a surface disinfected with the product and hand-to-mouth transfer (oral and dermal exposure).

Hand deposit concentration = 6.00 x10^{-3} mg/cm^2

Dermal systemic dose = 6.0 x 10^{-3} x 90% x 6,000 cm^2 x 4% / 10 kg = 1.30 x 10^{-1} mg a.s./kg bw/day

Oral systemic exposure= 6.0 x 10^{-3} x 10% x 6000 cm^2x 4% / 10kg= 1.44 x 10^{-2} mg a.s./kg bw/day

As the surfaces are not disinfected every day, and the substance on surface is rapidly wiped off e.g. by shoes, this exposure is considered to be medium-term.

Table 2.2-6: Estimation of oral and dermal exposure to disinfected surfaces

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 disinfected with ready to use wipes - Chronic dermal exposure**			
Tier 1: Without PPE	0.2%	1.30 x 10^{-1}	1.44 x 10^{-2}	1.44 x 10^{-1}

➔ **Risk characterisation for systemic effects**

Table 2.2-7: Summary of risk assessment for indirect exposure for an infant crawling on a surface disinfected with the product (systemic effects)

	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 disinfected with ready to use wipes**					
Tier 1 : Without PPE	1.44×10^{-1}	0.52	100	4	5.20×10^{-3}	**2769%**

Unacceptable risk has been identified for the infant crawling on surface cleaned with ready to use wipes, since MOE is lower than MOE_{ref} (100) and associated %AEL is above 100%, for the systemic effects.

Refinement of the assessment is not possible in absence of appropriate data. However, this situation of a crawling infant is not considered appropriate regarding the location of the application of the product.

➔ **Risk characterisation for local dermal effects**

The concentration of wipe liquor is below the concentration limit of sensitisation classification. Therefore, the risk for local effects is considered to be acceptable.

2.2.1.2.2.3 Indirect exposure via food

Secondary exposure after ingestion of PHMB transferred from treated surfaces and small husbandry equipments to livestock, and incidence on consumer safety following the consumption of contaminated commodities of animal origin, were assessed.

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.

2.2.1.2.2.3.1 Professional use / desinfection of small husbandry equipments

No experimental data/studies were provided. Consequently, the daily exposure to PHMB was assessed with a worst case scenario, using default values from the European draft guidance document (2014[8]) and additional proposed values from several technical institutes for husbandry.

As a general approach, a residue transfer of 100% was considered from the solution to the treated equipment, then from the treated equipment to the livestock. This is equivalent to say that the entire amount of active substance introduced in the tank would be found in the animal body or products of animal origin.

[8] ARTFOOD/DRAWG (2014) : Guidance on Estimating Transfer of Biocidal Active Substances into Foods – Professional Uses – 2014 - "Water film thickness on external surface of bottle") – draft not yet published

No information about a dipping scenario is currently available in the draft guidance. A volume of 100L was deemed practical for a daily or occasional treatment which could occur depending on the litter /material sanitary state during the breeding period. In addition, this volume was considered acceptable to cover the most common condition of use and livestock diversity probably involved (broiler chicken, beefs, calves, fattening pigs, and rabbit).

According to this approach, estimation show that the exposure to PHMB might be significant (above the trigger value of 0.004 mg as/kg bw/day defined in the DRAWG guidance[9]) for the majority of livestock considered (calf, fattening pigs, broiler chicken and rabbit).

These estimated exposures in mg/kg animal bw/day were then converted in mg/kg $_{\text{animal bw}}$ by multiplying with the corresponding duration of batch for each animal category to estimate the resulted residue in edible commodities of animal origin (tissues, milk and eggs).

Maximal residues estimated in tissues, eggs and milk were filled in the PRIMo model (Pesticide Residue Intake Model, commonly used for phytopharmaceutical products assessment, version 2) to calculate chronic and acute exposure to the consumer via the theoretical maximum daily intake (TMDI) and international estimated daily intake (IESTI).

Results of the risk assessment for a daily treatment, based on a maximalist approach, are that the risk is unacceptable: consumer exposure estimations is >> 100% of the ADI (SE general population) and >> 100% of ARfD for bovine meat, eggs and milk (including milk and milk products).

2.2.1.2.2.3.2 Ready to use (RTU) for professional: small scale disinfection of veterinary areas

The applicant does not provide any details about the size of the wipes and does not specify what was meant by "small scale disinfection of veterinary areas ".

Consequently, it was considered that wipe can be used for cleaning all washable surfaces in vicinity with the livestock and sufficiently cover small scale disinfection of veterinary areas. The secondary exposure is related to the transfer of the residues of PHMB to the livestock following handling of wipe containing 0.2% liquor of PHMB to their housing, transport vehicle and storage facilities.

An amount of 40 mg a.s./m² was determined by considering a film thickness of 20 µm of remaining solution on all treated surfaces (ARTFood/formerly DRAWG)[10].

Secondary exposure of livestock is estimated according to the step by step methodology proposed by ARTFood/formerly DRAWG)[11]. According to this approach, the calculated animal exposure to PHMB is above the trigger value of 0.004 mg a.s./kg b.w./day for all categories of livestock considered.

