Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report

diamine

(N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine)

Product-type 08
(Wood preservative)

January 2021

Portugal

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1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

This assessment report has been established as a result of the evaluation of the active substance N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine as product-type 08 (wood preservatives), carried out in the context of the work programme for the review of existing active substances provided for in Article 89 of Regulation (EU) No 528/2012[1], with a view to the possible approval of this substance.

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine (CAS no. 2372-82-9) was notified as an existing active substance, by Lonza Cologne GmbH, hereafter referred to as the applicant, in product-type 08.

Commission Regulation (EC) No 1062/2014 of of 4 August 2014[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process.

On 2004, Portugal competent authorities received a dossier from Lonza Cologne GmbH. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 2004.

On 9 November 2005 the Rapporteur Member State submitted to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the the "Agency" (ECHA). Revisions agreed upon were presented at the Biocidal Products Committee and its Working Groups meetings and the competent authority report was amended accordingly.

1.2. Purpose of the assessment report

The aim of the assessment report is to support the opinion of the Biocidal Products Committee and a decision on the approval of diamine for product-type 08, and, should it be approved, to facilitate the authorisation of individual biocidal products. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available from the Agency web-site shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Regulation (EU) No 528/2012, such conclusions may not be used to the benefit of another applicant, unless access to these data for that purpose has been granted to that applicant.

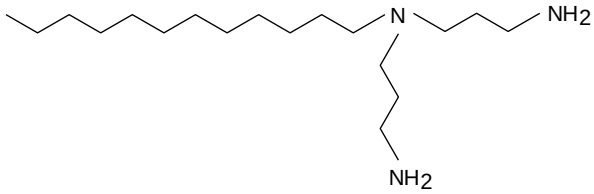
[1] Replace by Article 90(2) for a new active substance submitted under Article 11 of the BPD

[2] COMMISSION DELEGATED REGULATION (EU) No 1062/2014 of 4 August 2014 on the work programme for the systematic examination of all existing active substances contained in biocidal products referred to in Regulation (EU) No 528/2012 of the European Parliament and of the Council. OJ L 294, 10.10.2014, p. 1

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

2.1.1. Identity, Physico-Chemical Properties & Methods of Analysis

CAS-No.	2372-82-9
EINECS-No.	219-145-8
Other No. (CIPAC, ELINCS)	
IUPAC Name	N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine
Common name, synonyma	Not allocated. Same as IUPAC name.
Molecular formula	C18H41N3
Structural formula	
Molecular weight (g/mol)	299.54
Representative biocidal product(s)	[redacted] (proposed) Other code numbers: [redacted]

The N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine technical specification with a minimum purity of 91% w/w is supported by a non-validated analytical profile of batches at industrial scale.

Additional confirmation data was submitted using a validated HPLC-MS/MS one batch was analysed and the contents of the active and impurities were within the specified range (DOC IIIA 4.1 (confidential).

Two main impurities have been identified using validated GC-MS-MS and HPLC-MS methods. As neither of the impurities was considered to be of concern, the conclusion is that both impurities have been identified

Physical and chemical properties

N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine is a colourless liquid with low vapour pressure and at 20°C is highly soluble in water (highest concentration of a.s in water 95%:5% (822 g/L) forms a free flowing homogeneous liquid). It is completely soluble in organic solvents (methanol, acetone, ethyl acetate and n-octanol) The estimation of its partition coefficient n-octanol/water (Pow = 0.7) suggests that N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine does not have a tendency to bioaccumulate, however it has the characteristic of near irreversible binding or interaction with organic matter. N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine is not explosive nor oxidising nor flammable and it was found to be stable in its packaging.

All points were addressed and considered acceptable.

Analytical methods

Water was determined by Karl-Fisher, an accepted method.

A direct analytical method employing LC-MS/MS was validated with satisfactory results for the [redacted] (N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine) and impurities.

