Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

Cybutryne

Product type: 21

ECHA/BPC/065/2015

Adopted

17 June 2015

Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland | Tel. +358 9 686180 | Fax +358 9 68618210 | echa.europa.eu

Opinion of the Biocidal Products Committee

on the application for approval of the active substance Cybutryne for product type 21

In accordance with Article 89(1) of Regulation (EU) No 528/2012 of the European Parliament and of the Council 22 May 2012 concerning the making available on the market and use of biocidal products (BPR), the Biocidal Products Committee (BPC) has adopted this opinion on the non-approval in product type 21 of the following active substance:

Common name:	**Cybutryne**
Chemical name(s):	***N*^{2}-tert-butyl-*N*^{4}-cyclopropyl-6-methylthio-1,3,5-triazine-2,4-diamine**
EC No.:	**248-872-3**
CAS No.:	**28159-98-0**
Existing active substance	

This document presents the opinion adopted by the BPC, having regard to the conclusions of the evaluating Competent Authority. The assessment report, as a supporting document to the opinion, contains the detailed grounds for the opinion.

Process for the adoption of BPC opinions

Following the submission of an application by Ciba Specialty Chemicals Inc. (which was taken over during the evaluation by BASF in 2009) on 11 September 2006, the evaluating Competent Authority the Netherlands submitted an assessment report and the conclusions of its evaluation to the Commission on 7 April 2011. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC and the Commission via the Biocides Technical Meetings. Revisions agreed upon were presented and the assessment report and the conclusions were amended accordingly.

Information on the fulfilment of the conditions for considering the active substance as a candidate for substitution was made publicly available at ECHA's website on 10 February 2014, in accordance with the requirements of Article 10(3) of Regulation (EU) No 528/2012. Interested third parties were invited to submit relevant information by 11 April 2014.

Adoption of the BPC opinion

Rapporteur: the Netherlands

The BPC opinion on the non approval of the active substance Cybutryne in product type 21 was adopted on 17 June 2015.

The BPC opinion takes into account the comments of interested third parties provided in accordance with Article 10(3) of the BPR.

The BPC opinion was adopted by consensus.

Detailed BPC opinion and background

1. Overall conclusion

The overall conclusion of the BPC is that Cybutryne in product type 21 may not be approved. The detailed grounds for the overall conclusion are described in the assessment report.

2. BPC Opinion

2.1. BPC Conclusions of the evaluation

a) Presentation of the active substance including the classification and labelling of the active substance

This evaluation covers the use of Cybutryne in product type 21. Cybutryne acts by affecting the electron transport in the photosystem of algae and plants. This results in reduced CO_2 uptake and decreased carbohydrate production which inhibits the growth in target organisms. Specifications for the reference source are established.

The physico-chemical properties of the active substance and biocidal product have been evaluated and are deemed acceptable for the appropriate use, storage and transportation of the active substance and biocidal product.

Validated analytical methods are available for the active substance as manufactured and for the significant impurities. Validated analytical methods are required and available for drinking and sea water, marine sediment, fish and shellfish.

No harmonised classification for Cybutryne is available. The proposed classification and labelling for Cybutryne according to Regulation (EC) No 1272/2008 (CLP Regulation) is:

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Skin Sens. 1, H317 Aquatic Acute 1, H400 Aquatic Chronic 1, H410
Labelling	
Pictograms	GHS07, GHS09
Signal Word	Warning
Hazard Statement Codes	H317: May cause an allergic skin reaction H410: Very toxic to aquatic life with long lasting effects
Specific Concentration limits, M-Factors	M = 100 for Aquatic Acute 1 M = 1000 for Aquatic Chronic 1

b) Intended use, target species and effectiveness

Cybutryne is to be used as the active component in antifouling paints in product type 21.