The assessment was therefore refined by considering realistic worst case vs. screening scenario resulting from the sum of 3 exposure ways: oral/ animals licking surfaces, oral/direct treatment of feeding trough surface, dermal/rubbing against

[9] ARTFOOD/DRAWG (2014): Dietary Risk Assessment Working Group. « Guidance on estimating livestock exposure to biocidal active substances" – draft not yet published
[10] ARTFOOD/DRAWG (2014) : Guidance on Estimating Transfer of Biocidal Active Substances into Foods – Professional Uses – 2014 - "Water film thickness on external surface of bottle") – draft not yet published
[11] ARTFOOD/DRAWG (2014): Dietary Risk Assessment Working Group. « Guidance on estimating livestock exposure to biocidal active substances" – draft not yet published

surfaces. The range of calculated exposure with the models available for calculation is also above 0.004 mg a.s./kg b.w./day.

2.2.1.2.2.3.3 Conclusion of dietary risk assessment

Risks are deemed unacceptable by considering maximalist exposure scenarios. However, no data is avaible to refine the assessment. In addition, it should be noted that no rinsing step procedure is taken into account after the treatment. Therefore it is considered that all the remaining residues on treated surface will be transferred to the livestock. An intermediate tier approach could investigate the effect of a rinsing step procedure (with 1/10 dilution as default value). Nevertheless, based on:

- the chelating properties of PHMB,
- its mode of action,
- its high adsorption property (see environmental effects assessment section)
- difficulties to develop methods to analyse the PHMB

it is considered that removal of PHMB by rinsing cannot be demonstrated and therefore, an assessment that would consider removal by rinsing is not relevant in this context.

Acceptable dietary risk must be demonstrated at product authorisation stage. This may include data to refine the assumptions rinsing and transfer coefficients.

2.2.1.3 Overall conclusion for human health

The risks linked to the use of PHMB based products during the scenarios of mixing/loading and dipping of equipement, by professionals, are considered acceptable.The product should be handled by professionals only and PPE have to be worn, in order to consider the risk as accidental and managed.

The local and systemic risk during wiping with ready to use wipes by professionals is considered to be acceptable without wearing of PPE.

Concerning the secondary exposure by direct contact with residues on equipements, the risk is considered to be unacceptable. Concerning the secondary exposure by indirect exposure of an infant crawing on a surface cleaned with a wipe is unacceptable. Refinement of the assessment is not possible in absence of appropriate data. However, this situation of a crawling infant is not considered appropriate regarding the location of the application of the product.

Concerning dietary exposure, a maximalist approach shows unacceptable risks.,However,no refinement is possible, since the proposed use is not associated with experimental data/studies and since details, residue transfer information or default values are currently not well defined to give an exhaustive overview of the small equipment targeted for dipping and surfaces for wiping/mopping treatment and which one could be effectively in contact with animals or products from animal origin. Consequently, the dietary risk assessment is considered as not finalised. The demonstration of the relevance and effectiveness of a rinsing step would be required at product authorisation stage. Pending the submission of these elements, uses are considered acceptable only when disinfection is not done in vicinity of food, livestock or any products of animal origins.

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 VANTOCIL TG 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, it may be assumed that dermal exposure would occur only in accidental circumstances.

Therefore, the eCA considers that biocidal products containing up to 20% PHMB can be used provided that appropriate risk mitigation measures are applied during the mixing/loading of the product (VANTOCIL TG). 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 Table 2.2-8 below.

Table 2.2-8: Risk mitigation measures required to ensure safety of use (mixing/loading and post-application), due to local effects

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 into the dipping bath										
Medium	Skin Sens 1B (H317)	-	3	Professional users	Loading of the biocidal product (20% a.s.) into the dipping bath	Skin	Daily	<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	Acceptable: + Minimization 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**
									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).	
Medium	STOT Rep 1 (H372)	-	3	Professional users	Loading of the biocidal product (20% a.s.) into the dipping bath	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

2.2.2 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, as 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 K_{oc} 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 WG-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 2.2-9: PNEC values for active substance PHMB used for the risk assessment part

$PNEC_{water}$	0.743 $\mu g.L^{-1}$ of a.s.
$PNEC_{sediment}$	446.94 $\mu g.kg^{-1}$ 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 the active substance 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 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 an 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

The active substance is an antimicrobial agent which has a bactericidal effect. VANTOCIL TG containing 20% PHMB (w/w) in aqueous solution was proposed by the applicant as a representative biocidal product to illustrate the risk assessment of the active substance for the purpose of the approval.

The efficacy data presented in the dossier are only suspension laboratory tests which demonstrate the efficacy of the product applied by professional users by dipping. As a consequence, the environmental exposure assessment was performed initially only for the use of VANTOCIL TG by dipping of small equipment in livestock farming environment at the application rate of 0.2 % w/w a.s. and with a contact time of 30 minutes. After WG-I-2015 discussions, it was also decided to include surface treatments.