For monitoring purposes validated methods were submitted for the determination of active substance in all relevant environmental media:

In soil, the residues were determined by HPLC-MS/MS a fully validated method that allows the determination of the active in soil at a LOQ of 0.01 mg/kg. Soil samples were extracted with methanol:water:ammonia solution (90:10:1 v:v:v) containing 0.5M ammonium formate. An aliquot of the sample extracts was evaporated under nitrogen to a small volume, prior to reconstitution in methanol:water.formic acid (50:50:0.2 v:v:v). Quantitation was performed using liquid chromatography with tandem mass spectrometric detection (LC-MS/MS).

In water, the residues were determined by HPLC-MS/MS a fully validated method that allows the determination of the active in water at a LOQ of 0.1 µg/l in ground water; 1.0 µg/l in surface water and > 1.0 µg/l in drinking water. The fortified samples was mixed with an aliquot of methanol:water:formic acid (90:10:0.5 v:v:v) containing 0.5M ammonium formate. The analyte was removed from water samples using Strata-X SPE cartridges. Quantitation was performed using liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). Due to the matrix (presence of chlorine) it was not possible to validate the analytical method in the used drinking water at the required limit of detection.

It was not possible to fully validate an analytical method covering drinking, ground and surface water samples in accordance with 91/414/EEC as amended by 96/46/EC, SANCO/3029/99 rev.4 guidelines at the required limit of 0.1 µg/L but only at ≥ 1 µg/L due to chlorine interference (coming from the water itself).

The method was also tested with purified water and the LOQ achieved was 0.1 µg/L.

- Residues in air: the active substance is not volatile in air as its vapour pressure is low. In addition in the wood protection market, the product is sold as an aqueous solution of the a.s. and will not be used by spraying application; thus measurable concentrations in the air under normal use will not occur and are highly unlikely even under unusual circumstances (e.g. accidental releases). Thus, it is considered that the determination of analytical methods in air is not required.

- As N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine is not classified as toxic or highly toxic, analytical methods for human body fluids and tissues are not required.

- Residues in foodstuffs: wood treated with the a.s. in a biocidal product is not intended for use in areas where food for human consumption is prepared, consumed or stored, or where the feedingstuff for livestock is prepared, consumed or stored. Thus, it is considered that analytical methods for determination of residues in/on food or feedstuffs is not required.

Analytical methods for the determination of residues of a.s. and relevant metabolites

Sample	**Test substance**	**Analytical method**	**Fortification range / Number of measurements**	**Linearity**	**Specificity**	**Recovery rate (%)**			**Limit of determination**	**Reference**
						Range	Mean	St. dev.%		
Soil (clay loam)	N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine (88.7 w/w)	HPLC-MS/MS	0.01-0.1 mg/L 5 measurements per level	Y = 300.350X-46.586 R^2=0.9995	No interferences *	0.01 mg/L 73 - 94	80	RSD 10.1%	0.01 mg/L	[redacted] (2007)
						0.1 mg/L 84 - 99	92	RSD 7.2%		
Sandy loam	N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine (88.7 w/w)	HPLC-MS/MS	0.01-0.1 mg/L 5 measurements per level	Y = 300.350X-46.586 R^2=0.9995	No interferences *	0.01 mg/L 76 - 90	80	RSD 7.4%	0.01 mg/L	
						0.1 mg/L 93 - 101	97	RSD 3.4%		
						2.5 mg/L: 132-142	137	RSD 2.5%		
Ground water	N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine (88.7 w/w)	HPLC-MS/MS	0.1-1.0 µg/L 5 measurements per level	Y = 381.006X -10.626 R^2=0.9998	No interferences *	0.1 µg/L 72 - 78	77	RSD 3.4%	0.1 µg/L	[redacted] (2007)
						1.0 µg/L 72 - 85	78	RSD 5.9%		
Surface	N-(3-Aminopropyl)-N-	HPLC-MS/MS	0.1 – 10.0 µg/L 5	Y = 381.006-10.626	No interferences *	0.1 µg/L 60 -65	62	RSD 4.0 %	1.0 µg/L	[redacted] (2007)

