Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

Cyanamide

Product type: 3

ECHA/BPC/301/2021

Adopted

30 November 2021

Opinion of the Biocidal Products Committee

on the application for approval of the active substance Cyanamide for product type 3

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 3 of the following active substance:

Common name:	**Cyanamide**
Chemical name:	**Cyanamide**
EC No.:	**206-992-3**
CAS No.:	**420-04-2**

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 AlzChem AG on 4 July 2007, the evaluating Competent Authority Germany submitted an assessment report and the conclusions of its evaluation to the Commission on 30 July 2013. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC (BPC-16 and BPC-33) and its Working Groups (WG-I-2016 and WG-IV-2019). 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 *http://echa.europa.eu/addressing-chemicals-of-concern/biocidal-products-regulation/potential-candidates-for-substitution-previous-consultations* on 22 February 2016, 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 21 April 2016. A second consultation was launched on 26 June 2019 with an invitation to submit relevant information by 25 August 2019.

The BPC opinion on the approval of the active substance cyanamide in product type 3 was adopted on 16 June 2016. Due to the entry into force of Regulation (EU) 2017/2100[1] the Commission returned the BPC opinion to the Agency on 26 April 2018 in the frame of an Article 75(1)g) request to revise the opinion already adopted by the Biocidal Products Committee (BPC), related to the application of the criteria for endocrine disrupting properties

[1] Commission Delegated Regulation (EU) 2017/2100 of 4 September 2017 setting out scientific criteria for the determination of endocrine-disrupting properties pursuant to Regulation (EU) No 528/2012 of the European Parliament and Council.

as laid down in this regulation. The BPC opinion was then again adopted on 10 December 2019. In September 2020, ECHA received again an Article 75(1)g)[2] request of the Commission with the mandate to provide in the opinion a clear conclusion on the level of the risks of using cyanamide in relation to its ED properties. The Agency organised consultations in this regard via BPC-41 and its Working Group (WG-II-2021 and WG-III-2021)

[2] Mandate requesting ECHA opinions under Article 75(1)(g) of the BPR "Evaluation of the level of the risks for human health and for the environment of cyanamide used in biocidal products of product types 3 and 18" https://echa.europa.eu/documents/10162/2166576/Mandate+Opinion+Request+Cyanamide.pdf/2244732d-1341-1cae-5538-ca1e6613815a?t=1612172251443.

Adoption of the BPC opinion

Rapporteur: Germany

The BPC opinion on the application for approval of the active substance cyanamide in the product type 3 was adopted on 30 November 2021.

The BPC opinion takes into account the comments of interested third parties provided 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 position including its ground are published on the ECHA webpage: 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

The overall opinion of the BPC is that no final conclusion on whether the active substance cyanamide in product type 3 may be approved or not can be drawn. 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 cyanamide in product type 3. Cyanamide is regarded to be a multi-site inhibitor interfering with the respiratory metabolism. It is known to inhibit the activity of the enzymes catalase and dehydrogenase leading to accumulation of hydrogen peroxide in treated organisms.

The purity of the active substance is 96.8 % w/w (dry weight), but cyanamide is manufactured as aqueous solution with 50.5 % w/w. 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, drinking and surface water, body fluids and body tissues.

Commission Decision of 18 September 2008 (2008/745/EC)[3] concerning the non-inclusion of cyanamide in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance was taken in 2008. Commission Regulation (EU) of 17 October 2014 (1126/2014/EU) in accordance with Article 17 of Regulation (EC) No 396/2005 in conjunction with Article 14(1)(a) thereof deleted the MRLs set out for cyanamide in Annex III[4]. Cyanamide was also evaluated for the use of calcium cyanamide as fertiliser by SCHER[5]. The SCHER concluded that harmful effects for humans and for the environment could not be excluded when calcium cyanamide is used at the current rates of application as a fertiliser.

[3] OJ L 251, 19.9.2008, p.45.
[4] Commission Regulation (EU) No 1126/2014 of 17 October 2014 amending Annexes II, III and V to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for asulam, cyanamide, dicloran, flumioxazin, flupyrsulfuron-methyl, picolinafen and propisochlor in or on certain products.
[5] SCHER (Scientific Committee on Health and Environmental Risks), Potential risks to human health and the environment from the use of calcium cyanamide as fertiliser, 22 March 2016.