As a consequence, the environmental exposure assessment was performed for the use by dipping of VANTOCIL TG for small equipment disinfection, and for the small scale surface disinfection of veterinary areas with RTU wipes. It has to be highlighted that the risk assessment for the wiping use is done on the basis of a use dose that is not supported by any appropriate efficacy data. Therefore, the risk assessment does not reflect a realistic condition of use and has to be confirmed at product authorisation stage.

The solutions used for the small equipment disinfection by dipping will ultimately be discharged *via* two pathways:

- *via* the waste water; as a result of this, there will be a potential for exposure of both the aquatic (STP, surface water and sediment) and the terrestrial (soil and groundwater) compartments, the latter as a result of contaminated sewage sludge spreading on land;
- *via* the manure or slurry; as a result of this, there will be a potential for exposure of the terrestrial (soil and groundwater) compartments, following the spreading of contaminated slurry/manure on land.

No specific emission scenario for dipping is described in the Emissin Scenario Document (ESD) for PT03[12]. The process involves the disinfection of small equipment by dipping in a diluted aqueous solution of VANTOCIL TG (0.2% a.s. w/w). A scenario considering that the small equipment is disinfected in dipping baths with a capacity of up to 100 litres and that the bath content will be disposed of to drain or manure once per day was used. This volume of 100 L is proposed as a realistic worst case for the disinfection of small items of equipment in livestock farming environment by dipping. This volume was deemed practical for a daily or occasional treatment during the breeding period and to cover the most common conditions of use and livestock diversity (broiler chicken, beefs, calves, fattening pigs, and rabbit). Several smaller dipping tanks may also be used in the same location (e.g. 4 x 25 L). The use of one single container with a smaller volume seems unlikely in livestock farming environment where numerous animals are reared. The volume was discussed and approved at the WG-I-2015. The applied scenario is based on the emission scenario described in the ESD-PT03 (2011) for the disinfection of footwear modified with the volume proposed for the small equipment disinfection by dipping.

[12] Emission Scenario Document for Product Type 3 – Veterinary hygiene products. JRC Scientific and Technical Report (2011).

The solutions used for the small scale surface disinfection of veterinary areas with RTU wipes are considered to be ultimately discharged *via* the waste water. No release via the manure or slurry is expected due to the intended use in small scale veterinary areas. As a result of this, there will be a potential for exposure of both the aquatic (STP, surface water and sediment) and the terrestrial (soil and groundwater) compartments, the latter as a result of contaminated sewage sludge spreading on land.

The applicant initially considered that for the disinfection of surfaces, using RTU wipes induces no release to the environment, as the RTU wipes after use is considered as a solid waste. eCA disagrees with this assumption as it is the wipe that should be considered as a solid waste, not the solution of VANTOCIL TG that impregnates the wipes. As for mopping, eCA considers that VANTOCIL TG at an efficient dose rate will be left by RTU wipes onto the surfaces to be treated. As a consequence releases to the environment via the sewer system could occur when surfaces are cleaned with water.

No specific emission scenario for small scale surface disinfection by wiping is described in the ESD for PT03. eCA is of the opinion that the emission scenario for disinfection in industrial premises of the ESD-PT02 (table2, 2011)[13] can be applied for the PT03-use of PHMB for small scale surface disinfection of veterinary areas with RTU wipes.

2.2.2.7 Risk characterisation for the environment

To carry out a quantitative risk assessment for the environment for the use of PHMB in VANTOCIL TG as PT03 for small equipment disinfection by dipping and for small scale surface disinfection of veterinary areas with RTU wipes, the PEC values were compared to the respective PNEC values for the different compartments, resulting in the following PEC/PNEC ratios summarised in the Table below.

Table 2.2-10: PEC/PNEC ratios for PHMB used for small equipment disinfection by dipping and for small scale surface disinfection of veterinary areas with RTU wipes

	Small equipment disinfection by dipping		**Small scale surfaces disinfection of veterinary areas with RTU wipes**			
Application rate of the active substance	0.2% w/w		0.2% w/w			
			Surface area to be treated: **1000 m²**		Surface area to be treated: **145 m²** (reverse scenario)	
	Local PEC	**PEC/PNEC**	**Local PEC**	**PEC/PNEC**	**Local PEC**	**PEC/PNEC**
Freshwater [mg.L^{-1}]	1.27E-03	**1.71**	5.09E-04	0.685	7.38E-05	9.93E-02
Sediment [mg.kg^{-1} $_{wwt}$]	7.65	**17.12**	3.06	**6.58**	4.44E-01	0.99

[13] Emission Scenario Document for Product Type 2 – Private and public health area disinfectants and other biocidal products. JRC Scientific and Technical Report (2011).

STP [mg.L^{-1}]	1.80E-02	1.50E-03	7.20E-03	6.00E-04	1.04E-03	8.7E-05
Soil [mg.kg$^{-1}_{wwt}$]	3.39	0.95	1.36	3.79E-01	n.d.	n.d.
Groundwater [µg.L^{-1}]	< 0.001	< 0.1 [1]	< 0.001	< 0.1 [1]	n.d.	n.d.

