

## **Biocidal Products Committee (BPC)**

Opinion on the application for approval of the active substance:

**2,2-Dibromo-2-cyanoacetamide (DBNPA)**

**Product type: 4**

ECHA/BPC/300/2021

Adopted

30 November 2021



## Opinion of the Biocidal Products Committee

### on the application for approval of the active substance 2,2-Dibromo-2-cyanoacetamide (DBNPA) for product type 4

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 approval in product type 4 of the following active substance:

<b>Common name:</b>	<b>DBNPA</b>
<b>Chemical name:</b>	<b>2,2-Dibromo-2-cyanoacetamide</b>
<b>EC No.:</b>	<b>233-539-7</b>
<b>CAS No.:</b>	<b>10222-01-2</b>
<b>Existing active substance</b>	

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 the BPC opinion

Following the submission of an application by Specialty Electronic Materials Switzerland GmbH (former: DOW Europe GmbH) on 25 July 2007, the evaluating Competent Authority Denmark submitted an assessment report and the conclusions of its evaluation to the European Chemicals Agency (ECHA) on 27 December 2016. The assessment for endocrine disruption properties of DBNPA followed on 11 November 2018. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via BPC (BPC-26 and BPC-31) and its Working Groups (WG I 2017, WG I 2018 and WG II 2019). Additionally, the ED Expert Group was consulted on 10 October 2018. 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 on the ECHA website (at <https://echa.europa.eu/public-consultation-on-potential-candidates-for-substitution>) on 20 November 2018, in accordance with the requirements of Article 10(3) of Regulation (EU) No 528/2012. Interested parties were invited to submit relevant information by 18 January 2019.

On 8 July 2020 the European Commission submitted to the ECHA a mandate according to article 75(1)g of the Biocidal Products Regulation (EU) 528/2012 (BPR). The mandate requested the opinion of ECHA on the risks associated with the endocrine disrupting properties of DBNPA from the use in PT4. The Agency organised consultations in this regard via BPC-41 and its Working Group (WG II 2021 and WG III 2021).

## Adoption of the BPC opinion

### Rapporteur: Denmark

The BPC opinion on the application for approval of the active substance DBNPA in product type 4 was adopted on 30 November 2021.

No comments were received from interested third parties during the public consultation in accordance with Article 10(3) of BPR.

The BPC opinion was adopted by simple majority of the members present having the right to vote.

The opinion and the minority positions including their grounds are published on the ECHA webpage at: <http://echa.europa.eu/regulations/biocidal-products-regulation/approval-of-active-substances/bpc-opinions-on-active-substance-approval>.

## Detailed BPC opinion and background

### 1. Overall conclusion

DBNPA fulfils the exclusion criteria set in Article 5(1)(d) of Regulation (EU) No 528/2012 on the basis of the criteria defined in Regulation (EU) No 2017/2100. The overall conclusion of the BPC is that DBNPA should normally not be approved unless one of the conditions for derogation set in Article 5(2) of Regulation (EU) No 528/2012 is applicable. The process related to the demonstration of whether the conditions for derogation set in Article 5(2) are met, is not in the remit of the BPC<sup>1</sup>.

### 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 DBNPA in product type 4. 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 relevant and significant impurities. Validated analytical methods are required and available for the relevant matrices soil, air, water, blood and tissue and milk and beef. Analytical methods for detection of the metabolites cyanoacetamide (CAM) in blood and tissue and detection of dibromoacetic acid (DBAA) in milk and beef confirmatory methods are missing.

A harmonised classification according to Regulation (EC) No 1272/2008 is available for DBNPA. A CLH dossier was submitted in 2018 and was evaluated by the Risk Assessment Committee at RAC-49. The classification and labelling for DBNPA according to Regulation (EC) No 1272/2008 (CLP Regulation) is:

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox. 3 Acute Tox. 2 Skin Irrit. 2 Eye Dam. 1 Skin Sens. 1 STOT RE 1 Aquatic Acute 1 Aquatic Chronic 1

<sup>1</sup> See document: "Further guidance on the procedures related to the examination of the exclusion criteria and the conditions for derogation under Article 5(2) (CA-Nov14-Doc.4.5-Final).