The classification and labelling for cyanamide according to Regulation (EC) No 1272/2008 (CLP Regulation, 10th ATP) is:

Classification according to theCLP Regulation	
Hazard Class and Category Codes	Acute Tox. 3, H301 Acute Tox. 3, H311 Skin Corr 1, H314 Eye Dam. 1, H318 Skin Sens. 1, H317 Carc. 2, H351 STOT RE 2, H373 Repr. 2, H361fd Aquatic Chronic 3, H412
Labelling	
Pictogram codes	GHS05 GHS06 GHS08
Signal Word	Danger
Hazard Statement Codes	H301: Toxic if swallowed H311: Toxic in contact with skin H314: Causes severe skin burns and eye damage H317: May cause an allergic skin reaction H351: Suspected of causing cancer H373: Causes damage to organs through prolonged or repeated exposure (thyroid gland) H361fd: Suspected of damaging fertility. Suspected of damaging the unborn child H412: Harmful to aquatic life with long lasting effects
Specific Concentration limits, M-Factors	-

b) Intended use, target species and effectiveness

The intended use of the representative biocidal product is the disinfection against *Brachyspira hyodysenteriae* of the liquid manure stored underneath the slatted floor in pig stables in order to protect fattening pigs against the pig disease dysenteria. The biocidal product is applied by professional users only in empty pig stables. After dilution it is rinsed from the treated surfaces into the liquid manure where it exerts its effects.

The data on cyanamide and the representative biocidal product have demonstrated sufficient efficacy against the target species for the specific use. Further studies should be provided for product authorisation. Cyanamide is regarded to be a multi-site inhibitor. It is not expected that resistance to cyanamide develops from its use in pig stables under PT 3.

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

Human health

Cyanamide is acutely toxic after oral and dermal exposure. Cyanamide is considered irritating to eyes, corrosive to skin and to be a sensitiser via the skin. Cyanamide was considered non-genotoxic but was classified by RAC for carcinogenicity Cat. 2 and reproduction as well as developmental toxicity Cat. 2. RAC also proposed classification as STOT RE2 based on thyroid effects. Furthermore, cyanamide is considered to have endocrine disrupting properties with respect to humans.

In September 2020, 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 cyanamide used in biocidal products of product types 3 and 18".

The mandate states that the "BPC opinions do not contain any information as to whether a safe threshold may be derived in relation to ED properties and do not conclude clearly whether the risks could be considered acceptable or not acceptable."

Furthermore, regarding the risks for human health, the following questions were referred to ECHA:

a) Based on available information, clarify whether a safe level (threshold) can be determined for the ED properties of cyanamide 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. Assessing the level of risk for human health, either by a quantitative assessment or by a qualitative assessment.

2. Providing an opinion whether the risks can be considered acceptable or not.

Regarding a), it was discussed whether a threshold for the endocrine effects can be identified for the T modality as well as whether existing uncertainties can be addressed by the choice of appropriate Margins of Exposure. However, due to several uncertainities (missing DNT-Study, no conclusion on EAS modalities, no Guidance on ED risk assessment), the BPC=WG concluded, that a quantitative risk assessment could not be supported, and that the available data would not allow defining a threshold. The majority of the commenting members supported performing a qualitative assessment.

Point b) is addressed in the following as part of the overall risk assessment.

The table below summarises the exposure scenarios assessed.

Summary table: human health scenarios			
Scenario	**Primary or secondary exposure and description of scenario**	**Exposed group**	**Conclusion**
Application in animal housings	Primary inhalation and dermal exposure of a.s. in b.p. occurs during mixing & loading, application by watering can or half-automated movable cart and rinsing of floor and equipment in piggeries	Professional user	**Acceptable** with gloves, coverall, RPE, boots, safety goggles
Secondary exposure	Secondary inhalation and dermal exposure to a.s. in b.p. for any task inside the treated pig stables after application and cleaning are not expected as residues of the coloured procduct are rinsed-off after application.	Professional user	**Acceptable** without PPE
Secondary exposure of the general public –entry/ access to stables	Entry of (empty) piggeries (oral/dermal/inhalation)	General public	**Not assessed** as the general public has normally no access to piggeries.
Secondary exposure of the general public – via liquid manure	a) Bystander exposure during/after spreading of treated liquid manure on agricultural land (oral/dermal/inhalation) b) Resident exposure during/after spreading of treated liquid manure on agricultural land (oral/dermal/inhalation) c) Recreational exposure to surfaces where treated liquid manure was applied (oral/dermal)	General public	**No conclusion possible**

Professionals:

A quantitative risk characterisation for systemic effects was performed for the active substance in the representative biocidal product. In addition, due to the skin corrosive (comprising serious eye damage) and skin sensitisation properties of cyanamide in the representative biocidal product, a qualitative risk assessment for local effects was necessary.