Release via manure/slurry spreading on land						
Housing type	**Small equipment disinfection by dipping**					
	Grassland			**Arable land**		
	PIECgrs-N$_{worst-case}$ [mg.kg$^{-1}_{wwt}$]	**PEC/PNEC**	**PEC groundwater[1]**	**PIECgrs-N** [mg.kg$^{-1}_{wwt}$]	**PEC/PNEC**	**PEC groundwater[1]**
Dairy cow	1.18E+00	3.30E-01	< 0.001	2.95E-01	8.24E-02	< 0.001
Beef cattle	1.11E+00	3.10E-01	< 0.001	2.78E-01	7.75E-02	< 0.001
Veal calves	2.10E+01	**5.86**	< 0.001	5.25E+00	**1.47**	< 0.001
Sows, in individual pens	4.26E+00	**1.19**	< 0.001	1.07E+00	2.98E-01	< 0.001
Sows in groups	4.26E+00	**1.19**	< 0.001	1.07E+00	2.98E-01	< 0.001
Fattening pigs	3.29E+00	9.18E-01	< 0.001	8.22E-01	2.29E-01	< 0.001
Laying hens in battery cages without treatment	9.43E-01	2.63E-01	< 0.001	2.36E-01	6.58E-02	< 0.001
Laing hens in battery cages with aeration (belt drying)	1.05E+00	2.94E-01	< 0.001	2.63E-01	7.35E-02	< 0.001
Laying hens in batters cages with forced drying (deeppit, high rise)	1.05E+00	2.94E-01	< 0.001	2.63E-01	7.35E-02	< 0.001
Laying hens in compact battery cages	1.05E+00	2.94E-01	< 0.001	2.63E-01	7.35E-02	< 0.001
Laying hens in free range with litter floor (partly litter floor, partly slatted)	2.34E+00	6.53E-01	< 0.001	5.85E-01	1.63E-01	< 0.001
Broilers in free range -	1.28E+00	3.58E-01	< 0.001	3.21E-01	8.95E-02	< 0.001

litter floor						
Laying hens in free range - grating floor	1.17E+00	3.27E-01	< 0.001	2.92E-01	8.17E-02	< 0.001
Parent broilers in free range - grating floor	1.92E+00	5.36E-01	< 0.001	4.79E-01	1.34E-01	< 0.001
Parent broilers in rearing - grating floor	3.24E+00	9.06E-01	< 0.001	8.11E-01	2.27E-01	< 0.001
Turkey in free range - litter floor	8.30E-01	2.32E-01	< 0.001	2.07E-01	5.80E-02	< 0.001
Ducks in free range - litter floor	1.46E+00	4.08E-01	< 0.001	3.65E-01	1.02E-01	< 0.001
Geese in free range - litter floor	8.30E-01	2.32E-01	< 0.001	2.07E-01	5.80E-02	< 0.001

n.d. – not determined.

[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.

2.2.2.7.1 Aquatic compartment

The use of VANTOCIL TG for small equipment disinfection by dipping induced PEC/PNEC ratios > 1 for the following compartments:

- freshwater;
- sediment.

These results indicate that the predicted PHMB emission levels associated with the disinfection of small equipment by dipping will give rise to adverse effects to organisms present in the water column and the sediment.

In conclusion, the uses of VANTOCIL TG as PT03, for small equipment disinfection by dipping leads to unacceptable risks for the aquatic compartment (including sediment) *via* releases to wastewater.

The use of VANTOCIL TG for small scale surface disinfection with RTU wipes induced PEC/PNEC ratios > 1 for the sediment compartment when the typical scenarios for surface disinfection are considered. These results indicate that the predicted PHMB emission levels associated with use for disinfection of veterinary areas with RTU wipes will give rise to adverse effects in organisms present in the sediment.

Nevertheless, the use of RTU wipes can be considered more adapted to small scale surface disinfection, than for medium to large scale surface disinfection. As a consequence, the scenario applied for surface disinfection using a treated surface area of 1000 m² probably overestimated the risk for the use of RTU wipes. Based on the scenario for disinfection of veterinary areas, and by applying

a reverse calculation, the use of VANTOCIL TG would induce acceptable risk to sediment for treated surface < 145 m². eCA is of the opinion that treated surface < 145 m² could be considered as a small scale surface, and hence the use of RTU wipes for hard surface disinfection should be considered as acceptable for all relevant environmental compartments when used on a small scale surface as claimed by the applicant.

In conclusion, the use of VANTOCIL TG as PT03 for small scale surface disinfection of veterinary areas with RTU wipes leads to acceptable risks for the aquatic compartment (including sediment), if small scale treated surface is considered (*i.e.* < 145m²).

2.2.2.7.2 Sewage treatment plant organisms

The risk assessment estimates that the predicted PHMB emission levels associated with use of VANTOCIL TG for small equipment disinfection by dipping, and for small scale surface disinfection with RTU wipes, will not give rise to adverse effects to microorganisms present in STP.

As a consequence the risk following the use of PHMB in VANTOCIL TG for small equipment disinfection by dipping and small scale surface disinfection by wiping is considered acceptable for the STP.

2.2.2.7.3 Atmosphere

No risks are expected, considering that the active substance is not volatile.