<b>Labelling</b>	
Pictogram codes	GHS05, GHS06, GHS09
Signal Word	Danger
Hazard Statement Codes	H301, H330, H315, H318, H317, H372 (respiratory tract) (inhalation), H410
<b>Specific Concentration limits, M-Factors</b>	Oral ATE = 118 mg/kg bw Inhalation ATE = 0.24 mg/L (dust or mist) M = 1 (acute and chronic)

### b) Intended use, target species and effectiveness

DBNPA is intended for use in food processing vessels (e.g. industrial mayonnaise or yogurt producing facilities, fermenters for beer or other fermented products), which are periodically disinfected after use. The disinfection and processing exclusively takes place in industry and only industrial workers may come into contact with DBNPA.

DBNPA is a fast acting biocide and is exerting its biocidal action directly after its application via bromine, which inactivates enzymes by converting functional –SH groups to the oxidised S-S form. This reaction irreversibly disrupts the function of cell-surface components, interrupting transport across cell membranes, and inhibiting key biological functions.

The data on DBNPA and the representative biocidal product have demonstrated sufficient efficacy against the target species (bacteria). The risk of the development of resistance to the active substance is considered to be low due to the mode of action for the active substance which affects multiple cellular targets.

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

#### Human health

DBNPA is well-absorbed by oral administration, extensively metabolised, and rapidly excreted. It is harmful by the oral and inhalation route following acute exposure but is of low toxicity by the acute dermal route. It is both a skin irritant, skin sensitizer and causes eye damage.

In short term studies hemorrhage in the lumen of the colon was identified as the most critical effect. Dyspnoea<sup>2</sup> and subsequent death was observed in gavages studies due to a bolus effect of the test material.

DBNPA is not mutagenic, carcinogenic or a reproductive toxicant. There is no evidence that it is neurotoxic or immunotoxic.

DBNPA is considered to have endocrine-disrupting properties with respect to humans as it meets the criteria set out in section A of Regulation (EU) No 2017/2100. The conclusion is based on the observed adverse effects in the thyroid gland in the studies on rats and dogs combined with data obtained from a literature search conducted on bromide effects on the thyroid. Bromide may substitute iodide in the sodium/iodide symporter of the thyroid, thus creating a relative iodide insufficiency for further synthesis of thyroid hormones. This shows a link between the observed adverse effects in the thyroid and endocrine activity, which is relevant for humans and non-target species.

<sup>2</sup> Difficult or labored breathing; shortness of breath.

The European Commission mandated ECHA to provide an opinion on the "Evaluation of the level of the risks for human health and for the environment of DBNPA used in biocidal products of product type 4."

The mandate requests ECHA to evaluate the risks associated with the ED properties of DBNPA-derived bromide. Regarding human health, the following questions were referred to ECHA<sup>3</sup>.

- (a) Based on available information, clarify whether a safe level (threshold) can be determined for the ED properties of DBNPA-derived bromide for human health, and if such threshold can be established, what would be this level.
- (b) Clarify the level of the risks for humans by:
  - 1. Considering the acceptable daily intake for bromide derived by WHO and the European Medicines Agency for bromide salts used as anti-epileptics in humans, and considering them in the risk assessment if relevant.
  - 2. Taking into account the levels of bromide that are considered essential for human life.
  - 3. Assessing the contribution of the use of DBNPA as a biocide to the average daily bromide consumption.
  - 4. Assessing the level of risk for human health, either by a quantitative assessment or a qualitative assessment
  - 5. Providing an opinion whether the risks can be considered acceptable or not.

### **Evaluation of risk for human health from the endocrine disruptive properties of DBNPA**

With regard to the fact that DBNPA is considered to have endocrine disrupting properties, there is no currently agreed methodology for undertaking a risk assessment based on such properties.

The endocrine disrupting effects of DBNPA is attributed to the bromide ion and therefore the risk assessment focused on evaluating relevant information on bromide. A semi-quantitative risk assessment was performed.

