

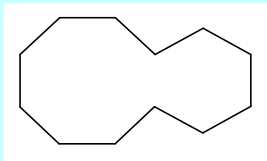
## Cyclododecane

Cyclododecane substance was classified as PBT according to the ECB. This makes it a good example to validate the algorithm since the aim of the algorithm is to be used as screening for potential PBT.

An assessment of the PBT status of Cyclododecane using the algorithm described in the toolbox is explained below step by step.

### Step 1: Substance identification

Identifiers on cyclododecane have been obtained from the most recent reliable sources ([www.chemfinder.com](http://www.chemfinder.com)) which is listed in step1. The smiles notation for cyclododecane was obtained from [chemspider](http://chemspider) source. These identifiers are shown in Table1 below.

<b>Identifier of Cyclododecane</b>	
EINECS or ELINCS number	206-033-9
CAS name and CAS number	294-62-2
Name(s) in the IUPAC nomenclature or other international chemical name(s)	Cyclododecane
Other names (usual name, trade name, abbreviation)	Cyclododecane
<b>Information related to molecular and structural formula of Cyclododecane</b>	
Molecular Formula	C <sub>12</sub> H <sub>24</sub>
Structural formula	
Smiles Notation	C1CCCCCCCCCCC1

**Table1:** Cyclododecane 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<sub>50</sub>, NOEC)

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

#### 1- Information on the physical-chemical properties for Cyclododecane

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 Cyclododecane 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
Water solubility	10 mg/l at 20°C (study not evaluated so the data can not be reliable)	The solubility in water is reported in the industry <a href="#">IUCLID</a> .
Partition coefficient n-octanol/water	No measured logK <sub>ow</sub> is available. Log K <sub>ow</sub> = 6.7 (calculated)	IUCLID
Soil Adsorption Coefficient (Koc/Kd)	No measured log Koc value is available for Cyclododecane.	
Henry's Law Constant	No experimentally determined Henry's law constant information is available only calculated.  1.54atm m <sup>3</sup> /mol	

**Table2:** Physical chemical data available for Cyclododecane.

#### 2- Accumulation data of Cyclododecane

According to MITI result (Biodegradation and Bioaccumulation Database on Existing Chemicals, Japan (MITI), see step 3 for link), bioaccumulation of cyclododecane was studied with common carp (*Cyprinus carpio*). The mean BCF measured from this study was approximately 13,700. Although it is not clear if the study was conducted according to EU-approved methods but this value is considered to give sufficient evidence on a very high bioaccumulation of Cyclododecane.

### 3- Degradation data of Cyclododecane

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 Cyclododecane along with the source for these data. As explained in the algorithm, the data should be reliable.
3. The data gap which is highlighted as red in the table.

Required Property	Value	Source
Biodegradation	On the basis of the available data, Cyclododecane is considered to be not readily biodegradable. (study conducted according to OECD TG 301C guideline)	MITI and IUCLID
<b>Half lives-t<sub>1/2</sub></b>		
1-Hydrolysis as a function of pH	No experimental aquatic degradation data are available for Cyclododecane.	IUCLID
2-Photolysis (Atmospheric OH Rate Constant)	No experimental data are available for Cyclododecane only calculated one Rate Cons = 1.67 *10 <sup>-11</sup>	

**Table3:** Degradation data available for Cyclododecane.

### 4- Environmental Partitioning (MacKay)

According to calculations using a Mackay level I fugacity model, Cyclododecane will, after release to a specific environmental compartment, distribute in the environment as following:

Air: 7.201 %, Soil: 47.882 %, Sediment: 44.764 5, Water: 0.122 %, Biota: 0.031 %.

(source from IUCLID).

## 5- Aquatic toxicity information of Cyclododecane

The results of toxicity tests carried out with Cyclododecane on fish (acute), aquatic invertebrates (acute and chronic), and algae (acute/chronic) have been collated from IUCLID. The data are summarised below and in Table 4.

