Cetyltrimethylammonium bromide

Cetyltrimethylammonium bromide is a cationic surfactant. It is widely used as topic antiseptics, and may be found in many household products such as shampoos, hair conditioning product and cosmetics. According to the Directive 67/548/EEC, this chemical is not classified. Nevertheless in one of the available MSDS related to CTB (%99), dangerous to the environment classification with the risk phrase (R50) and hazard symbol N was found. Its PBT status is unknown. (R50) substances are not necessarily PBT but under the new EU chemical legislation REACH; they will be recognized as potential PBT. An assessment of the PBT status of Cetyltrimethylammonium bromide using the algorithm described in the toolbox is explained below step by step.

Step 1: Substance identification

Identifiers on Cetyltrimethylammonium bromide have been obtained from the most recent reliable sources (chemfinder) which is listed in step1. The smiles notation for Cetyltrimethylammonium bromide was obtained from chemspider source. These identifiers are shown in Table1 below.

Identifier of Cetyltrimethylammonium bromide	
EINECS or ELINCS number	200-311-3
CAS name and CAS number	57-09-0
Name(s) in the IUPAC nomenclature or other international chemical name(s)	Hexadecyltrimethylammonium bromide
Other names (usual name, trade name, abbreviation)	Centimide; Cetab; Cetrimide; Cetrimonium bromide; Cetyltrimethylammonium Bromide; Hexadecyltrimethylammonium bromide; CTAB; CTABr; Hexadecanaminium, N,N,N-trimethyl-, bromide; HTAB; N-Hexadecyltrimethylammonium Bromide; N,N,N-trimethyl-1-Hexadecanaminium bromide;
Information related to molecular and structural formula of Cyclododecane	
Molecular Formula	$C_{19}H_{42}BrN$

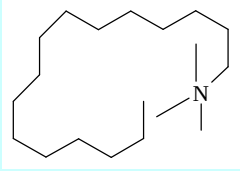
Structural formula	
Smiles Notation	[Br⁻].C(CCCC[N+](C)(C)C)CCCCCCCCCC

Table1: Cetyltrimethylammonium bromide identification parameters.

Step 2: Data needed for the assessment

These are divided into the followings:

- Physical-chemical properties (water solubility, Partition coefficient n-octanol/water, Soil Adsorption Coefficient (Koc/Kd), and Henry's Law Constant)
- Degradation, (biodegradation, half lives)
- Accumulation (BCF)
- Environmental Partitioning (MacKay)
- Ecotoxicity data of the substance (LC_{50}, NOEC)

Step 3: Collecting the available information and identifying the data gap

1- Information on the physical-chemical properties for Cetyltrimethylammonium bromide

The following table provides a summary of the

1. Chemical and physical properties required for the assessment as explained in the algorithm.
2. The available chemical and physical properties of Cetyltrimethylammonium bromide along with the source for these data. Upon conducting the search, no IUCLID data sheet was found for this compound.
3. The data gap which is highlighted as red in the table.

Required Property	Value	Source
Water solubility	0.3g/100ml water (20°C)	Chemfinder, chemspider and MSDS
Partition coefficient n-octanol/water	$LogK_{ow}$ = 2.26. Log Kow = 3.180 (estimated)	Literature: García et al (1994) Toxnet
Soil Adsorption Coefficient (Koc/Kd)	No measured log Koc value is available for CTB.	
Henry's Law Constant	No experimentally determined Henry's law constant information is available	

Table2: Physical chemical data available for Cetyltrimethylammonium bromide.