On the risk from ED properties related to human health the following was concluded:

- (a) Bromide is a natural occurring and essential halogen for humans. It is considered that a threshold of adversity exists for the ED effects (T-modality) for bromide. Below this threshold of toxicity the biological response in the human body will be beneficial (or adaptive). However, a *quantifiable* threshold cannot be set due to multiple uncertainties. The identification of a point of departure in the terms of suitable data and toxicological endpoints from which a potential reference value could be derived was not possible. Additionally, insufficient clarity regarding the appropriate assessment factor which should be applied exists. Furthermore, it is considered that the threshold of adversity is affected by the presence of other halogens and by the availability of bromide to humans.
- (b) Already established reference values from other institutions (e.g. the ADI derived by EMA and WHO) are not appropriate to be used when assessing the level of risk against the endocrine disruptive properties of bromide as they are established based on the evaluation of the acute neurotoxic effects of bromide and do not focus on its

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<sup>3</sup> It was confirmed by the Commission that the assessment shall refer only to DBNPA in PT 4.

endocrine disruptive effects.

- (c) Bromide is an essential trace element for human life and development, and systemic bromide levels are within a defined range. It is not possible to determine the minimum systemic levels of bromide essential for human life based on the information available.
- (d) Exposure from PT 4 DBNPA-derived bromide further contributes to the average daily dietary exposure of the general population by 0.03-1.33% and the primary user by 5.1% if considering the normal average daily intake from a total diet study (the UK 1997 Total Diet Study, Rose *et. al*, 2001<sup>4</sup>). If considering the average daily intake reference values presented in the 2019 European Union report on pesticide residues in food, exposure from PT 4 DBNPA-derived bromide contributes to the average daily dietary exposure of the general population by 0.2-6.6% and the primary user by 25% considering the lower bound average daily dietary intake, of the general population by 0.02-1.1% and the primary user by 4% considering the middle bound average daily dietary intake and of the general population by 0.01-0.6 and the primary user by 2.1% considering the upper bound average daily dietary intake.

The table below summarises the contribution of DBNPA-derived bromide exposure from PT 4 to the dietary average daily intake of bromide in percentage.

Average daily intake	General population (% contribution to average daily intake)	Primary exposure when workers are wearing PPE and RPE (% contribution to average daily intake)	Reference
Value 0.06 mg/kg bw/day	0.03-1.33	5.1	UK 1997 Total Diet study (Rose et al 2001)
Value 0.012 mg/kg bw/day Lower bound approach: samples with non-quantified residues (i.e. samples with residue levels < LOQ) are treated as if the residues are not present in the food product analysed *	0.2-6-6	25	2019 Annual European Union report on pesticide residues in food <sup>5</sup>
Value 0.075 mg/kg bw/day Adjusted middle bound approach: samples with non-quantified residues (i.e. samples with residue levels < LOQ) are present in the sample at level of half of the LOQ	0.02-1.1	4	
Value 0.145 mg/kg bw/day Adjusted upper bound approach: samples with non-quantified residues are present in the sample at the level of LOQ **	0.01-0.6	2.1	

<sup>5</sup> 2019 EU report on pesticide residues in food, EFSA Journal 2021;19(4):6491 (<https://www.efsa.europa.eu/en/efsajournal/pub/6491>).



- (e) Only automated transfer of the reference product into closed systems is considered relevant for exposure calculation for the primary (industrial) user. The use of the input value for dermal and inhalation exposure is a worst case assumption, as it would otherwise be considered negligible. Furthermore, the primary user wears coveralls, gloves and respiratory equipment due to local effects of DBNPA.
- (f) The calculated secondary exposure of the general public via food (bottles) can be considered worst case, as bottles are rinsed after disinfection with the PT 4 DBNPA reference product. The scenario was originally included in the DBNPA CAR for PT 4 as no measurements of the actual residues within the bottles were available, but it is clearly stated in the original assessment that this exposure is highly unrealistic. As stated in section 2.4.b, more data can be submitted in order to demonstrate the relevance and effectiveness of this rinsing step at the product authorisation stage.

Considering the conclusions on the risk from ED properties related to human health, no endocrine disruptive effects in humans are expected from exposure to DBNPA-derived bromide from the use in PT 4, as this contribution to the average daily intake is within the natural variation and the exposure calculations for the representative uses of DBNPA in PT 4 should be regarded as overestimates. Therefore, no unacceptable risks from the ED properties are associated with exposure to DBNPA-derived bromide from the use in PT 4.

