Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

Amines, N-C_{10}–C_{16}-alkyltrimethylenedi-, reaction products with chloroacetic acid

Product type: PT 3

ECHA/BPC/054/2015

Adopted

15 April 2015

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Opinion of the Biocidal Products Committee

on the application for approval of the active substance Amines, N-C10–C16-alkyltrimethylenedi-, reaction products with chloroacetic acid 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:	**Amines, N-C_{10}–C_{16}-alkyltrimethylenedi-, reaction products with chloroacetic acid**
Chemical name(s):	**Amines, N-C_{10}–C_{16}-alkyltrimethylenedi-, reaction products with chloroacetic acid**
EC No.:	**N/A**
CAS No.:	**139734-65-9**
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 Evonik Industries AG (formerly Goldschmidt GmbH) on 30th July 2007, the evaluating Competent Authority Ireland submitted an assessment report and the conclusions of its evaluation to the Commission on 30th August 2013. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC and its Working Groups. Revisions agreed upon were presented and the assessment report and the conclusions were amended accordingly.

Adoption of the BPC opinion

Rapporteur: Ireland

The BPC opinion on the approval of the active substance Amines, N-C_{10}–C_{16}-alkyltrimethylenedi-, reaction products with chloroacetic acid in product type 3 was adopted on 15 April 2015

The BPC opinion was adopted by consensus.

Detailed BPC opinion and background

1. Overall conclusion

The overall conclusion of the BPC is that the Amines, N-C_{10}–C_{16}-alkyltrimethylenedi-, reaction products with chloroacetic acid in product type 3 may 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 Amines, N-C10–C16-alkyltrimethylenedi-, reaction products with chloroacetic acid, which is also known under the synonym Ampholyt, in product type 3. Ampholyt acts by a relatively unspecific mode of action. As an amphoteric surfactant part of the mode of action includes surface activity with the cell or viral surfaces. The charged character of the molecule, amphotheric agents effectively bind to cellular or viral surfaces, and disrupt the barrier that ensures impermeability. The surfactant mixture is considered to be a UVCB substance (substance of Unknown, Variable Composition, or Biological origin). The active substance is considered to be made up of ~24 individual components having long chain alkanes (C_{10}-C_{16} with C_{12} and C_{14} predominating) with amine, or amine and carboxyl functional groups. The individual components and specification ranges for the components that make up the active substance are reported. A minimum specification content of 100% w/w for total active substance was determined for the dry purified active substance material (TC). The specification range for the technical material as manufactured (TK) is 16–22% w/w (average of 19% w/w) for total active substance content in aqueous solution. 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. A number of physical and chemical properties could not be experimentally determined because of the surfactant properties of the active substance and some properties for the individual components have been determined by QSAR. The substance is not considered flammable, explosive or oxidising.

Analytical methods are available for the active substance as manufactured. The HPLC-CAD method is used to determine all components of the active ingredient in Ampholyt, except the HPLC-UV method for acetic acid and a method will be required for the analysis of water content. Ampholyt is a UVCB substance and therefore does not contain impurities as such. Analytical methods are available for the relevant matrices that include soil, drinking water, food of plant and animal origin (meat, milk, fat, wine and beer), however deficiencies remain relating to some of the components of the active substance and further method validation will be required as the applicant has only used a single ion transition for method validation. The applicant should validate the lead components for an additional ion transition. Validated analytical methods are missing and required for surface water and sediment matricies and body fluids and tissues at product authorisation (refer to the section 2.5).

No harmonised classification for Ampholyt is available according to regulation (EC) No 1272/2008. A CLH dossier to ECHA will be submitted by the evaluating CA in 2016.

The proposed classification and labelling for Ampholyt according to Regulation (EC) No 1272/2008 (CLP Regulation) is:

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox Cat. 4, *H302 Skin Corrosion, Cat. 1, *H314 STOT RE Cat. 1, *H372 Repr. Cat. 2, *H361f Aquatic Acute Cat. 1, *H400 Aquatic Chronic Cat. 1, *H410
Labelling	
Pictograms	GHS05, GHS08, GHS09
Signal Word	Danger
Hazard Statement Codes	H302 Harmful if swallowed H314 Causes severe skin burns and eye damage H361f Suspected of damaging fertility H372 Causes damage to (eyes, mesenteric lymph nodes, male/female genital systems) through prolonged or repeated exposure H410 Very toxic to aquatic life with long lasting effects EUH401 To avoid risks to human health and the environment, comply with the instructions for use
Specific Concentration limits, M-Factors	M = 10 (acute) M = 1 (chronic)

b) Intended use, target species and effectiveness

Ampholyt is used as a hard surface disinfectant in treatments to surfaces, walls, and floors in animal health and veterinary areas (including footbaths) by professionals to prevent the spread of various micro-organisms. The spectrum of antimicrobial activity is focused on the destruction of gram-positive and gram-negative bacteria, yeasts, as well as a limited viruicide activity against enveloped viruses and against the non-enveloped adenovirus. The effectiveness of Ampholyt observed in tests under a range of conditions on bacteria, moulds and viruses to demonstrate innate activity of the active substance against a selection of representative target organisms, indicated effective concentrations in the ranges 0.125-0.5%, 0.125-0.25% and 0.2-1.0%, respectively.