2.2.2.7.4 Terrestrial compartment

Considering releases via the wastewater only, the use of VANTOCIL TG for small equipment disinfection by dipping, and for small scale surface disinfection of veterinary areas with RTU wipes induced PEC/PNEC ratios < 1 for the terrestrial compartment. These results indicate that the predicted PHMB emission levels associated with the use for small equipment disinfection by dipping and for the small scale surface disinfection of veterinary areas will give rise to no adverse effects to organisms present in the soil, considering releases via the wastewater.

Considering releases via the manure/slurry spreading on land, the use of VANTOCIL TG for small equipment disinfection by dipping induced PEC/PNEC ratios > 1 for the terrestrial compartment:

- For veal calves breeding with manure spreading on grassland or arable land;
- For sows in individual pens or in groups with slurry spreading only on grassland.

For all other housing types mentioned in the ESD-PT03, the use of VANTOCIL TG for small equipment disinfection by dipping with releases via the manure/slurry spreading on land induced PEC/PNEC ratios < 1 for the terrestrial compartment (grassland and arable land).

These results indicate that the predicted PHMB emission levels associated with the use for small equipment disinfection by dipping will give rise to adverse effects to organisms present in the soil, considering releases via manure/slurry, only for veal calves breeding and for sows in individual pens or in groups.

In conclusion:

- if only releases via the waste water are considered, the use of VANTOCIL TG as PT03 for the small equipment disinfection by dipping and for small scale surface disinfection of veterinary areas with RTU wipes, leads to acceptable risks for the terrestrial compartment,

- if releases via the manure/slurry spreading on land are considered, the use of VANTOCIL TG as PT03 for the small equipment disinfection by dipping leads to unacceptable risks for the terrestrial compartment, only for veal calves breeding and for sows in individual pens or in groups.

2.2.2.7.5 Groundwater

With regard to predicted PHMB concentrations in groundwater, these did not exceed the 0.1 µg/L limit set by the EU Groundwater Directive following all PT03-uses of PHMB-based product VANTOCIL TG.

As a consequence the risk following the use of PHMB in VANTOCIL TG as PT03 is considered **acceptable** for groundwater.

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

It is believed that there is no significant potential for secondary poisoning because the low log octanol/water partition coefficient of -2.29, and the high molecular weight of PHMB.

2.2.2.9 Overall conclusion for the environment

The environmental risk assessment of PHMB used for small equipment disinfection by dipping, and for small scale surfaces disinfection of veterinary areas with RTU wipes is summarised in the table below.

Table 2.2-11: Summary of the environmental risk assessment of PHMB used for equipment disinfection by dipping and wiping

Scenario		STP	Aquatic compartment	Terrestrial compartment	Groundwater	Air	Secondary poisoning
Professional application: equipment disinfection by dipping							
Application rate of the active substance	0.2% w/w a.s. (bactericidal activity)	Acceptable	Unacceptable	Acceptable (1), (2)	Acceptable	Not relevant	
Professional application: small scale surfaces disinfection of veterinary areas with RTU wipes							
Application rate of the active substance	0.2% w/w a.s. (bactericidal activity)	Acceptable	Acceptable (3)	Acceptable	Acceptable	Not relevant	

(1) Considering release via the wastewater only.

(2) Considering release via the manure/slurry spreading on land only, except for veal calves breeding and for sows in individual pens or in groups .

(3) Only for small scale surface disinfection (treated surface < 145 m²).

Considering that:

- The efficiency of PHMB used in VANTOCIL TG − *i.e.* aqueous concentrate containing 20% (w/w) of PHMB − was demonstrated for the disinfection of small equipment by dipping and for the surface disinfection at the application rate of 0.2% of a.s. (w/w) for a bactericidal activity;
- The solutions of diluted VANTOCIL TG used for the small equipment disinfection by dipping, and for the small scale surface disinfection of veterinary areas with RTU wipes will be discharged to drain and will enter a municipal sewage treatment plant (STP), or in the case of the small equipment disinfection by dipping will be discharged to land via the spreading of manure/slurry;
- In accordance with the realistic case scenarios applied for the risk assessment,
    - For the small equipment disinfection by dipping with releases *via* wastewater,
        - the derived PEC/PNEC ratios for freshwater, sediment are above the trigger value of 1 for the efficient application rate;
        - the derived PEC/PNEC ratio for sewage treatment plant, and soil compartment are below the trigger value of 1 for the efficient application rate;
        - the calculated groundwater concentration is below the maximum permissible concentration set for drinking water by the Directive 98/83/EC of 0.1 µg/L;

The environmental risk is unacceptable for freshwater including sediment for the small equipment disinfection by dipping with releases *via* wastewater.