The table below summarises the exposure scenarios assessed for DBNPA and bromide:

<b>Summary table: human health scenarios</b>			
<b>Scenario</b>	<b>Primary or secondary exposure and description of scenario</b>	<b>Exposed group</b>	<b>Conclusion</b>
Disinfection of industrial equipment – Loading by connecting IBC drum to vacuum suction	Primary exposure by the dermal and inhalation routes  Ready-to-use product  In use concentration: 100%  PPE: Gloves and coated coverall and face screen/goggles	Professionals	Acceptable with PPE/RPE
Disinfection of industrial equipment - Drinking water	Secondary exposure by the oral route  Drinking water from disinfected bottles after being rinsed	General public	Acceptable

For professional users, all primary exposure scenarios show acceptable risks with PPE/RPE. The foreseen local effects due to skin irritation and skin sensitisation properties of the active substance as well as the endocrine disrupting properties of bromide require the use of PPE in order to provide sufficient protection, including chemically resistant gloves, coated coverall, and face screen/goggles when loading machinery.

For the general public an acceptable risk was identified for infants, toddlers and adults drinking water from bottles, which had been disinfected with a 20% solution of DBNPA. It was assumed that disinfected bottles are thoroughly rinsed before filled with water for consumption. This risk mitigation measure is a requirement as the risk assessment includes a rinsing step.

## Environment

According to its chemical properties, DBNPA can be degraded via two pathways; hydrolysis and nucleophilic reaction. For PT 4 nucleophilic reaction is the relevant pathway after DBNPA comes into contact with sulphur containing reducing species (“nucleophiles”), light or organic material (e.g., proteins, bacteria, humus/fulvic acids, etc.). DBNPA will quickly be degraded to cyanoacetamide (CAM).

DBNPA is not readily biodegradable. Based on a weight of evidence approach including several studies from the open literature a degradation half life in soil (DT<sub>50</sub>) of 20.9 hours at 12 oC was used for the risk assessment. In addition, the default value of inherent biodegradable substances was included.

Exposure of the atmospheric compartment to DBNPA is considered not to raise a concern, as DBNPA has a very low vapour pressure, a low Henry’s law constant and is additionally not used in a manner, which leads to direct release to the atmosphere.

There is no risk of bioaccumulation of DBNPA in aquatic organisms as indicated by the log Pow and supported by the results of the bioconcentration study in fish.

The toxicity of DBNPA to aquatic organisms is well documented by acute and long-term studies.

The Predicted No Effect Concentration (PNEC) calculation for sediment is based on the equilibrium partitioning method.

The mixing and loading process takes place in completely closed systems. Thus, the environmental exposure during mixing and loading is considered to be negligible compared to the actual application of DBNPA. The emission estimations for the use of DBNPA in PT 4 have been determined using two different scenarios (a tonnage-based scenario and a consumption-based scenario) and a tiered approach. For CAM only the consumption-based scenario, representing the realistic worst-case scenario is evaluated.

QSAR and results from the literature used in a weight of evidence (WoE) approach indicate that CAM is readily biodegradable; however, as a realistic worse case CAM was considered as inherently biodegradable in the exposure assessment. Based on WoE a DT<sub>50</sub> in soil for CAM can be assumed to be around 30 days. However, it was decided to consider CAM as inherently biodegradable (using a k-rate of 0.1h<sup>-1</sup> in STP and DT<sub>50</sub> value of 300 days for soil by default). Acute aquatic toxicity studies/QSAR estimations clearly shows that CAM has a significantly lower toxicity to aquatic organisms, compared to DBNPA.

DBNPA has endocrine disrupting properties with respect to non-target organisms as it meets the criteria set out in section B of Regulation (EU) No 2017/2100. This conclusion is based on evidence from studies conducted on DBNPA in rats and studies conducted on bromide in rat, guppy and medaka in combination with additional information showing that the postulated Mode of Action affects amphibian metamorphosis, which is considered relevant at population level.

The European Commission mandated ECHA to provide an opinion on the “Evaluation of the level of the risks for human health and for the environment of DBNPA used in biocidal products of product type 4.”