2- Accumulation data of Cetyltrimethylammonium bromide

According to MITI result (Biodegradation and Bioaccumulation Database on Existing Chemicals, Japan (MITI), see step 3 for link), bioaccumulation of CTB was studied with common carp (*Cyprinus carpio).* The mean BCF measured from this study was approximately 600. Although is not clear if the study was conducted according to EU-approved methods but this value is considered to give sufficient evidence that Cetyltrimethylammonium bromide is not highly bioaccumulative

3- Degradation data of Cetyltrimethylammonium bromide

The following table provides a summary of the

1. Degradation properties required for the assessment as explained in the algorithm.
2. The available degradation data of Cetyltrimethylammonium bromide along with the source for these data. As explained in the algorithm, in this step you have to make sure that the data studies were conducted according to EU-approved methods (e.g. those specified in Annexes V and VIII of Directive 67/548/EEC, or REACH Annex X methods) and in compliance with the principles of GLP.

3. The data gap which is highlighted as red in the table.

Required Property	Value	Source
Biodegradation	On the basis of the available data, Cetyltrimethylammonium bromide is considered to be readily biodegradable under aerobic conditions. (study conducted according to OECD TG 301C guideline)	MITI Literature; García et al (1994) and Guo Ying(2006
Half lives-$t_{1/2}$		
1-Hydrolysis as a function of pH	No experimental aquatic degradation data are available for Cetyltrimethylammonium bromide	
2-Photolysis (Atmospheric OH Rate Constant)	No experimental data are available for CTB, only estimated one Rate Cons = 3.42E-11 cm^3/molecule-sec at 20 C^0	Toxnet

Table3: Degradation data available for Cetyltrimethylammonium bromide.

4- Environmental Partitioning (MacKay)

Not found. It will be calculated using EPIWIN programe, see below.

5- Aquatic toxicity information of Cetyltrimethylammonium bromide

The results of toxicity tests carried out with Cetyltrimethylammonium bromide (%99) on fish (acute), aquatic invertebrates (acute), have been collated from MSDS and literature (M. T. Gracia et al (1994) and Ying (2006)). The data are summarised below in Table 4. In the MSDS, only the values of the LC50 and EC50 are reported nor the tests neither the methods. Therefore, these data will not be reliable due to the lack of information with regard to its method used. Gracia et al (1994) found LC_{50}(24h) of 0.22 mg/l for *Daphnia* in a test described in the Frenach norm test NF-T90-30. However, test conditions for the whole set of substances tested were not provided and therefore the result is considered as not valid.

Required Property	Value	Source
Fish Acute toxicity to fish (96hrs LC_{50}) mg/l Long term toxicity to fish (28days NOEC) mg/l	LC_{50}(96h) > 0.3 mg/l Data are not reliable No data available	MSDS
Daphnia Acute toxicity to Daphnia (48hrs EC_{50}) mg/l Long term toxicity to Daphnia (21days NOEC) mg/l	EC_{50} = 0.03mg/l Data are not reliable (24hrs, LC50) = 0.22mg/l No data available	MSDS Gracia et al.
Algae Acute toxicity to algae (72hrs EC_{50}) mg/l	No data available	

Table4: Aquatic toxicity data available for Cetyltrimethylammonium bromide

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Step 4: Filling the data gap by using QSAR

In this step the above endpoints (both the available and not) will be predicted using QSARs tools and software (EPIWIN, Danish(Q)SAR data base and PBT profiler). The reason for doing this is to compare the QSAR results with the experimental one to identify the accuracy of the QSAR.

1- Results obtained by using EPIWIN

Table 5 provides the predicted values for the above endpoints using EPIWIN software along with the name of the program used. The output obtained by EPIWIN for each end point is given. Also included are explanations which could be obtained by clicking on a link to view.

Required Property	EPI QSAR Programme	Predicted Value
Water solubility	WSKOW (result output)	9.651 mg/l at 25 C
Partition coefficient n-octanol/water	KOWWIN	Log K_{ow} = 3.18