Required Property	Value	Source
<b>Fish</b> Acute toxicity to fish (96hrs LC <sub>50</sub> ) mg/l  Long term toxicity to fish (28days NOEC) mg/l	LC <sub>50</sub> (96h) > 1 mg/l Data are not reliable  No data available	IUCLID
<b>Daphnia</b> Acute toxicity to Daphnia (48hrs EC <sub>50</sub> ) mg/l  Long term toxicity to Daphnia (21days NOEC) mg/l	No data available  No data available	
<b>Algae</b> Acute toxicity to algae (72hrs EC <sub>50</sub> ) mg/l	EC <sub>50</sub> >2 mg/l (Study conducted according to Directive 87/302/EEC following GLP. However it is not evaluated and therefore is considered as not valid.	IUCLID and PBT summary sheet for Cyclododecane.

**Table4:** Aquatic toxicity data available for Cyclododecane.

### 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 listed in step 4 (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 programme used. The output obtained by EPIWIN for each end point is

given. Also included are explanation which in the toolbox would be obtained by clicking on a link to view.

Required Property	EPI QSAR Programme	Predicted Value																				
Water solubility	WSKOW <a href="#">(result output)</a>	0.1075 mg/l at 25 C																				
Partition coefficient n-octanol/water	KOWWIN	Log K <sub>ow</sub> = 6.12																				
Bioconcentration Factor (BCF)	BCFWIN	LogBCF = 4.014 (BCF = 1.033e+004)																				
Soil Adsorption Coefficient (K <sub>oc</sub> /K <sub>d</sub> )	(PCKOCWIN)	K <sub>oc</sub> = 6513																				
Henry's Law Constant	HENRYWIN	1.54 atm·m <sup>3</sup> /mole																				
<b>Half lives-t<sub>1/2</sub></b>																						
1-Hydrolysis as a function of pH	HYDROWIN	Can not be estimated																				
2-Photolysis (Atmospheric OH Rate Constant)	AOPWIN	Atmospheric Oxidation Rate Constant = 16.9566 E-12 cm <sup>3</sup> /molecule-sec Half-Life = 7.569 hrs																				
(Atmosph. Oxidation, Ozone)	AOPWIN	No Ozone Reaction Estimation																				
<b>Biodegradability</b>																						
BIOWIN1	BIOWIN	0.6674 (Biodegrades fast)																				
BIOWIN2	BIOWIN	0.6499 (biodegrades fast)																				
BIOWIN3 (Ultimate biodegradation)	BIOWIN	2.8272 (weeks)																				
BIOWIN4 (Primary Biodegradation)	BIOWIN	3.6049 (weeks)																				
BIOWIN5	BIOWIN	0.4481(Not readily Degradable)																				
BIOWIN6	BIOWIN	0.623(Biodegrades fast)																				
BIOWIN7	BIOWIN	-0.1644 (Does not biodegrade fast)																				
Ready Biodegradability Prediction:	BIOWIN	NO																				
<b>Environmental Partitioning</b>																						
(MacKay)	EPI V3.2 <a href="#">(Results output)</a>	Level III Fugacity Model: <table border="1"> <thead> <tr> <th></th> <th>Mass Amount (percent)</th> <th>Half-Life (hr)</th> <th>Emissions (kg/hr)</th> </tr> </thead> <tbody> <tr> <td>Air</td> <td>1.21</td> <td>15.1</td> <td>1000</td> </tr> <tr> <td>Water</td> <td>7.07</td> <td>360</td> <td>1000</td> </tr> <tr> <td>Soil</td> <td>31.5</td> <td>720</td> <td>1000</td> </tr> <tr> <td>Sediment</td> <td>60.2</td> <td>3.24e+003</td> <td>0</td> </tr> </tbody> </table>		Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)	Air	1.21	15.1	1000	Water	7.07	360	1000	Soil	31.5	720	1000	Sediment	60.2	3.24e+003	0
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<b>Fish</b> Acute toxicity to fish (96hrs LC50) mol/l Long term toxicity (28days NOEC) mol/l	ECOSAR	LC <sub>50</sub> (96hrs) = 0.017 mg/l (not reliable as chemical is outside the model domain, log Kow>5.0)  LC <sub>50</sub> (14 days) = 0.058mg/l (not reliable because Chemical may not be soluble enough to measure this predicted effect)  ChV(30days)= 0.004 mg/l, where CHV is chronic toxicity value
<b>Daphnia</b> Acute toxicity to Daphnia (48hrs EC <sub>50</sub> ) mol/l Long term toxicity (21days NOEC) mol/l	ECOSAR	LC <sub>50</sub> (48hrs) = 0.024 mg/l (not reliable as chemical is outside the model domain, log Kow>5.0)  EC <sub>50</sub> (16-day)= 0.007 mg/l
<b>Algae</b> Acute toxicity to Algae (72hrs EC <sub>50</sub> ) mol/l	ECOSAR	EC <sub>50</sub> (96-hr) = 0.019 mg/l