Sample	Test substance	Analytical method	Fortification range / Number of measurements	Linearity	Specificity	Recovery rate (%)			Limit of determination	Reference
						Range	Mean	St. dev.%		
water	dodecylpropane-1,3-diamine (88.7% w/w)		measurements per level	R^2=0.9998		1.0 µg/L 72 - 77	74	RSD 2.9 %		[redacted]
						10.0 µg/L 82 - 109	97	11.5 %		
Drinking water	N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine (88.7% w/w)	HPLC-MS/MS	0.1 – 1.0 µg/L 5 measurements per level	Y = 381.006-10.626 R^2=0.9998	No interferences *	0.1 µg/L 50 - 59	54	RSD 6.4 %	>1.0 µg/L	[redacted] (2007)
						1.0 µg/L : 62 - 66	64	RSD 3.1%		
Ultra pure (UP)	N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine (88.7% w/w)	HPLC-MS/MS	0.1 – 1.0 µg/L 5 measurements per level	Y = 381.006-10.626 R^2=0.9998	No interferences *	0.1 µg/L : 81 - 93	89	RSD 5.2 %	1.0 µg/L	[redacted] (2004)
						1.0 µg/L : 74 - 94	88	RSD 9.5 %		

2.1.2. Intended Uses and Efficacy

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 summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious.

N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine is intended to be used as an active substance against wood destroying basidiomycetes, with preventive protection of wood and construction timbers of use classes (UC) 1 to 4a. The active substance was considered in the assessment for use by industrial users, in industrial pre-treatment of timber by vacuum pressure impregnation and dipping/surface treatment. In addition, in order to facilitate the work of Member States in granting or reviewing authorisations, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

Related to the concentrations at which the active ingredient will be used laboratory tests with an aqueous solution of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine, according to EN 113 at a range of 0.4 – 0.8% w/w (2.6- 5.3 kg a.s. /m3) was found to be sufficient to protect the wood against destroying basidiomycete fungi.

The accompanying product [redacted] contains 4,41 % of active substance. The formulation showed a sufficient level of efficacy to protect constructional timbers in areas with moderate or subtropical climate, and is to be used exclusively in industrial applications. The method of application depends on the class of hazard to be protected. It includes the short term dipping (use class 1-2), long term dipping (use class 1-3) and industrial impregnation vacuum/pressure (use class 1-4a).

An uptake of 2.3-3.6Kg/m3 resp. 30-40 g/m2 should be achieved by these application methods in order to ensure the protection level for the use class required.

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine is a non-ionic surfactant type active substance. Since it is surface active, it has fair wetting properties and reacts strongly with cell walls of micro-organisms. Its mode of action, therefore, is to destroy the cell walls by chemical reaction with the exterior structures and by entering and disintegrating the inner phospholipid-bilayer based membrane structures. Due to its interaction with phospholipid-bilayer structures, it severely alters the cell wall permeability, disturbs membrane-bound ion-translocation mechanisms and may facilitate the uptake of other biocides. It is effective against Gram+ bacteria. Weak activity is shown against Gram- bacteria and against fungi there exists a selective activity spectrum.

2.1.3. Classification and Labelling

The following classification and Labelling is proposed in accordance with Regulation (EC) Nº 1272/2008 as amended, and Commission Regulation (EC) Nº 547/2011

Proposed classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox. 3 Skin Corr. 1B STOT RE 2

	Acute Aquatic 1
Labelling	
Pictogram codes	GHS05, GHS06, GHS08, GHS09
Signal Word	Danger
Hazard Statement Codes	H301 H314 H373 H400
Specific Concentration limits, M-Factors	M = 1
Justification for the proposal	
Acute Tox. 3 H301: Toxic if swallowed, based on the oral LD50 in rats of 261 mg a.s./kg bw. Because of the corrosive effects of the undiluted product Skin Corr. 1B, H314: Causes severe skin burns and eye damage is assigned. The risk of severe damage to eyes is considered implicit. STOT RE 2, GHS08, H373: May cause damage to organs through prolonged or repeated oral exposure. (nephrotoxicity: moderate proximal tubular changes with evidence of degeneration, regeneration and hyperplasia at 90 mg/kg bw/day). Acute Aquatic 1; H400: Very Toxic to aquatic life based on the EbC50 of 0.012 mg/l on the most sensitive aquatic organism tested (algae); active ingredient can be considered as readily biodegradable and does not merit additional classification for chronic effects to aquatic life.	