Since no applicable models are available to assess an application by watering can, an operator exposure study was conducted as a higher tier study to determine realistic occupational exposure conditions. In the study, a Pro-Chem® I"C" Typ3 coverall and Camatril® 732 gloves proved to be suitable protective clothing. In addition, some other coveralls were tested which did not result in the same level of protection.

According to the systemic and local risk assessment for cyanamide, exposure to cyanamide should be minimized with the following protection measures: effective chemically protective

gloves, protective coverall, chemically protective boots, respiratory protective equipment (RPE) against gaseous cyanamide including full face mask or half face mask with safety goggles. If the prescribed risk mitigation measures are implemented, handling and use of the active substance cyanamide do not lead to concern for professionals.

Based on the results of a performed operator exposure study (Rath, 2011) the following specific personal protective equipment proved to be suitable to reduce dermal exposure to an acceptable level:

- chemically protective gloves (Camatril 732, Cat.III, EN 374 AJL, thickness ca. 0,40 mm, length ca. 400 mm);
- chemically protective suit, Cat. III, Type 3 (Pro-Chem I “C” has proven to be suitable to reduce the exposure to an acceptable level according to the study of Rath, 2011).

It is noted that the above specifications are an example of appropriate personal protective equipment to be worn when handling the product. However, if different PPE are proposed at product authorisation stage material test have to be provided demonstrating the same level of protection.

In relation to the questions (b) 1 and 2 of the Commission’s Article 75(1) g) request, the following is concluded for the professional user.

For the qualitative exposure assessment, based on the available exposure study, it is assumed that inhalation and dermal exposure of hands and body occurs during mixing and loading, pouring of in-use solutions onto slatted floors, and rinsing of slatted floors and equipment with water. Exposure of the eyes via splashes might be possible as well.

After the treatment, residues of the coloured product are rinsed off. Therefore, it is assumed that secondary inhalation and dermal exposure inside the pig stable as well as the direct contact with residues in the manure are highly unlikely.

Professional users represent a defined sub-population that is considered to not comprise particularly sensitive sub-groups. As appropriate risk mitigation measures (chemically protective gloves, protective coverall, boots, respiratory protective equipment, eye protection, rinsing with water after application and use in well-ventilated areas) are in place to ensure minimised exposure, the **risk regarding the ED properties of cyanamide is considered acceptable for professional users**.

Non-Professionals and general public:

The representative biocidal product is only used by professionals inside empty pig stables. The general public has normally no access to these buildings; thus, exposure inside stables is also not expected and has not been assessed.

With regard to the questions mandated to ECHA regarding the endocrine disrupting properties of cyanamide, the potential exposure of the general public to cyanamide following liquid manure application on agricultural land was considered relevant and was assessed. As there is no agreed methodology for risk assessment for ED properties and no models for the application of liquid manure are available, exposure was described based on exposure scenarios developed for the application of plant protection products, i.e. bystander and resident exposure as well as recreational exposure.

For these scenarios, exposure cannot be excluded for the general public. There is only the possibility of reducing the exposure by potential risk mitigation measures, e.g.: i) prolonged storage of liquid manure, ii) warning signs or other measures to restrict access to treated areas and iii) incorporation into soil as additional consideration.

These measures may in principle be expected to lead to a reduction of exposure of the general public, but the exposure cannot be generally excluded. Therefore, it cannot be concluded whether these measures are sufficient to ensure an acceptable risk with regard to the ED properties of the active substance. The RMM "prolonged storage of liquid manure" has been discussed and considered unsuitable. In addition, the "incorporation into soil is already considered in the models for environmental exposure assessment and can hence not be a RMM".

It is concluded that exposure might be low but cannot be excluded. It is noted that there is no information on how low the exposure should be in order to exclude risks as no threshold for ED effects of the active substance can be identified. Therefore, it is not possible to conclude on the risk assessment.

For the representative use, residues in food and feed are not expected as due to the fast degradation of cyanamide, transfer of cyanamide residues from treated manure into agricultural crops is considered unlikely.