- For the small equipment disinfection by dipping with releases via manure/slurry spreading on land
  - the derived PEC/PNEC ratios for soil is above the trigger value of 1 for the efficient application rate for uses in veal calves breeding, and in sows breeding only if slurry is spread on grassland;
  - For all other housing types mentioned in the ESD-PT03 (2011), the derived PEC/PNEC ratios for soil is below the trigger value of 1 for the efficient application rate;
  - the calculated groundwater concentration is below the maximum permissible concentration set for drinking water by the Directive 98/83/EC of 0.1 µg/L for all housing type mentioned in the ESD-PT03 (2011);

The environmental risk is acceptable for the soil compartment (the only relevant compartment) for the small equipment disinfection with releases via manure/slurry spreading on land, except for uses in veal calves and sows breeding housings.

- For the small scale surface disinfection of veterinary areas with RTU wipes with releases *via* wastewater:
  - The derived PEC/PNEC ratios for all relevant environmental compartments is below the trigger value of 1, if small scale treated surface is considered (i.e. < 145m²);
  - the calculated groundwater concentration are below the maximum permissible concentration set for drinking water by the Directive 98/83/EC of 0.1 µg/L for all assessed uses.

The environmental risk is acceptable for all relevant environmental compartments for the use for small scale surface disinfection of veterinary areas with RTU wipes (i.e. treated surface < 145m²).

In conclusion, the uses of VANTOCIL TG as PT03 are cause for no concern for the environment only:

- **For the small equipment disinfection by dipping:**
  - **If no release to wastewater is allowed in order to prevent risk for the sediment compartment.**
  - **If releases *via* the manure/slurry is expected, VANTOCIL TG should not be released in veal calves breeding manure if spread on grassland or arable land, and in sows breeding if slurry is spread on grassland, in order to prevent risk for the soil compartment.**
- **For surface disinfection of veterinary areas with RTU wipes if the treated surface area is < 145 m².**

It should be noted, for the surface disinfection of veterinary areas with RTU wipes, that a dummy product was only proposed (*i.e.* a solution containing 20% w/w of PHMB). Hence, the biocidal product considered for the risk assessment is

not the RTU wipe, but the solution impregnating the wipes. As a consequence, a worst case approach was conducted considering the lack of data about the description of a RTU wipe (e.g. amount of impregnation fluid per tissue, size of the tissues, number of tissues required per m², etc) provided by the applicant at the substance approbation stage. Such data was not requested by eCa, as it was decided at a late stage of the process (*i.e.* WG-I-2015 decision) that surface disinfection uses should be included in the risk assessment of PHMB.

As a consequence, the following data must be provided at the product authorisation level for a more realistic risk assessment, as the applicant intended a dummy product at the substance approbation level, and as the environmental risk is acceptable for all relevant environmental compartments for the surface disinfection of veterinary areas with RTU wipes only if small scale treated surface is considered (*i.e.* < 290m²):

- The biocidal product should be the RTU wipe itself, not the impregnating solution;
- Data on the transfer rate from the wipe to the treated surface should be provided by the applicant;

2.2.3 ASSESSMENT OF ENDOCRINE DISRUPTOR PROPERTIES

PHMB (1600; 1.8) is not included in the priority list of substances for further evaluation of their role in endocrine disruption established within the Community Strategy for Endocrine Disrupters (COM (1999) 706, COM (2001) 262). Available evidence at this time indicates that PHMB (1600; 1.8) does not have endocrine-disrupting properties (classification criteria specified in Art. 5(3) of Regulation 528/2012 are not met, no effects on endocrine organs and/or reproduction were observed in standard toxicity studies to raise a concern for potential endocrine disruption).

2.3 OVERALL CONCLUSION OF THE RISK ASSESSMENT

The outcome of the assessment for PHMB (1600; 1.8) in product-type 1, 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 primary exposure		Human secondary exposure		Environment					
	Professional	Non professional	Worker	General public	STP	Aquatic compartment	Terrestrial compartment	Groundwater	Air	Secondary poisoning
Disinfection of small equipment (livestock farming environment) by dipping – Bactericide (efficacy not demonstrated for mycobacteria and bacteria spore)										
Dipping 0.2 % w/w a.s. Temperature 10 to 30°C, contact time of 30 minutes	Acceptable (1)	NR	**Not acceptable**	Acceptable (2)	Acceptable	**Not acceptable**	Acceptable (4), (5)	Acceptable	NR	NR
Ready to use wipes for small scale disinfection of vetenrinary areas										
Wiping 0.2% w/w a.s.	Acceptable	NR	NR	Acceptable (2), (3)	Acceptable	Acceptable (6)	Acceptable	Acceptable	NR	NR

NR: Not relevant.

Polyhexamethylene biguanide (Mn = 1600; PDI =1.8) (PHMB)	**Product-type 3**	**June 2015**

Conditions:

(1) Due tot he local effects, the product should be handled only by professionals adequately trained to use them and PPE have to be worn, in order to consider the risk as acceptable.

(2) Acceptable risk related to food consumption when disinfection is done in vinicity of food, livestock or any products of animal origins cannot be confirmed. Further data should be provided to demonstrate an acceptable risk (such as rinsing efficiency data).

(3) Where there is the potential of children to be exposed to residues of PHMB (1600; 1.8) after disinfection of surfaces with ready-to-use wipes, special attention shall be given to the potential risks. .

(4) Considering release via the wastewater only.