The mandate requests ECHA to evaluate the risks associated with the ED properties of DBNPA-derived bromide. Regarding the environment, the following questions were referred to ECHA<sup>6</sup>:

- (a) Based on available information, clarify whether a safe level (threshold) can be determined for the ED properties of DBNPA-derived bromide for the environment, and if such threshold can be established, what would be this level.
- (b) Determine the background level of bromide in the environment
- (c) Determine the exposure of non-target organisms to DBNPA-derived bromide.
- (d) Clarify the level of the risks to the environment by:
  1. Assessing the level of risk for the environment, either by a quantitative assessment or by a qualitative assessment by considering among others the DBNPA-derived bromide concentration and the background level of bromide.
  2. Providing its opinion whether the risks can be considered acceptable or not.

For uses of DBNPA where the release is to an off-site STP with the relevant dissipation rate in sewer applied and the daily use concentration is 4 kg or less (consumption-based scenario), the requirements for acceptable risk are met for all environmental compartments: the PEC/PNEC values are below the trigger value of 1. However, for the worst-case situation using a  $DT_{50\text{soil}}$  of 300 days, a risk for groundwater was identified based on the pore water concentrations. Therefore, to refine the assessment the groundwater concentrations were calculated also with FOCUS PEARL. Based on these calculations, risks are considered acceptable (as groundwater concentrations are below 0.1 µg/L) for most of the FOCUS scenarios even under this worst-case situation.

Considering a CAM-only (i.e., worst case) scenario, the PEC/PNEC values are below the trigger value of 1 for all environmental compartments except for groundwater: a risk for groundwater was identified based on the pore water concentrations. Therefore, to refine the assessment the groundwater concentrations were also calculated with FOCUS PEARL. Based on these calculations acceptable risks can be demonstrated (as groundwater concentrations are below 0.1 µg/L) for most of the FOCUS scenarios.

### **Evaluation of risk for the environment from the endocrine disruptive properties of DBNPA**

With regard to the fact that DBNPA is considered to have endocrine disrupting properties, there is no currently agreed methodology available on how to consider the data used for the identification of whether this substance is an endocrine disruptor in risk assessment. The endocrine disrupting effects of DBNPA is attributed to the bromide ion.

Bromide is a naturally occurring substance in the environment, and therefore a threshold for the endocrine disrupting effects must be assumed. However, there is currently no scientific consensus how such a threshold might be established and there are several uncertainties to consider. Uncertainties for setting a threshold for non-target organisms include a lack of clarity on the data that would be considered necessary to ensure that the most sensitive species as well as life stage is sufficiently protected. Furthermore, it is unclear how assessment factors can be applied to address the uncertainty presented in the available data set.

The conclusion on the ED effects for non-target organisms in the environment of DBNPA in PT4 is based on mammalian data, and the data available for bromide on NTOs is scarce, which further contributes to the challenge of setting a threshold. Bromide is a naturally

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<sup>6</sup> It was confirmed by the Commission that the assessment shall refer only to DBNPA in PT 4.

occurring substance and a threshold for the ED effects must therefore exist, but it is not possible to quantify such threshold at the moment in a scientifically sound manner.

The background concentrations of bromide in the aquatic environment shows a large variety and is influenced by natural factors (distance to the sea, geology, seasonal fluctuations) and anthropogenic sources (chemical industry, pharmaceutical industry, mining, waste incineration). A fixed value for the background concentrations of bromide in the environment could not be established.

The concentration of bromide in the environment can also be influenced by many different anthropogenic sources. Bromide can be released from different sectors e.g. chemical industry, pharmaceutical industry, mining, waste incineration etc.

Although data is very limited, it is clear that concentrations of bromide is higher in areas of industrial activity. From an available study, it was estimated that 2 % of the bromide load to a Swiss water body in 2016 could be attributed to a general biocides use (i.e. not DBNPA-specific).

The exposure concentration of bromide following PT 4 representative use is within the background concentrations in the environment, although in the high end of the large range reported in literature. Considering that the representative use of this product is for industrial application, the exposure from this use can also be considered a minor contributor to the environmental bromide concentration compared to other anthropogenic sources.

Since release to the environment of DBNPA occurs via wastewater from industrial use a risk related to ED properties cannot be excluded, however the risk is considered acceptable when considering the anthropogenic sources of bromide and the natural variation of bromide in the environment. In an area of industrial activity, the emission of bromide from DBNPA in PT 4 to the environment would only contribute a fraction of the total bromide emission in the area.