The active ingredient Cybutryne present in the biocidal PT21 antifouling product is an algicide. The antifouling product is applied to hulls of ships (commercial deep sea and coastal vessels only >25m in length), to be used by professionals only. The active ingredient Cybutryne is an antifoulant against marine algal species causing soft fouling. The active ingredient Cybutryne from the antifouling paint affects the electron transport in the photosystem of algae and plants. This results in reduced CO_2 uptake and decreased carbohydrate production which inhibits the growth in target organisms.

The efficacy of the antifouling paint was shown in a raft test of panels applied with a

suitable anti-corrosive primer, a tie coat and the antifoulant. The settlement and growth of marine fouling organisms were determined. Besides, the antifouling performance of the antifouling product applied on a vessel sailing in a heavy fouling area during 34 months is shown.

c) Overall conclusion of the evaluation including need for risk management measures

At the 55th meeting of the representatives of Member State Competent Authorities for the implementation of Regulation (EU) No 528/2012 it was agreed to utilise generic conditions in approval regulations for all product type 21 substances evaluated as part of the EU Review Programme[1].

Human health

Cybutryne did not have an acute toxic potential. It was non-irritating to the skin and eye, but is considered to be a skin sensitizer (Xi, R43 (according to Directive 1999/45/EC) or Skin Sens. 1, H317 (according to Regulation 1272/2008/EC)). Toxicokinetic studies with Cybutryne show that the systemically available (absorbed) dose was considered to be at least 50%. Cybutryne is predominately excreted via faeces, and is distributed mainly into blood and highly perfused organs. In the 7-day repeated dosing oral study no plateau was reached, indicating possible accumulation at (semi-) chronic exposure. In repeated dose studies in rat with Cybutryne, the predominant effects were reduced food consumption and body weight at higher doses. Neither genotoxic nor a carcinogenic potential was identified in a number of studies, the latter based on structurally related Terbutryn. In the 1-year dog study with Terbutryn a local effect was noted in the intestine, (irritation and enterotoxicity), which cannot be excluded for Cybutryne in chronic studies. Form this study, a NOAEL of 2.7 mg/kg bw/day was derived, in which the effects in the gastro-intestinal tract were considered local. Reproductive performance in a 2-generation rat study was unaffected by treatment with Cybutryne. In addition, no teratogenic potential was detected in developmental toxicity studies with rats and rabbits. A NOAEL of 15 mg/kg bw/day was derived from a rabbit teratogenicity study, based on marked maternal toxicity, i.e. body weight loss and reduced food consumption, was seen at 45 mg/kg bw/day. Based on the NOAEL derived from the repeated dose studies which were in the same range, no effect of time duration was concluded. Therefore, one overall AEL was derived for short-, medium- and long-term deruation. The AEL was derived from the NOAEL of 15 mg/kg bw/day, including a factor of 100 for inter- and intra-species variations, and a correction for oral absorption (50%), resulting in a value of 0.08 mg/kg bw/day.

The table below summarises the exposure scenarios assessed.

Summary table: human health scenarios	
Scenario **Primary or secondary exposure: exposed group** **Description of scenario**	**Acceptable or unacceptable**
Airless spraying Primary exposure: Professionals Spraying antifouling paint on a boat on a shipyard	Acceptable with protective gloves and clothing (double coverall, 1% clothing penetration)

[1] See document: Antifouling (PT21); the way forward for the management of active substances and the authorisation of biocidal products. (CA-March14-Doc.4.2 - Final).