Based on the discussions with the member states in the context of the HH WG, question (a) of the COM's mandate, relating to the existence of a safe level (threshold) can be answered as follows:

> *With respect to the T-modality, a threshold for biological adversity through TPO inhibition by cyanamide was discussed, but a threshold for the ED properties was not supported due to a variety of uncertainties (*missing DNT-Study, no conclusion on EAS modalities, lacking guidance on ED risk assessment).

In relation to item (b) 1 of the Commission's request asking for either a quantitative or a qualitative risk assessment, the following is concluded:

> *Based on the available information, a quantitative risk assessment on the ED properties of cyanamide was conducted. Although there are several uncertainties within the current database, a threshold for the ED effects of cyanamide as well as a risk assessment approach using the margin of exposure approach is not supported.*
>
> *A qualitative risk assessment was based on the description of scenarios available for plant protection products due to lack of harmonised exposure scenarios for the application of liquid manure. In addition to the exposure of professionals, the exposure of general public including bystanders, residents and during recreational exposure was considered. None of the proposed RMMs allowed to exclude the exposure of the general public. Due to the lack of a safe level (threshold),* ***the level of risk could not be determined in the scope of the qualitative assessment for the general public whereas the risk regarding the ED properties of cyanamide is considered acceptable for professional users***

In relation to item (b) 2 of the Commission's request asking for providing an opinion whether the risks can be considered acceptable or not, the result of the discussions is summarized as follows:

> *Regarding the acceptability of the risk, no final conclusion is possible. It is concluded that given the uncertainties of the assessment and lack of methodology, it is currently not possible to determine whether the risk is acceptable or not for the general public.*

Environment

Cyanamide is hydrolytically stable and is not classified as "readily biodegradable". However, rapid degradation was shown in aerobic water/sediment systems, the active substance can be considered to have a low persistence in aquatic systems. In soil, low and moderate persistence has been observed under aerobic and anaerobic conditions, respectively. It was

concluded that cyanamide will be subject to significant levels of mineralisation in both the aquatic and terrestrial environments. Cyanamide can be considered as very mobile in soil. Cyanamide is harmful to aquatic organisms with long lasting effects. As the active substance is not considered to be volatile, the air compartment is not considered in the exposure assessment.

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusion**
Aqueous solution used in animal housings (only indoor in pig fattening) directly in manure (professional use)	Application to • the liquid manure via the slatted floor of pig fattening housings using a watering can or a half-automated movable cart after the end of a fattening cycle Emission to • soil due to liquid manure applications carried out according to maximum nitrogen immission limits, afterwards to groundwater and aquatic compartment (surface water and sediment)	**No conclusion possible**

In a conventional risk assessment (excluding ED properties), the intended use of the representative biocidal product as disinfectant in animal housings indicates no unacceptable risk for the aquatic and terrestrial compartments. Thus, for the environment, an acceptable risk for all compartments would be demonstrated for the use as direct manure application by professionals in piggeries. However, cyanamide is considered to have endocrine disrupting properties with respect to non-target organisms.

Therefore, the European Commission initiated a mandate according to Article 75(1)(g) of the BPR as the initial BPC opinion on cyanamide for PT 3 did not provide a clear conclusion on the level of the risks associated with the use of cyanamide in relation to its ED properties.

In the light of the available data the eCA provided a proposal that integrated the hazard caused by the ED properties of cyanamide.

Based on the discussions with the member states in the context of the ENV WG, question (a) of the COM's mandate, relating to the existence of a safe level (threshold) can be answered as follows:

> *Currently no thresholds/safe concentration limits with regard to environmental non-target organisms can be derived for the ED properties of cyanamide due to a variety of uncertainties associated with such an approach.*

In relation to item (b) 1 of the Commission's request asking for either a quantitative or a qualitative risk assessment, the following is concluded:

A risk assessment in the strict sense is not possible for cyanamide at this point in time. Neither a quantitative nor a qualitative risk assessment can be conducted as no safe threshold can be derived with which the exposure can be compared to. The only option is an assessment of the exposure situation with particular focus on whether the exposure can be considered negligible or not. However, it needs to be considered in this context, that the term "negligible" has not yet been defined within the frame of the BPR.