The table below summarises the exposure scenarios assessed for DBNPA, CAM and bromide.

<b>Summary table: environment scenarios</b>		
<b>Scenario</b>	<b>Description of scenario including environmental compartments</b>	<b>Conclusion</b>
Tonnage based scenario: ESD for PT 4: Assessment of entire plants off-site treatment. DBNPA	Food processing vessels. Based on amount of DBNPA (4000 ppm) supported by the efficacy data submitted and taking degradation in the sewer system into account.  Direct exposure to STP via drains. Indirect exposure to surface water (including sediment) via STP effluent; to soil (including groundwater) via STP sludge application to land; and biota via surface water and soil.	Acceptable
Tonnage based scenario: ESD for PT 4: Assessment of entire plants off-site treatment. DBNPA	Bottle washing. Based on amount of DBNPA (4000 ppm) supported by the efficacy data submitted and taking degradation in the sewer system into account.  Direct exposure to STP via drains. Indirect exposure to surface water (including sediment) via STP effluent; to soil (including groundwater) via STP sludge application to land; and biota via surface water and soil.	Acceptable

Summary table: environment scenarios		
Consumption based scenario. DBNPA	Food processing vessels or bottle washing (4 kg for both food vessels and bottle washing. Taking degradation in the sewer system into account. Using a DT50 soil of 20.9 hours). Direct exposure to STP via drains. Indirect exposure to surface water (including sediment) via STP effluent; to soil (including groundwater) via STP sludge application to land; and biota via surface water and soil.	Acceptable
Consumption based scenario. DBNPA	Food processing vessels or bottle washing (4 kg for both food vessels and bottle washing. Taking degradation in the sewer system into account. Using the default value of 300 days for DT50 soil (as for inherent biodegradable substances). Direct exposure to STP via drains. Indirect exposure to surface water (including sediment) via STP effluent; to soil (including groundwater) via STP sludge application to land; and biota via surface water and soil.	Acceptable
Consumption based scenario. CAM	Based on 100% transformation of DBNPA to CAM in the influent of the STP (0.448 kg DBNPA/d = 0.156 kg CAM/d). Rate constant in STP of 0.1 and a DT50 soil of 300d). Direct exposure to STP via drains. Indirect exposure to surface water (including sediment) via STP effluent; to soil (including groundwater) via STP sludge application to land; and biota via surface water and soil.	Acceptable
Consumption based approach. Bromide.	Based on 100% transformation of DBNPA to bromide in the influent of the STP. Direct exposure to STP via drains. Indirect exposure to surface water (including sediment) via STP effluent.	Acceptable

The above results show that an acceptable risk was demonstrated for the assessment of the entire plant for all scenarios for DBNPA with respect to non-target organisms.

### Overall conclusion

Without considering that DBPNA has endocrine-disrupting properties, the risk assessment performed using the usual methodology showed no unacceptable risks for DBNPA for humans and for the environment including the environmental relevant metabolite CAM.

DBNPA is however considered to have endocrine disrupting properties relevant for both humans and non-target organisms in the environment. There is no currently agreed methodology for undertaking a risk assessment for human health based on such properties and no agreed methodology available on how to consider the data used for the identification of whether this substance is an endocrine disruptor in risk assessment for the environment. Although a threshold must exist for the ED effects of bromide for human health and the environment, it was not possible to quantify such a threshold.

The risk of ED effects associated with the exposure to DBNPA-derived bromide use in PT 4 is considered acceptable for humans, as this contribution to the average daily intake is within the natural variation and the exposure calculations for the representative uses of DBNPA in PT 4 are overestimates. The data available is considered adequate to reach this conclusion.

The risk associated with the ED effects of bromide are considered to be acceptable for the non-target organisms in the environment, due to the natural variation of bromide, and anthropogenic sources of bromide from many other uses. The exposure from DBNPA-derived bromide is within the range of these values. The data available is scarce, but is considered adequate to reach this conclusion.

Disinfection by-products (DBPs) can be formed as a consequence of the use of DBNPA. An assessment of the risks of disinfectant by-products was not performed at active substance approval level. At product authorisation level it must be demonstrated that no DBPs will be formed. Otherwise, an assessment of the risks of DBP will have to be performed.