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against the target organism(s) and the evaluation of the data provided in support of the efficacy of the accompanying product, establishes that the products containing the active substance are expected to be efficacious. Specific resistance to Ampholyt has not been recorded to date and is not expected due to the relatively unspecific mode of action of amphoterics, which is at least partly based on surface activity.

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

Human health

Ampholyt is harmful when administered by the acute oral route and was determined to have a rat oral LD50 value between 300 and 2,000 mg/kg body weight. When administered repeatedly by the oral route, repeated dose studies on the 90-day rat study, the 90-day dog study and the two year mouse study indicate Ampholyt can cause damage to organs (eyes, mesenteric lymph nodes, male/female genital systems) through prolonged or repeated exposure. Toxicological studies carried out on Ampholyt indicate that the substance is corrosive based on in vivo corrosivity and irritation studies on rabbit. Based upon the results of the 90 day dog dietary study and 18 month mouse dietary study Ampholyt may also potentially affect fertility.

The table below summarises the exposure scenarios assessed.

Summary table: human health scenarios			
Scenario	**Primary or secondary exposure and description of scenario**	**Exposed group**	**Safe use for scenario**
Spraying: Mixing and loading	Primary exposure: handling containers and diluting with water for low pressure spraying. Low-pressure spraying: Spray Model 1 (TNsG 2002) incorporates mixing and loading with an exposure time combining mixing and loading and application of 120 min. Tier I with no PPE. Tier II with PPE (coveralls and gloves, 10%).	Prof.	No safe use identified at 120 mins and Tier II PPE
Spraying: Application	Primary exposure: Low-pressure spraying: Spray Model 1 (TNsG 2002) which incorporates mixing and loading with an exposure time for mixing and loading and application of 120 min. Tier I with no PPE. Tier II with PPE (coveralls and gloves, 10%).	Prof.	No safe use identified at 120 mins and Tier II PPE
Spraying: Post Application	Primary exposure: Wash-down, disposal of the remaining cleaning solution/waste water and disposal of empty containers. Post- application time assumed: 9 minutes. Tier I with no PPE. Tier II with PPE (coveralls and gloves, 10%).0%).	Prof.	Acceptable use identified at Tier II
Spraying: Combined exposure	Primary exposure: mixing and loading, application and post application (coveralls and gloves, 10%) for low-pressure spraying,	Prof.	No safe use identified when combined with 10% PPE
Footbath: Mixing and loading for preparation	Primary exposure: handling containers and diluting with water for footbath preparation and, where relevant, pouring of the prepared solution from a mixing bucket to the footbath tray. EUROPOEM II DB for manual pouring and loading (up to 20L). Tier I with no PPE. Tier II with PPE (coveralls and gloves, 10%).	Prof	Acceptable use identified at Tier II
Footbath:Post Application	Primary exposure: Wash-down, disposal of the remaining cleaning solution/waste water and disposal of empty containers. Tier I with no PPE. Tier II with PPE (coveralls and gloves, 10%).	Prof.	Acceptable use identified at Tier II
Footbath: Combined exposure	Primary exposure: mixing and loading, application and post application (coveralls and gloves, 10%) for footbaths	Prof.	Acceptable use identified at Tier II

RTU: Combined exposure from spraying by RTU	Primary exposure: application and post application of ready-to-use trigger spray. Application: Model TNsG Consumer Spraying and Dusting Model 2 – hand held trigger spray. Wash-down, disposal of the remaining cleaning solution/waste water and disposal of empty containers. Application time assumed: 30 minutes (total exposure including application and post-application). Wiping step (Surface disinfection model 1): 15 minutes. Tier I with no PPE. Tier II with PPE (coveralls and gloves, 10%).	Prof.	Acceptable use identified at Tier II
Secondary exposure	Secondary exposure: child in contact (oral and dermal exposure) with residues following disinfection procedure.	Child	No safe use identified

Skin and eye corrosive properties were observed in the tests using Ampholyt. Therefore, the classification of Ampholyt as H314 "Causes severe skin burns and serious eye damage", according to CLP Regulation 1272/2008, warrants the incorporation of a qualitative local risk assessment to address the potential risks associated with its use to the skin and to the eye. Study data suggests that the technical active substance and products may cause corrosion to skin and eyes under the normal conditions of use through the mixing and loading phase of an application process. The use of PPE including protective eyewear is recommended because of corrosive and irritant local effects.