Bioconcentration Factor (BCF)	BCFWIN	LogBCF = 1.85 (BCF = 70.79)
Soil Adsorption Coefficient (Koc/Kd)	(PCKOCWIN)	K_{oc} = $2.21*10^5$
Henry's Law Constant	HENRYWIN	$2.32*10^{-10}$ atm-m^3/mole
Half lives-$t_{1/2}$		
1-Hydrolysis as a function of Ph	HYDROWIN	Can not be estimated
2-Photolysis (Atmospheric OH Rate Constant)	AOPWIN	Atmospheric Oxidation Rate Constant = 34.1642 E-12 cm^3/molecule-sec Half-Life = 3.757 hrs
(Atmosph. Oxidation, Ozone)	AOPWIN	No Ozone Reaction Estimation
Biodegradability		
BIOWIN1	BIOWIN	0.6674 (Biodegrades fast)
BIOWIN2	BIOWIN	0.6499 (Does not biodegrade fast)
BIOWIN3 (Ultimate biodegradation)	BIOWIN	2.8272 (weeks-months)
BIOWIN4 (Primary Biodegradation)	BIOWIN	3.6049 (days-weeks)
BIOWIN5	BIOWIN	0.4481(Not readily Degradable)
BIOWIN6	BIOWIN	0.623(Not readily Degradable)
BIOWIN7	BIOWIN	-0.1644 (Does not biodegrade fast)
Ready Biodegradability Prediction:	BIOWIN	NO
Environmental Partitioning		
(MacKay)	EPI V3.2 (Results output)	Level III Fugacity Model: Mass Amount (percent) / Half-Life (hr) / Emissions (kg/hr) Air 0.142 / 7.5 / 1000 Water 15.2 / 900 / 1000 Soil 84.1 / 1.8e+003 / 1000 Sediment 0.522 / 8.1e+003 / 0
Fish Acute toxicity to fish (96hrs LC50) mol/l Long term toxicity (28days NOEC) mol/l	ECOSAR	LC_{50} (96hrs) = 2.214 mg/l LC_{50}(14 days) = Can not be estimated
Daphnia Acute toxicity to Daphnia (48hrs EC_{50}) mol/l Long term toxicity (21days NOEC) mol/l	ECOSAR	LC_{50} (48hrs) = 3.508 mg/l EC_{50}(16-day)= Can not be estimated
Algae Acute toxicity to Algae (72hrs EC_{50}) mol/l	ECOSAR	EC_{50} (96-hr) = Can not be estimated

Table5: EPIWIN predictions of the required endpoints

2- Results obtained from Danish(Q)SAR database

Unfortunately, no data was found for Cetyltrimethylammonium bromide using the Danish(Q)SAR database. The search revealed no matches; however other QSAR databases could be used such as chemspider or PBT profiler. Chemspider provides an online access to structure based predictions of systematic identifiers and physicochemical based predictions. You only need to type the name of your chemical, click on search and the predictions result will appear. The problem in using this source is that information about the QSARs models used for the prediction is not available. On the other hand, PBT Profiler is a no-cost computer based tool to screen chemicals lacking experimental data in order to help identify if they are potentially may persist, bioaccumulate, and be toxic to aquatic life, i.e., PBT chemicals. The good thing with PBT profiler, is that it provides a straight-forward estimate of persistence, bioaccumulation, and aquatic toxicity based on widely accepted criteria along with the explanation of the results. It is important to know that the PBT Profiler is a screening level predictive tool and cannot be used for all chemical substances.

PBT profiler estimates that CTB is persistent and not accumulative. The toxicity of CTB could not be estimated by PBT profiler.

Step 5: Assess your substance to identify whether it is PBT or vPvB

Is your substance persistent? (Degradation properties)

The assessment of persistence is based on the degradation (biotic and chemical) and half life data. As seen above, no measured data are available on the rate of degradation of Cetyltrimethylammonium bromide in the environment. Where no measured environmental degradation data are available, the predicted one can be used as a screen to indicate persistence.