Painter using brush and roller Primary exposure: Professionals Applying antifouling paint with brush and roller in a shipyard, spot appliation	Acceptable with protective gloves and clothing (impermeable coverall, 10% clothing penetration)
Mixing and loading (Potman) Primary exposure: Professionals The potman works together with the sprayer.	Acceptable with protective gloves and clothing (impermeable coverall, 5% clothing penetration)
Removal of paint (Blast worker) Primary exposure: Professionals performs a total or partial removal of the expired coating from the ship hull using abrasive or high-pressure water.	Acceptable with protective gloves and clothing (impermeable coverall, calculation based on actual data values)
Grit filler Primary exposure: Professionals The grit filler works together with the person removing the paint.	Acceptable with protective gloves and clothing (impermeable coverall, 5% clothing penetration)
Bystanders Secondary exposure: Professionals Workers at the shipyard where spray application of antifouling paint is used	Acceptable with warning sign*
Residues Secondary exposure: Professionals General public drinking water or eating fish/seafood.	Acceptable

*To protect bystanders in the shipyard, the area where spray painting is performed should be labelled with "Unprotected persons should be kept out of treatment areas".

No unacceptable human health risks were identified for professional users of antifouling paint containing 2.3% Cybutryne provided personal protective equipment (PPE) is used.

Access of unauthorised persons to professional shipyards is considered to be unlikely. To keep unauthorised persons from entering the treatment area, the product label should carry the phrase "Unprotected persons should be kept out of treatment areas".

Based on the environmental exposure assessment, no relevant residues are expected in matrices for human consumption. Although not considered relevant, a reverse reference scenario was performed to calculate the amount of fresh fish eaten by a person every day of his life before the Acceptable Daily Intake (ADI) is exceeded, which resulted in 171 kg wet fish a day for a lifetime. This value is considered to be worst-case for shellfish as the value for wet fish is considered for a fish containing 5% fat (in which Cybutryne could potentially accumulate).

Environment

The table below summarises the exposure scenarios assessed. Use of Cybutryne containing antifouling paints is limited to commercial marine vessels. Therefore expected routes of environmental exposure are limited to releases into marine waters in either harbours, the wider environment, shipping lanes or open sea. The main routes of entry into the environment is *via* leaching of the active substance during service life and *via* discharge from docks or marine lifts as a result of application and removal of antifouling. Thus the dominant receiving compartment will be sea water.

Summary table: environment scenarios	
Scenario	**Description of scenario including environmental compartments**
	Commercial ships
New building – application	Direct releases to marine surface water following spray application by professionals
Maintenance and repair – application and removal of paint	Direct release to marine surface water following spray application and high pressure washing by professionals
In-service life stage	OECD-EU commercial harbour and wider environment OECD-EU shipping lane OECD-EU open sea
Aggregated exposure	Application and in-service releases were summed up. Removal and in-service releases were summed up.
For all scenarios evaluated the exposure is estimated within the harbour as well as adjacent to the harbour (defined as the wider environment). The model MAMPEC is used to estimate the exposure. Worst case and typical case situations were evaluated.	

Marine compartment (including sediment)
A tier one assessment based on a 0.9 application factor (the application factor aims to correct the exposure calculation for the market share of cybutryne in PT 21 products) showed unacceptable risks.

For the in-service life stage an unacceptable risk is identified in sediments in the wider environment outside commercial harbours, in water and sediments of commercial harbours. According to the risk characterisation, no unacceptable risks are identified for water and sediment in the shipping lane or in open sea.

For aggregated exposure from in service use, maintenance and repair, an unacceptable risk was identified in the commercial harbour and wider environment including typical case situations where removal releases were summed up with service-life releases.

Since multiple antifouling active substances are in use both in Europe and worldwide, an application factor of 0.2 seems to be more appropriate. The MAMPEC calculations were repeated with the lower application factor of 0.2, a risk was estimated in commercial harbours , while an acceptable risk was estimated in the wider environment.

Historical monitoring data, however, show significantly higher concentrations in the marine environment than expected by using the 0.2 application factor.

Monitoring studies show that Cybutryne is detected in marine waters in harbours, but also at more distant areas (coastal and/or transitional water) at concentrations between < 1 and 1700 ng/L and in sediments at concentrations between 0.07 and 42 ng/g dw (median 0.46 ng/g dw) of the United Kingdom, France, Spain, Greece, the Netherlands, Switzerland, Germany, Portugal and Sweden. These monitoring concentrations are above the predicted no-effect concentration (PNEC) for the marine and freshwater environments, which include open sea and shipping lane.