For professional users exposure to Ampholyt was evaluated for the scenarios summarized in the table above.

- Spraying application

In the tier II assessment for low-pressure spraying, considering the use of appropriate PPE (coveralls and gloves, 10%) acceptable risk were identified for post-application processes; but risks were identified for individual phases of the scenarios for mixing and loading, and application. Risks were identified for professionals when all phases were combined (mixing/loading, application and post-application) for the spraying scenario.

- Ready-to-use (RTU) trigger spray spot application

For professional users application by RTU trigger spray using PPE is acceptable for all phases (application and post-application) when combined.

- Footbath application

In the tier II assessment, considering the use of appropriate PPE (coveralls and gloves, 10%) acceptable uses were identified for all individual phases of the scenarios for footbaths that include mixing and loading, application and post application. Acceptable uses were also identified when all individual phases were combined.

Application in animal housings and other veterinary areas might result in exposure of humans to residues of the active substance via food. Currently there is no guidance available for conducting dietary risk assessments and it is proposed that issues relating to dietary risk are undertaken at product authorisation.

A risk of secondary exposure is identified based on the worst case exposure of a crawling child on a floor in contact (oral and dermal exposure) with residues following hard surface disinfection. However, for industrial or cross-contamination prevention application scenarios like the footbath application this situation of a crawling child is not considered relevant.

Environment

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios	
Scenario	**Description of scenario including environmental compartments**
Disinfection of animal housing	Sows in groups, fattening pigs and broilers in free range. Emissions from spraying to slurry/manure. The slurry/manure will be spread on grassland or arable land and lead to exposure of soil and groundwater. Broilers in free range also lead to emission to surface water and sediment via STP.
Disinfection of vehicles used for animal transport	Animal transport for mammals and poultry. Waste water emissions from spraying to the STP. Emissions to slurry/manure. The slurry/manure will be spread on grassland or arable land and lead to exposure of soil and groundwater.
Veterinary hygiene	Footbath for humans (in animal housing for sows in groups, fattening pigs and broilers in free range) and animal hooves (dairy cows). Emissions from spraying to slurry/manure. The slurry/manure will be spread on grassland or arable land and lead to exposure of soil and groundwater. Broilers in free range also lead to emission to surface water and sediment via STP.

- Disinfection of animal housing

An acceptable risk was identified for the disinfection of animal housing (both in sows in group and fattening pigs) where there are no direct emissions to the STP.

A risk was identified for animal housing containing broilers as a result of exposure to the surface water and sediment compartments when water is released from the STP. This risk could be mitigated by directing the emission to slurry/manure rather than to the STP. As such, biocidal products containing the active substance, Ampholyt, should not be applied in animal housings where direct releases of the active substance to surface water cannot be prevented and/or where safe releases of the active substance to an STP cannot be identified.

- Application of ampholyt by ready-to-use (RTU) products used for the spot treatment of surfaces was not considered for the animal housing scenario but it should be noted that such uses could be applicable for applications at product authorisation. Disinfection of vehicles used for animal transport

Risks to the environment were identified for the soil, sediment and surface water compartments when Ampholyt is applied for the disinfection of vehicles used for animal transport (both mammals and poultry). Acceptable risks were identified for the same scenarios for groundwater and the STP.

- Veterinary hygiene (footbaths)

Risks were identified for the STP and surface water for use of a footbath to disinfect footwear in the broiler, sows in groups and fattening pig housing scenarios and for the disinfection of animals' hooves (dairy cows) in veterinary hygiene situations. However, acceptable risks were identified for the disinfection of footwear via a footbath for humans in a veterinary hygiene scenario (for broilers, sows in group and fattening pigs) where there are no direct emissions to the STP and emissions were directed to slurry/manure for subsequent spreading to the land.

Given the risks identified they should be mitigated by directing the emission to slurry/manure rather than to the STP. As such, biocidal products containing the active substance, Ampholyt, should not be applied to footbaths where direct releases of the active

substance to surface water cannot be prevented and/or where safe releases of the active substance to an STP cannot be identified.

Application of ampholyt by ready-to-use (RTU) products used for the spot treatment of surfaces was not considered for the veterinary hygiene purposes but it should be noted that such uses could be applicable for applications at product authorisation.

Additionally, the risk of secondary poisoning after the application of Ampholyt is not considered to be of concern for the aquatic or terrestrial food chain owing to Ampholyt being both highly water-soluble and readily biodegradable in the environment.