The predicted rate constant and estimated half-life for the reaction of hydroxyl radicals with Cetyltrimethylammonium bromide in the atmosphere indicated that when Cetyltrimethylammonium bromide is released to the atmosphere is likely to be **degraded** (not persistence) by this fate process. Moreover no data was available with regards to aquatic degradation. As a result a definitive conclusion cannot be reached

regarding persistence of Cetyltrimethylammonium bromide in the environment. Further testing would be needed to determine the rate of aquatic degradation. However, the PBT Profiler has estimated that Cetyltrimethylammonium bromide is expected to be found predominantly in soil and its persistence estimate is based on its transformation in this medium. Its half-life in soil, 75 days, exceeds the EPA criteria of >= 2 months but not the EU one (>120 days). As expected, this result is similar to EPIWIN v3.2 estimate for Level III Fugacity Model (since PBT profile uses EPIWINV3.2 for this). Therefore, Cetyltrimethylammonium bromide is estimated to be persistent in the environment.

With regard to the biotic degradation assessment, the ready biodegradability result can be used to determine if a substance meets the P criteria. Based on the biodegradability screening tests available (MITI and Gracia et al), CTB is considered to be readily biodegradable at low concentration (2.5mg/l). However at high concentration (10mg/l) a very slow and incomplete degradation were observed. On the other hand the BIOWIN v4.02 gives an overall prediction that the substance is **not readily biodegradable**. However, some degradation is expected to occur according to the models.

As a conclusion, based on the half life in soil prediction results (PBT profile and EPIWIN), Cetyltrimethylammonium bromide is considered to meet the screening criteria for persistence based on EPA criteria.

Is your substance bioaccumlative?

The available study provides a BCF of 600 for *Cyprinus carpio*. BCFWIN v2.17 and PBT profiler predicts BCF of 71. These BCF values do not exceed the bioconcentration criteria and suggest the potential for bioconcentration in aquatic organisms is low. Therefore Cetyltrimethylammonium bromide is considered not fulfilling the B criterion.

Based on the above measured and estimates data, Cetyltrimethylammonium bromide is not expected to bioaccumulate in the food chain and therefore is not considered to meet the screening criteria for bioaccumulation.

Is your substance toxic to the environment organisms?

The acute toxicity values L(E)C50 for *fish and Daphnia reported in MSDS* were 0.3 mg/l and 0.03 mg/l respectively. The EC50 value for Daphnia is clearly below 0.1 mg/l and therefore it is considered reasonably to conclude that the EU criteria for toxicity may be met. However, Ying claimed that most surfactants are not acutely toxic to organisms at environmental concentrations and their aquatic chronic toxicity occurs usually at concentrations above than 0.1mg/l apart of alkylphenols surfactants.

With regards to the predictions values, ECOSARv0.99 predicts acute L(E)C_{50} values for fish and Daphnia (LC_{50}(96h) of 2.214 mg/l for fish and LC_{50}(48hrs) of 3.508mg/l for Daphnia). These acute toxicity predictions are higher than the measured one. No other acute or chronic toxicity estimates of Cetyltrimethylammonium are freely available to compare with.

In conclusion, based on the available toxicity data, Cetyltrimethylammonium bromide is not potentially considered fulfilling the T screening criterion. Further tests are required and needed for the assessment.

Is your chemical classified as potential PBT?

Based on the available data, the substance has been shown to have a half-life of 75 <120 days in soil. Therefore the substance does not fulfil the P-criterion. The estimated BCF for the substance in fish is 72. Therefore the substance does not fulfil the B-criterion. The estimated aquatic toxicity data for Cetyltrimethylammonium bromide are clearly above 0.1mg/l, therefore the substance does not fulfil the T-criterion.

Therefore on the basis of the predictions data the substance is not considered as a PBT substance under EU criteria but it is considered as P under the EPA criteria.

What is the preferred environmental compartment of your chemical? (Environmental Distribution)

Adsorption:

The substance has a high K_{oc} value of $2.21*10^5$ indicating that the substance is likely to adsorb onto soil. This is also in agreement with the Mackay level III predictions, which shows that that soil is the preferred environmental compartment (85%). Therefore the persistence of Cetyltrimethylammonium bromide in soil is probably more significant than the persistence in water.