The conclusions of the qualitative assessment of the exposure situation are:

i. the data submitted by the applicant on the natural occurrence of cyanamide in certain plant species does not allow to assess reliably the environmental background levels and distribution of cyanamide in the environment and

ii. releases to the environment from the intended uses of cyanamide cannot be excluded.

In relation to item (b) 2 of the Commission's request asking for providing an opinion whether the risks can be considered acceptable or not, the result is summarized as follows:

Regarding the acceptability of the risk no final conclusion is possible. It is agreed that, given the uncertainties of the assessment and lack of methodology, it is currently not possible to determine whether the risk is acceptable. Nevertheless, it is agreed that, since exposure cannot be excluded, also the risk coming from this exposure cannot be excluded.

Overall conclusion

Due to uncertainties associated with the endocrine disrupting properties of cyanamide, it is not possible to conclude whether risks for both, human health and the environment for the only applied use (disinfection in empty pig stables by professionals, application by using watering cans or half-automated movable carts) are acceptable or not. The risk for the professional user is acceptable with adequate PPE.

Since it was not possible to derive a safe threshold with respect to the ED properties of cyanamide, no conclusion can be drawn on whether cyanamide fulfils the approval conditions.

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)	Cat. 2	Cyanamide does not fulfil criterion (a), (b) and (c) of Article 5(1)
	Mutagenicity (M)	no classification required	
	Toxic for reproduction (R)	Cat. 2	
PBT and vPvB properties	Persistent (P) or very Persistent (vP)	Cyanamide is not P and not vP The relevant major metabolites urea,	Cyanamide does not fulfil criterion (e) of Article

Property		Conclusions	
		dicyandiamide and guanidine are not P and not vP The minor metabolite thiourea is P and vP	5(1) and criterion (d) of Article 10(1)
	Bioaccumulative (B) or very Bioaccumulative (vB)	Cyanamide is not B and not vB The minor metabolite thiourea is not B and not vB	
	Toxic (T)	Cyanamide is T The minor metabolite thiourea is not T	
Endocrine disrupting properties	Section A of Regulation (EU) 2017/2100: ED properties with respect to humans	Yes	Cyanamide fulfils criterion (d) of Article 5(1) and criterion (e) of Article 10(1)
	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	
	Intended mode of action that consists of controlling target organisms via their endocrine system(s).	No	
Respiratory sensitisation properties	No classification required. Cyanmide does not fulfil criterion (b) of Article 10(1).		
Concerns linked to critical effects other than those related to endocrine disrupting properties	Cyanamide does not fulfil criterion (e) of Article 10(1).		
Proportion of non-active isomers or impurities	Cyanamide has a purity of 96.8 % w/w (dry weight) and does therefore not fulfil criterion (f) of Article 10(1)		

The major metabolites dicyandiamide and guanidine were only found in relevant amounts in the liquid manure study and were quickly degraded in soil. Therefore, they do not meet the P or vP criteria. For soil, effect values for dicyandiamide were available for earthworms; the value of 3000 mg/kg indicates that the T criterion is not fulfilled. In addition, urea, dicyandiamide and guanidine are not expected to fulfil the B and vB criteria based on their low log Kow value.

Consequently, the following is concluded:

Cyanamide meets the exclusion criteria laid down in Article 5(1)(d) of Regulation (EU) No 528/2012.

Cyanamide meets the conditions laid down in Article 10(1)(a) and (e) of Regulation (EU) No 528/2012 and is therefore 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" [6], with "Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR"[7] and with "Implementation of scientific criteria to determine the endocrine-disrupting properties of active substances currently under assessment"[8] 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).

According to the CA guidance[6] for draft CARs submitted before 1st September 2013, the exclusion and substitution criteria as defined in the BPR have to be assessed, but the principles of the BPD will apply for the decision-making. This means that though cyanamide fullfills Article 5(1)(d) of Regulation (EU) No 528/2012, Article 5(2) of Regulation (EU) No 528/2012 is not of relevance for the approval decision.

2.2.2. POP criteria

Cyanamide does not fulfil the criteria for being a persistent, organic pollutant.

The minor metabolite thiourea does not fulfil the criteria for being a persistent, organic pollutant.

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

Two public consultations were carried out to determine if any chemical or non-chemical alternatives are available for the intended use. According to the applicant, cyanamide is used for the disinfection of liquid manure in animal houses (pig stables) against the bacterium *Brachyspira hyodysenteriae* (use in PT 3) and to control fly larvae in liquid manure in animal houses (pig stables) (use in PT 18).