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)	Repr. Cat. 2 (H361f)
Respiratory sensitisation	No classification required	
PBT and vPvB properties	Persistent (P) or very Persistent (vP)	Not P or vP
	Bioaccumulative (B) or very Bioaccumulative (vB)	Not B or vB
	Toxic (T)	T
Endocrine disrupting properties	Effects on organ systems in studies with Ampholyt suggest a systemic toxicity mediated by perturbations in the lymphatic system. The male and female genital systems are not selectively impacted but rather are part of a group of organs impacted by Ampholyt's systemic toxicity. Ampholyt is not considered not have endocrine disrupting properties.	

Consequently, the following is concluded:

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

Ampholyt does not meet the conditions laid down in Article 10 of Regulation (EU) No 528/2012, and is therefore not 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[1]" and in line with "Further guidance on the application of the substitution criteria set out under article 10(1) of

[1] 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)

the BPR"[2]agreed at the 54th and 58th meeting 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[3]. 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 and d).

2.2.2. POP criteria

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

Ampholyt does not have potential for long-range transboundary atmospheric transport.

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

In view of the conclusions of the evaluation, it is proposed that Amines, N-C10–C16-alkyltrimethylenedi-, reaction products with chloroacetic acid (Ampholyt) shall be approved and be included in the Union list of approved active substances, subject to the following specific conditions:

1. Specification: minimum purity of the active substance evaluated: The active substance as manufactured is an aqueous solution of 160-220 g/kg (16-22 %, by wt) solution of Ampholyt. The theoretical (calculated) dry weight specification: minimum purity of Ampholyt is 1000 g/kg (100.0 %, by wt).

2. The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any use covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.

3. For professional users, safe operational procedures and appropriate organisational measures shall be established. Products shall be used with appropriate personal protective equipmen where exposure cannot be reduced to an acceptable level by other means.

4. Products should not be applied by low-pressure spraying unless it can be demonstrated at product authorisation that risks to human health can be reduced to an acceptable level.

5. Products used for disinfection of animal housings as well as footwear disinfection shall not be authorised for uses where direct release via waste water to STP and/or surface water cannot be prevented unless it can be demonstrated at product authorisation that risks to the surface water and sediment can be reduced to an acceptable level..

6. Products used for disinfection of vehicles for animal transport as well as for disinfection of animal hooves shall not be authorised unless it can be demonstrated at product authorisation that risks to the environment can be reduced to an acceptable level.

7. 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 of the European Parliament and of the Council or Regulation (EC) No 396/2005 of the European Parliament and of the Council shall be verified, and any appropriate risk mitigation measures shall be taken into account to ensure that the applicable MRLs are not exceeded.

[2] 2 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)

The active substance does not fulfil the criteria according to Article 28(2)(a) to enable inclusion in Annex I of Regulation (EU) 528/2012.

2.4. Elements to be taken into account when authorising products

1. When authorising products containing Ampholyt Member States will need to determine the potential risk presented following secondary exposure to contaminated food or food products.

2. For the calculation of the concentration in soil (manure/slurry application the Emission Scenario Document for PT3 was used. This means that the amount of biocide present in the manure is related to the nitrogen content and the nitrogen load, which is allowed according to the immission standard. Some Member States may have derogations in relation to certain aspects of the EU Nitrates Directive. Where relevant this information should be taken into account at product authorisation.

3. When authorising products containing Ampholyt special attention shall be given, where relevant, to the potential risks for children to be exposed to residues of Ampholyt.

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 Ampholyt. However, further data shall be required as detailed below. The data should be provided to the evaluating Competent Authority (Ireland) as soon as possible but no later than 6 months before the date of approval of the active substance.

2.5.1. Physical and chemical properties

The applicant needs to confirm their specification proposals for the C10 components (including C10-diGly) in the active matter. The C10 components were not analysed as part of the 7-batch analysis.

The applicant should provide a study or make a statement in relation to the corrosivity of Ampholyt to metals.

2.5.2. Methods of analysis

The applicant should provide further validation of the active substance in the technical material as manufactured regarding the HPLC-CAD method. Following deficiencies should be addressed: the use/synthesis of certain reference standards for method validation and the lack of validation data for a number of components which are considered to be part of the active substance.

The applicant needs to provide a validated method of analysis for water in the technical material as manufactured. The applicant should also experimentally determine the LOQ of acetic acid down to a level of 0.9% w/w for the HPLC-UV method.

The applicant should provide validation data for a second ion transition for the "three lead components" included in the residue analysis method and definition for monitoring in soil and drinking water. Additionally, the applicant needs to provide a validated method of analysis for sediment, body fluids and tissue (the LOQ should allow determination at the NOAEL).