(5) Considering releases via manure/slurry spreading on land, risk for terrestrial compartment is acceptable except for veal calves breeding and for sows in individual pens or in groups.

(6) Only for small scale surface disinfection (treated surface < 145 m^2).

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 1.8
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 and 32289-58-0
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- (CH2)6- [C8H18N5Cl]n [C7H16N3Cl]m - terminal function

Possible terminal functions:
NH2 (amine)
C2H3N4 (cyanoguanide)
CH5N3Cl (guanidine)

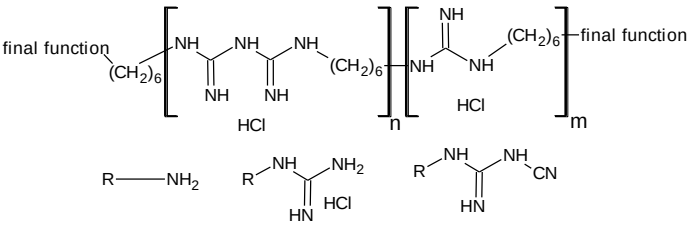
		range	average
m+n		2-40	11
n /(m+n) [biguanide %]		90.8 - 91.9%	91.3 %
m /(m+n) [guanide %]		8.1 - 9.2 %	8.6 %
Terminal function	amino	35% - 46%	39%
	guanidine	22% - 29%	25%
	cyanoguanide	31 - 39%	35%

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	426 g/L at 25°C (41% w/w)

temperature)	
Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1)	Methanol: 41% w/w at 25°C 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, point 4.2)	Not technically feasible for an enforcement method
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 required
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 NOAEL	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 effect	Rabbit – no developmental effects related to 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	Exposure estimates based on "worst" case assumptions regarding magnitude of the residue, transfer to food and consumption do not indicate a concern for human health when disinfection is not realized in vicinity of food, livestock or any products of animal origins Effectiveness of a rinsing step must be demonstrated.
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 population	No data available.
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	Concerning the dipping of farming equipments with VANTOCIL TG, the risks linked to the use of PHMB based products during the scenarios of mixing/loading and dipping, by professionnals, are considered as acceptable. Concerning the local dermal effects, the product should be handled by professionals only and PPE have to be worn, in order to consider the risk as accidental and managed. Concerning the wiping for small scale of disinfection of veterinary areas with ready to use wipes, due to the high maximum number of wipes can be used per day, the risk for systemic effects is acceptable for professionals and non professionals wiping with ready to use wipes for small scale disinfection.
Non-professional users	Non-professional or consumer direct exposure to treatment fluids containing PHMB used in the agriculture for PT03 applications is not relevant since these biocidal products are sold for professional use only.
Indirect exposure as a result of use	Concerning exposure by dermal contact with residues on equipments, the maximum rubbed area without risk of systemic effects would be 0.7 m^2. The situation where a person rubs 0.7 m^2 of equipements daily is realist. the risk is unacceptable. Concerning exposure of infant crawling on cleaned surface with wipe, the risk is considered to be unacceptable. Where there is the potential of children to be exposed to residues of PHMB (1600; 1.8) after disinfection of surfaces with ready-to-use wipes, special attention shall be given to the potential risks Exposure estimates based on "worst" case assumptions regarding magnitude of the residue, transfer to food and consumption do not indicate a concern for human health when disinfection is not realized in vicinity of food, livestock or any products of animal origins. Effectiveness of a rinsing step must be demonstrated. Furthermore, should applications be made for authorisation of products containing PHMB that may lead to residues in food or feed, Member States shall verify the need to set new or to amend existing maximum residue levels (MRLs) according to Regulation (EC) No 470/2009 or Regulation (EC) No 396/2005, and take any appropriate risk mitigation measures ensuring that the applicable MRLs are not exceeded.

[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 and temperature)	50°C, pH 4, 7 and 9: hydrolytically stable (<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.i. (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 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)
Leaching of PHMB from PT02 products	No Leaching studies conducted.

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 with terrestrial plants (Annex IIIA, point XIII.3.2)	Not required.

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 standardization 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)	$BCF_{aquat\ c\ organism}$ 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 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		
Small equipment (livestock farming environment)	VANTOCIL TG	Bacteria	SL*	20% w/w	Dipping (immersion)	-	-	Concentration of in-use solution (dipping): up to 0.2 % w/w active substance. The time delay is extracted from the efficacy data (30 minutes)	Professional use only
Small scale surfaces in veterinary areas			RTU wipes	0.2% w/w	Wiping	-	-	0.2 % w/w	-