During the first consultation, six contributions were received. All contributions stated that cyanamide is particularly suited for the intended use due to its unique characteristics. Most contributors emphasized that no suitable chemical or non-chemical alternatives are available.

According to the submitted statements, swine dysentery caused by *B. hyodysenteriae* is a major cause of loss to pig industry throughout the world. *B. hyodysenteriae* is transmitted by flies and rodents or when pigs come into contact with contagious manure.

The following reasons for the need of a disinfection of the liquid manure were given. To

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[6] 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).

[7] 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).

[8] See document: Implementation of scientific criteria to determine the endocrine-disrupting properties of active substances currently under assessment (available from https://circabc.europa.eu/ui/group/e947a950-8032-4df9-a3f0-f61eefd3d81b/library/48320db7-fc33-4a91-beec-3d93044190cc/details).

prevent the spread of swine dysentery a strict program of antibiotic treatment and biosafety/ hygiene measures has to be followed. The treatment of the infected animals with antibiotics alone is not sufficient because *B. hyodysenteriae* can survive and proliferate in the liquid manure for months and re-infect newly housed animals when they come into contact with even small amounts of the contagious manure. Furthermore, *B. hyodysenteriae* has already developed resistances against a variety of antibiotics. Because the animals excrete 70-90% of the administered antibiotics unchanged or as active metabolites the risk of the development of further antibiotic resistances increases if *B. hyodysenteriae* is present in the manure.

According to the contributions, cyanamide is essential for the disinfection of the liquid manure to prevent the spread of swine dysentery caused by *B. hyodysenteriae.* It is emphasized that cyanamide, in contrast to other active substances, is effective even under the difficult circumstances of the intended use (e.g. it is effective at a high organic load in the liquid manure and at low temperatures, which is important if the treatment is carried out in winter). Furthermore, treatment of the liquid manure with cyanamide is effective against *B. hyodysenteriae* as well as against fly larvae, which can function as a vector. Consequently, it is suitable to interrupt the re-infection cycle without the use of a (second) larvaecide. No resistances of fly larvae or *B. hyodysenteriae* against cyanamide have been reported although the active substance has been used for decades. The development of resistance is not to be expected because cyanamide acts as a multi-site inhibitor.

Except for two submissions the validity of the submitted statements could not be checked because no references were given or can easily be found by literature research. It remains unclear whether cyanamide is the only active substance suitable for the intended use.

In the second public consultation in 2019, 10 contributions (8 non-confidential and 2 confidential) were received, mainly from Germany but also from Austria and Spain. In general, the statements in the newly submitted documents are very similar to the documents submitted in the first public consultation.

It is stated that cyanamide is the only active substance that combined the effects against *B. hyodysenteriae* and its vector, the fly larvae in liquid manure. According to the contributions, the use of other larvicides (e.g. diflubenzuron or cyromazine) is not necessary. Other larvicided approved for the same use are limited and are generally characterized by a specific mode of action entailing the risk of resistence build-up. It is claimed that if cyanamide is not used, more antibiotics will be necessary, resulting also in a greater risk for antibiotic resistance. Furthermore, one contribution claims that cyanamide is a biodegradable and natural occurring substance synthesized by plants, allowing the use of the pig slurry as manure.

In none of the contributions received, neither in the first nor in the second round of the consultation, an alternative is mentioned.

In Denmark and Norway, cyanamide is not used in pig stables. Instead, the pig stables are cleaned and afterwards the clean surfaces are treated with a surface disinfectant. The manure itself is never treated.

<u>Potential alternative active substances:</u>

For PT 3 the following active substances have already been approved: active chlorine generated from sodium chloride by electrolysis, active chlorine released from calcium hypochlorite, active chlorine released from hypochlorous acid, active chlorine released from sodium hypochlorite, alkyl (C12-16) dimethylbenzyl ammonium chloride (ADBAC/BKC (C12-16)), amines, N-C10-16-alkyltrimethylenedi-, reaction products with chloroacetic acid (Ampholyt 20), bacillus amyloliquefaciens, benzoic acid, biphenyl-2-ol, calcium dihydroxide, calcium magnesium oxide, calcium magnesium tetrahydroxide, calcium oxide, chlorocresol, didecyldimethylammonium chloride (DDAC), formaldehyde, glutaraldehyde, hydrogen peroxide, iodine/polyvinylpyrrolidone iodine, L-(+)-lactic acid, peracetic acid, peracetic acid

generated from tetra-acetylethylenediamine (TAED) and sodium percarbonate, PHMB(1600;1.8) and reaction mass of peracetic acid and peroxyoctanoic acid.