**Table5:** EPIWIN predictions of the required endpoints

## 2- Results obtained from Danish(Q)SAR database

Unfortunately, no data was found for Cyclododecane 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 cyclododecane is persistent, bioaccumulative and toxic.

### 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 data. As seen above, no measured data are available on the rate of degradation of Cyclododecane 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 Cyclododecane in the atmosphere indicated that when Cyclododecane 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 Cyclododecane in the environment. Further testing would be needed to determine the rate of aquatic degradation.

In this case the ready biodegradability result can be used to determine if a substance meets the P criteria. 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. Moreover, the PBT Profiler has estimated that Cyclododecane is expected to be found predominantly in sediment and its persistence estimate is based on its transformation in this medium. Its half-life in sediment, 140 days, does not **exceed the EU criteria of  $\geq 180$  days but exceed the EPA criteria of  $\geq 2$  months** . Therefore, Cyclododecane is estimated to be persistent in the environment.

As a conclusion, based on the ready biodegradability prediction results (Biowin) and PBT profiler, **Cyclododecane is considered to meet the screening criteria for persistence.**

### **Is your substance bioaccumulative?**

No measured BCF data are available. The potential for bioaccumulation was therefore assessed on the basis of a calculated BCF.

BCFWIN v2.17 predicts BCF of  $1.033 \times 10^4$  ( $>5000$ , very accumulative) based on logKow of 6.12. Moreover, the estimated bioconcentration factor (BCF) for Cyclododecane from PBT

profiler is 10000, which exceeds the BCF criteria. BCF estimate from chemspider for Cyclododecane is also in consistent with BIOWIN and PBT profiler.

Based on the above estimates, Cyclododecane is expected to bioaccumulate in the food chain and therefore is considered to meet the screening criteria for bioaccumulation.

### **Is your substance toxic to the environment organisms?**

No ecotoxicity data are available for fish or Daphnia of Cyclododecane and the results of the available acute toxicity to algae studies are not considered reliable. Furthermore, QSARs predict acute L(E)C<sub>50</sub> values for fish and Daphnia (LC<sub>50</sub>(96h) of 0.017 mg/l for fish and LC<sub>50</sub>(48hrs) of 0.024mg/l for Daphnia). However, these acute toxicity predictions are not reliable as chemical is outside the model domain. Only the chronic toxicity data for Daphnia and fish (EC<sub>50</sub>(16-day)= 0.007 mg/l, CHV(30days = 0.04mg/l ) and acute toxicity for Algae (EC<sub>50</sub> (96-hr) = 0.019 mg/l ) can be considered. These values are clearly below 0.1mg/l. It is therefore considered reasonably to conclude that the EU criteria for toxicity may be met. This is in consistent with PBT profiler ecotoxicity estimate for Cyclododecane.

In conclusion, in the absence of reliable toxicity data, Cyclododecane is considered fulfilling the T screening criterion based on the QSAR predictions.

### **Is your chemical classified as potential PBT?**

Based on the predictions data, the substance has been shown to have a degradation (mineralization) half-life of >180 days in marine sediment and to be not readily biodegradable. Therefore the substance fulfils the P-criterion. The estimated BCF for the substance in fish is 10.330. Therefore the substance fulfils the B-criterion. The estimated aquatic toxicity data for Cyclododecane are clearly below 0.1mg/l, therefore the substance fulfils the T-criterion.

Therefore on the basis of the predictions data the substance should be considered as a potential PBT substance.

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

**Adsorption:**

The substance has a high  $K_{ow}$  value of 1318256 and relatively low water solubility (0.175 mg/l).

These properties indicate that, in water, the substance is likely to adsorb onto sediment. This is also in agreement with the Mackay level III predictions which shows that that sediment is the preferred environmental compartment (60%). Therefore the persistence of Cyclododecane in sediment is probably more significant than the persistence in water.