* (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	Organisms controlled	Formulation		Application			In use concentration claimed (% w/v a.s. in the in-use solution)	In use concentration conclusion of the assessment of the efficacy data (% w/v a.s. in the in-use)	Remarks
			Type	Conc [% PHMB]	Method	Number	Interval			
Example 1: Animal housing	VANTOCIL TG	Bacteria,	SL*	20 % w/w	Dipping (footbath for footwear),	Dipping: 2 per visit (entry and exit)	Dipping: solution would be replenished when heavily soiled – assume once per day but usually less frequently.	Concentration of in-use solution (dipping): up to 0.2 % w/w active substance.	Efficacy not demonstrated	Professional use only
					Fogging	Fogging: see 'Interval'	Fogging: at turnaround between flocks or at intervals during the flock lifetime.	Concentration of in-use solution (fogging): up to 0.25 % w/v active substance.	Efficacy not demonstrated	Professional use only
Example 2: Veterinary establishments	VANTOCIL TG	Bacteria,	SL*	20 % w/w	Mopping, Wiping, Trigger Spray	1	One hour to several hourly intervals	Concentration of in-use solution: up to 0.1 % w/w active substance.	Efficacy not demonstrated	Professional use only
	READY TO USE SPRAY	Bacteria,	SL* (RTU SPRAY**)	0.1 % w/w	Trigger Spray	1	As required	Concentration of in-use solution: up to 0.1 % w/v active substance.	Efficacy not demonstrated	Professional and non professional
	READY TO USE WIPES	Bacteria,	SL* (RTU WIPES**)	0.1 % w/w	Wiping	1	As required	Concentration of in-use solution: up to 0.1 % w/v active substance.	Efficacy not demonstrated	Professional and non professional

Object and/or situation	Product name	Organisms controlled	Formulation		Application			In use concentration claimed (% w/v a.s. in the in-use solution)	In use concentration conclusion of the assessment of the efficacy data (% w/v a.s. in the in-use)	Remarks
			Type	Conc [% PHMB]	Method	Number	Interval			
Example 3: Teat dip	VANTOCIL TG	Bacteria,	SL*	20 % w/w	Dipping	2 dips per day	As per milking schedule	Concentration of in-use solution: up to 0.2 % w/v active substance.	Efficacy not demonstrated	Professional use only
	READY TO USE teat dips	Bacteria,	SL*	0.2 % w/w	Dipping	2 dips per day	As per milking schedule	Concentration of in-use solution: up to 0.2 % w/v active substance.	Efficacy not demonstrated	Professional use only

Note *: SL (Soluble concentrate): A liquid homogenous preparation to be applied as a true solution of the active substance after dilution with water.
Note **: READY TO USE SOLUTION in trigger spray bottle or impregnated into wet wipes

APPENDIX III: LIST OF STANDARD ABBREVIATIONS

List of standard terms and abbreviations (adapted from: (i) Guidelines and criteria for the preparation of PPP dossiers[14]; (ii) TNsG on Data Requirements[15]).

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

[14] 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

[15] 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
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
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

Stand. term / Abbreviation	Explanation
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
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

Stand. term / Abbreviation	Explanation
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)
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

Stand. term / Abbreviation	Explanation
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
ip	intraperitoneal

Stand. term / Abbreviation	Explanation
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

Stand. term / Abbreviation	Explanation
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
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

Stand. term / Abbreviation	Explanation
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
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

Stand. term / Abbreviation	Explanation
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
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

Stand. term / Abbreviation	Explanation
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})
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})

Stand. term / Abbreviation	Explanation
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
SBLC	shallow bed liquid chromatography

Stand. term / Abbreviation	Explanation
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

Stand. term / Abbreviation	Explanation
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
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
Tlm	median tolerance limit
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TMRC	theoretical maximum residue contribution

Stand. term / Abbreviation	Explanation
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
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

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 3: Veterinary hygiene

FINAL CAR

June 2015

eCA: FRANCE

This document is a list of all the studies submitted by the Applicant to support the PT03 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
B3-5	McGeechan P.	2005	Evaluation of the Bactericidal Efficacy of VANTOCIL IB. Arch UK Biocides Microbiology Group, Manchester, UK. Report no. 001. Not GLP, Unpublished	Arch Chemicals Inc	YES: Data on existin A.s. submitted for the first time for entry into Annex I.	ARCH B3-5-01		No
B3-5	McGeechan P.	2006 Revised 2008	Evaluation of the Bactericidal Efficacy of VANTOCIL TG. Arch UK Biocides Microbiology Group, Manchester, UK. Report no. 016. Not GLP, Unpublished.	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I.	ARCH B3-5-04		No
B3-5	McGeechan P.	2006 Revised 2008	Evaluation of the Bactericidal Efficacy of VANTOCIL TG. Arch UK Biocides Microbiology Group, Manchester, UK. Report no. 017. Not GLP, Unpublished.	Arch Chemicals Inc	YES: Data on existing a.s. submitted for the first time for entry into Annex I.	ARCH B3-5-05		No
IIIB5.10.08 (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: (EN1656 (2000) Chemical Disinfectants and antiseptics – Quantitative suspension test for the evaluation of the bactericidal activity of chemical disinfectants and antiseptics used in the veterinary area - Phase 2, step1)	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

Document/ Section	Author	Year	Description/Title	Owner	Data Protection	Doc IV Code	KS/ IUCLID/ Other	Study relied on
IIIB5.10.09 (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: (EN1656 (2000) Chemical Disinfectants and antiseptics – Quantitative suspension test for the evaluation of the bactericidal activity of chemical disinfectants and antiseptics used in the veterinary area - Phase 2, step1)	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