None of these active substances was evaluated with the same intended use as cyanamide. Therefore, it cannot be concluded whether any of these active substances might be an alternative for the disinfection of liquid manure in pig stables against the bacterium *Brachyspira hyodysenteriae*.

2.3. BPC opinion on the application for approval of the active substance cyanamide in product type 3

In view of the results of the evaluation and the data available, it is not possible to conclude whether cyanamide shall be approved and be included in the Union list of approved active substances. Neither a positive nor a negative conclusion can be drawn on whether cyanamide fulfils the approval conditions of Article 4(1) of Regulation (EU) No 528/2012, in particular with regard to the criteria referred to in Article 19(1)(b)(iii) and (iv).

With respect to human health, it was not possible to decide on a safe level (threshold), mainly due to the uncertainties regarding the EAS modalities. Cyanamide was already shown to fulfil the ED criteria with respect to the T modality and the ED guidance does not require exploring all modalities in full detail for reasons of animal welfare when the ED properties for one modality are already demonstrated. However, the approach for a quantitative risk assessment as it was proposed by the eCA was considered unsuitable due to the high level of uncertainty. Thus, no quantitative risk assessment neither for the professional user nor for the general public could be agreed on. For the general public, same applies for a qualitative risk assessment which considered possible RMMs, where uncertainties on the magnitude of exposure and the lack of a threshold did not allow to draw a conclusion whether the risk is acceptable for the general public or not. In contrast, the risk regarding the ED properties of cyanamide is considered acceptable for professional users.

With respect to the environment, the diversity of non-target organisms and the lack of suitable test methods did not allow to derive a safe level (threshold) for cyanamide. Data provided by the applicant were considered insufficient to reliably assess the environmental background levels and distribution of cyanamide. Thus, the magnitude of exposure from biocidal uses in combination with the lack of a threshold did not allow a quantitative risk assessment for cyanamide. With regard to a qualitative risk assessment, exposure from biocidal uses could not be excluded nor is a definition available when risks from exposure are considered negligible. Thus, given the uncertainties, it was not possible to conclude whether the risk is acceptable for the environment or not.

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

1. Specification: minimum purity of the active substance evaluated: minimum purity in 96.8 % w/w (dry weight), manufactured as an aqueous solution with 50.5 % w/w.

2. The authorisations of biocidal products are subject to the following condition(s):
    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. In addition, pursuant to point 10 of Annex VI to Regulation (EU) No 528/2012, the product assessment shall include an evaluation as to whether the conditions of Article 5(2) of Regulation (EU) No 528/2012 can be satisfied.

    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.

c. According to point (d) of Article 19(4) of Regulation (EU) No 528/2012, products shall not be authorised for making available on the market for use by the general public.

d. In view of the risks identified for the uses assessed, the product assessment shall pay particular attention to:

    i. professional users;

    ii. general public.

e. For products that may lead to residues in food or feed, the need to set new or to amend existing maximum residue levels (MRLs) in accordance with Regulation (EC) No 470/2009 or Regulation (EC) No 396/2005 shall be verified, and any appropriate risk mitigation measures shall be taken to ensure that the applicable MRLs are not exceeded.

3. 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 cyanamide 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 as it is classified as Carc. 2, Repr. 2, Acute Tox. 3 via dermal and oral route, Skin Sens. 1 and STOT RE2. Furthermore, the active substance is considered to have endocrine disrupting properties according to Section A and B of Regulation (EU) 2017/2100.

2.4. Elements to be taken into account when authorising products

1. The active substance cyanamide is considered as a candidate for substitution, and consequently the competent authority shall perform a comparative assessment as part of the evaluation of an application for national authorisation.

2. The 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 is identified for professional users, 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 taking into account the properties of cyanamide.

3. 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.

4. Similar to active substances approved according to Article 5(2) of Regulation (EU) No 528/2012, the use of biocidal products containing cyanamide should be subject to appropriate risk mitigation measures to ensure that exposure of humans, animals and the environment is minimised taking into account that it is considered to have endocrine disrupting properties.

2.5. Requirement for further information

Sufficient data have been provided to verify the conclusions on the active substance.

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