The main source of Cybutryne in most of these areas can only be explained by the use as an antifouling agent. Back-calculation in MAMPEC, based on these monitoring data, indicates an application factor closer to 0.9.

The MAMPEC model in this case underestimates the actual concentrations in various compartments. Monitoring data should be considered as higher tier data in this respect. It is known from laboratory studies that the substance is persistent and this has been confirmed by the monitoring data.

Although it is claimed that a low volume of Cybutryne is placed on the European market today and only for commercial ships, there is no guarantee or mechanism to ensure that this volume (application factor) will not increase in the future. Cybutryne is also flagged for substitution according to Article 10(1) of the BPR due to its persistent and toxic properties.

Therefore a non-approval is proposed based on the properties of the substance and the monitoring data supporting the potential environmental risk posed by the use of the substance as an antifouling booster biocide.

Terrestrial compartment and groundwater
Considering that use of Cybutryne is restricted to commercial coastal and ocean-going vessels treated in a floating dock or marine lift (in the open air, on a hard standing area, enshrouded), no direct emissions to soil or groundwater are expected from the use of Cybutryne in antifouling products. Predicted concentrations in soil and groundwater are therefore considered negligible. No risk to terrestrial organisms and groundwater is expected due to the lack of exposure.

Risk characterisation for the atmospheric compartment
No direct emission to air is expected from the use of Cybutryne in antifouling products for commercial coastal and ocean-going vessels. In addition, Cybutryne has a low vapour pressure and low Henry's law constant, so no significant volatilisation is expected. The concentrations in air are therefore considered negligible and consequently, in the absence of exposure, no risk is expected.

Secondary poisoning
No unacceptable risks from Cybutryne use in antifouling products by secondary poisoning are identified for top predators (birds, mammals).

2.2. Exclusion, substitution and POP criteria

2.2.1. Exclusion and substitution criteria

The table below summarises the relevant information with respect to the assessment of exclusion and substitution criteria:

Property		Conclusions
CMR properties	Carcinogenicity (C)	No classification required
	Mutagenicity (M)	No classification required
	Toxic for reproduction (R)	No classification required
PBT and vPvB properties	Persistent (P) or very Persistent (vP)	P
	Bioaccumulative (B) or very Bioaccumulative (vB)	Not B
	Toxic (T)	T
Endocrine disrupting properties	Xeno-estrogenic effects of Cybutryne were observed in a study with snails, similar to known endocrine disrupters such as Bisphenol A and Ethinylestra-diol. The molecular mode of action is, however, unknown. It should also be kept in mind that invertebrate endocrine systems are different from those in vertebrates. In a 2 generation reproduction study with rats and two development toxicity studies with rats and rabbits no endocrine disruptive effects were observed.	

	The information available on endocrine disruption in snails cannot be discarded but the study results do not provide sufficient evidence to identify Cybutryne as endocrine disrupter. Since no approval is proposed no further action is required. Otherwise additional studies should be initiated to provide definitive evidence on the endocrine disrupting propterties of Cybutryne.
Respiratory sensitisation properties	No classification required.
Reasons for concern linked to the nature of critical effects in combination with the use patterns	Cybutryne does not fulfil criterion (e) of Article 10(1).
Proportion of non-active isomers or impurities	Cybutryne does not fulfil criterion (f) of Article 10(1).

Consequently, the following is concluded:

Cybutryne does not meet the exclusion criteria laid down in Article 5 of Regulation (EU) No 528/2012.

Cybutryne does meet the conditions laid down in Article 10 of Regulation (EU) No 528/2012, and is therefore considered as a candidate for substitution by being T and P.