## 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	DBNPA does not fulfil criterion (a), (b) and (c) of Article 5(1)
	Mutagenicity (M)	No classification required	
	Toxic for reproduction (R)	No classification required	
PBT and vPvB properties	Persistent (P) or very Persistent (vP)	Not P or vP (DBNPA) Potential P and vP (CAM)	DBNPA and CAM do not fulfil criterion (e) of Article 5(1) and do not fulfil criterion (d) of Article 10(1)
	Bioaccumulative (B) or very Bioaccumulative (vB)	Not B or vB (DBNPA) Not B or vB (CAM)	
	Toxic (T)	T (DBNPA) Not T (CAM)	
Endocrine disrupting properties	Section A of Regulation (EU) 2017/2100: ED properties with respect to humans	Yes	DBNPA fulfils Article 5(1)(d) and 10(1)(e)
	Section B of Regulation (EU) 2017/2100: ED properties with respect to non-target organisms	Yes	
	Article 57(f) and 59(1) of REACH	No	

Property		Conclusions	
	Intended mode of action that consists of controlling target organisms via their endocrine system(s)	No	
Respiratory sensitisation properties	DBNPA does not fulfil criterion (b) of Article 10(1). No classification required.		
Concerns linked to critical effects	DBNPA does not fulfil criterion (e) of Article 10(1).		
Proportion of non-active isomers or impurities	DBNPA does not fulfil criterion (f) of Article 10(1).		

Consequently, the following is concluded:

DBNPA meets the exclusion criteria laid down in Article 5 of Regulation (EU) No 528/2012 with regard to its endocrine disrupting properties related to humans.

DBNPA meets the conditions laid down in Article 10 of Regulation (EU) No 528/2012 with respect to its endocrine disrupting properties, which are relevant for non-target organisms and humans, and is therefore also considered as a candidate for substitution.

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"<sup>7</sup>, "Further guidance on the application of the substitution criteria set out under Article 10(1) of the BPR"<sup>8</sup> and "Implementation of scientific criteria to determine the endocrine –disrupting properties of active substances currently under assessment"<sup>9</sup> agreed at the 54th, 58th and 77th 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).

<sup>7</sup> 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>).

<sup>8</sup> 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](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)).

<sup>9</sup> See document: Implementation of scientific criteria to determine the endocrine –disrupting properties of active substances currently under assessment (<https://circabc.europa.eu/sd/a/48320db7-fc33-4a91-beec-3d93044190cc/CA-March18-Doc.7.3a-final-%20EDs-%20active%20substances%20under%20assessment.docx>).

### 2.2.2. POP criteria

DBNPA does not fulfil the criteria for being a persistent organic pollutant (POP).

### 2.2.3 Identification of potential alternative substances or technologies, including the results of the public consultation for potential candidates for substitution

As DBNPA is considered a potential candidate for substitution ECHA launched the public consultation in accordance with Article 10(3) of Regulation (EU) 528/2012, which took place from November 2018 to January 2019. No information was submitted during the public consultation. Currently, several other active substances have been approved in PT 4, all of which have bactericidal activity.

#### Potential alternative active substances

2-phenoxy ethanol, Active chlorine (generated from sodium chloride by electrolysis or released from hypochlorous acid), Active chlorine (released from calcium hypochlorite), Active chlorine (released from sodium hypochlorite), Bromoacetic acid, C(M)IT/MIT, Decanoic acid, Glutaraldehyde, Hydrogen peroxide, Iodine, L(+) lactic acid, Octanoic acid, Peracetic acid, Peracetic acid generated from tetraacetythylenediamine (TAED) and sodium percarbonate, PHMB (1415;4.7), PHMB (1600;1.8), Polyvinyl-pyrrolidone iodine, Propan-1-ol, Propan-2-ol, Salicylic acid.<sup>10</sup>

### 2.3. BPC opinion on the application for approval of the active substance DBNPA in product type 4

In view of the conclusions of the evaluation, DBNPA should normally not be approved unless one of the conditions for derogation set in Article 5(2) of Regulation (EU) No 528/2012 is applicable.