The exclusion and substitution criteria were assessed in line with the "Note on the principles for taking decisions on the approval of active substances under the BPR"[2] and in line with "Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR"[3] agreed at the 54th and 58th meeting respectively, of the representatives of Member States Competent Authorities for the implementation of Regulation 528/2012 concerning the making available on the market and use of biocidal products. This implies that the assessment of the exclusion criteria is based on Article 5(1) and the assessment of substitution criteria is based on Article 10(1)(a, b, d, e and f).

During the public consultation one non-confidential comment was received from a third party containing additional monitoring data for Cybutryne. There are several other active substances intended for use in the same product type already approved or currently being reviewed under Regulation (EU) No 528/2012.

2.2.2. POP criteria

The initial criteria for long-range transport potentially are met, and Cybutryne is persistent and toxic. Cybutryne and its metabolite, however, do not bioaccumulate. Therefore this substance is not a POP candidate as defined in the Annex D of the Stockholm Convention 2001.

2.2.3. Water Framework Directive (WFD)

Cybutryne was included as a priority substance in Directive 2013/39/EU, which amends Directive 2000/60/EC and Directive 2008/105/EC as regards priority substances in the field of water policy.

Under this Directive, two types of quality standards are established to ensure good water quality: AA-EQS (annual average environmental quality standard) and MAC-EQS (maximum

[2] See document: Note on the principles for taking decisions on the approval of active substances under the BPR (available from https://circabc.europa.eu/d/a/workspace/SpacesStore/c41b4ad4-356c-4852-9512-62e72cc919df/CA-March14-Doc.4.1%20-%20Final%20-%20Principles%20for%20substance%20approval.doc)

3 See document: Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR (available from https://circabc.europa.eu/d/a/workspace/SpacesStore/dbac71e3-cd70-4ed7-bd40-fc1cb92cfe1c/CA-Nov14-Doc.4.4%20-%20Final%20-%20Further%20guidance%20on%20Art10(1).doc)

allowable concentration environmental quality standard).

In the case of Cybutryne the AA-EQS is 2.5 ng/L (inland surface waters, and marine waters). According to the WFD the arithmetic mean of all measured concentrations over a twelve month monitoring period within a body of water should not exceed this value.

According to historical monitoring data the AA-EQS is exceeded.

2.3. BPC opinion on the application for approval of the active substance Cybutryne in product type 21

The following conclusions can be drawn from the evaluation:

1. Cybutryne is toxic and persistent.
2. Using a first tier assessment with the MAMPEC model, exposure to Cybutryne arising from in-service use of antifouling paint and activities (application/removal phase losses and in-service losses) associated with commercial coastal and ocean-going vessels causes unacceptable risks to marine water and sediment organisms in the environment. A higher tier assessment using the concentrations of Cybutryne in the environment from monitoring data shows that the actual concentrations are higher than expected by the MAMPEC model and exceed the PNEC. Therefore, it is concluded that unacceptable risks are identified from the in-service life stage.
3. Cybutryne is a priority substance under the Water Framework Directive (WFD). Historical monitoing data exceed the AA-EQS (annual average environmental quality standard) derived under the WFD.
4. It is not possible to propose measures to mitigate the identified risks resulting from the in-service life stage.
5. A low volume is currently placed on the European market for commercial ships. However, there is no guarantee or mechanism to control whether a higher volume could be brought on the market in the future.

In view of these conclusions it is proposed that Cybutryne shall not be approved for use in product type 21 and therefore not be included in the Union list of approved active substances as the overall conclusion is that biocidal products containing Cybutryne as an active substance may not be expected to meet the criteria laid down in point (iv) of Article 19(1)(b).

According to Article 28(2) of Regulation (EU) No 528/2012, Cybutryne gives rise to the following concerns: it is classified as skin sensitizer (Skin Sens. 1) and toxic to aquatic life of acute category 1 (Aquatic Acute 1). In addition, it fulfils the substitution criteria P and T. Therefore inclusion in Annex I of Regulation (EU) No 528/2012 is not acceptable.

o0o