DBNPA fulfils the criteria for having endocrine disrupting properties laid down in Article 5(1)(d) of Regulation (EU) No 528/2012 as defined in Regulation (EU) No 2017/2100. This implies that biocidal products containing DBNPA should not be used for the general public according to Article 19(4)(d) of Regulation (EU) No 528/2012 (see note "The implementation of scientific criteria for the determination of endocrine-disrupting properties in the context of biocidal product authorisation" (CA-March18-Doc.7.3.b-final)).

If DBNPA is approved, the approval shall be subject to the following conditions:

1. Specification: minimum purity of the active substance evaluated: 98.0 % w/w.
2. Relevant impurities: dibromoacetonitrile (DBAN) 0.14 % w/w.
3. DBNPA is considered a candidate for substitution in accordance with Article 10(1)(a) and (e) of Regulation (EU) No 528/2012.
4. The authorisations of biocidal products are subject to the following conditions:
  - a. The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.
  - b. Products shall only be authorised for use in Member States where at least one of the conditions set in Article 5(2) of Regulation (EU) No 528/2012 is met.

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<sup>10</sup> The proposed alternative active substances have not been assessed for endocrine disrupting properties according to the scientific criteria set out in Regulation (EU) No 2017/2100.



- c. In view of the risks identified for the uses assessed, the product assessment shall pay particular attention to:
    - i. Professionals
  - d. For products containing DBNPA that may lead to residues in food or feed, Member States shall verify the need to set new or amended 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.
  - e. Products containing DBNPA shall not be incorporated in materials and articles intended to come into contact with food within the meaning of Article 1(1) of Regulation (EC) No 1935/2004, unless the Commission has established specific limits on the migration of DBNPA into food or it has been established pursuant to that Regulation that such limits are not necessary
5. The placing on the market of treated articles is subject to the following condition(s):
- a. The person responsible for the placing on the market of a treated article treated with or incorporating the active substance DBNPA shall ensure that the label of that treated article provides the information listed in the second subparagraph of Article 58(3) of the Regulation (EU) No 528/2012.

The active substance does not fulfil the criteria according to Article 28(2) to enable inclusion in Annex I of Regulation (EU) 528/2012. DBNPA gives rise to concern for human health and the environment, i.e. it is classified as Acute Tox 2, Skin Sens 1, STOT RE 1 and Aquatic Acute 1. DBNPA furthermore meets the exclusion criteria in Article 5(1) and substitution criteria in Article 10(1) in Regulation (EU) 528/2012.

#### **2.4. Elements to be taken into account when authorising products**

1. The active substance DBNPA is considered a candidate for substitution in accordance with Article 10(1)(a) and (e) of Regulation (EU) No 528/2012, and consequently a comparative assessment shall be carried out as part of the evaluation of an application for national authorisation.
2. Following recommendations and risk mitigation measures have been identified for the uses assessed. Authorities should consider these risk mitigation measures when authorising products, together with possible other risk mitigation measures, and decide whether these measures are applicable for the concerned product
  - a. If an unacceptable risk for professionals is identified, safe operational procedures and appropriate organizational measures shall be established. Products shall be used with appropriate personal protective equipment where exposure cannot be reduced to an acceptable level by other means.
  - b. Indirect exposure via food consumption was assessed considering a rinsing step after treatment. More data are expected to demonstrate the relevance and effectiveness of this rinsing step at product authorisation stage.
  - c. An assessment of the risk in food and feed areas may be required at product authorisation where use of the product may lead to contamination of food and feeding stuffs.
  - d. Disinfection by-products (DBPs) can be formed as a consequence of the use of DBNPA. An assessment of the risks of disinfectant by-products was not performed at active substance approval level. At product authorisation level it

must be demonstrated that no DBPs will be formed. Otherwise, an assessment of the risks of DBP will have to be performed.

## **2.5. Requirement for further information**

Sufficient data have been provided to verify the conclusions on the active substance, permitting the proposal for the approval of DBNPA. However, the following further data must be submitted to the evaluating Competent Authority (DK) as soon as possible but no later than 6 months before the date of approval of the active substance:

- Confirmatory method on determination of CAM in animal and human body fluids and tissues;
- Confirmatory method on determination of DBAA in food and feeding stuff;
- Ready biodegradation test for CAM to clarify the P/vP status. Determination of degradation of DBNPA in soil, including identification of relevant metabolites and determination of DT<sub>50</sub> values in soil.

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