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard identification and effects assessment

Toxicokinetics and metabolism
Studies performed in rats:

[redacted]

Urine was not analysed as the total radioactivity excreted in the urine was < 0.3 %

There were 6 minor faecal metabolites found each 1-3% of the applied dose. One metabolite was identified as 1-dodecylamine. The major compound excreted in faeces was identified as the parent compound (7-13% of the applied dose). There is evidence that the substance may have a cumulative effect on the renal tubule, intermediate concentrations of radioactivity were detected in the renal cortex 120 hours after administration. Around 81% of the radioactivity excreted in the faeces were not identified, according to the applicant ”the results of the Toxicokinetic study showed that 90 to 97% of the administered radioactivity is excreted in the faeces. Taking into account the very limited gastrointestinal absorption after oral administration, it can be concluded that the most of the metabolites detected in the faeces by TLC radiochromatography is formed by the intestinal flora.”.

[redacted]

A study to identify the tissue distribution and depletion of the test substance after oral administration was performed. After an oral dose of 3 mg/kg, 14C-N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine related material was slowly absorbed and distributed in the tissues and organs investigated. Peak concentrations generally occurred at Tmax = 12 hours post dosing. Radioactive concentrations were highest in the different gastrointestinal parts (without contents) and to a lesser extend in the richly vascularised organs (i.e. adrenals, heart, kidney, liver, lung, pancreas and spleen). Concentrations were also found high in the mesenteric lymph nodes. Concentrations in those tissues/organs were higher than blood concentrations.

At the time point of TCmax for most of the tissues, i.e. 12 hours post dosing, in total 1.70 % of the administered radioactivity was found absorbed and distributed in tissues and organs. Highest amounts were found in muscle (0.60%), liver (0.48%), kidney (0.15%) ,and skin (0.15%). A remarkable amount of the radioactivity was measured in the tissue of the GI-tract accounting for about 4% of the dose. The radioactivity in question was not due to contamination with feces, but was associated to the tissue of the GI-tract after cleaning and rinsing.

[redacted]

An additional study to determine absorption and excretion showed that following oral administration of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine to bile duct cannulated male rats absorption was low and represented 2.24% of the administered dose. The retained dose corresponded to 1.9%, 0.08% was recovered in urine and 0.23% in bile. A mean of 1.43% of the administered dose was still present in the carcass (without GI-tract) 48 hours after administration. Radioactivity recovered in the GI-tract (without contents) accounted for approximately 0.48% of the administered dose.

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine related material was almost entirely excreted with feces, i.e. mean of 98.1% of the administered dose within 48 hours after administration. Altogether, approximately 0.31% of the administered dose was recovered in urine and bile.

Approximately 2.2% of the administered dose was found absorbed. Excretion via bile was low and there is no indication for enterohepatic circulation.

As a conservative approach based on the available study data a rate of 2.5% was applied to oral absorption.

Study performed in vitro Human skin:

[redacted]

In vitro dermal absorption of the radio-labelled active substance indicated that 22.8% of the applied dose was associated with the stratum corneum and the absorption and dermal delivery were < 0.01% and 0.92% of the applied dose respectively, for risk assessment RMS did consider (the sum of these values) 24% for dermal absorption.

In vitro dermal absorption of the radio-labelled active substance indicated that 22.8% of the applied dose was associated with the stratum corneum and the absorption and dermal delivery were < 0.01% and 0.92% of the applied dose respectively,

The rate of dermal absorption was confirmed in a second in vivo study. The study indicated that a maximum of 15% of the dose remained in/on the treated skin area, predominantly in the stratum corneum (between 12.7 and 14.6% at the 4 time points; 14.5% at 72 hours). Low amounts of the applied dose were found in the lower skin levels of the application site after skin stripping, i.e. less than 1% of the dose.

The material in tapes strips I-II was 0.67 – 0.71 – 0.91 – 0.63% of the applied dose at 6, 24, 48 and 72 hours. At the same time points, the material in tape strips III – IV was 12.03 – 13.86 – 13.14 – 13.84 % of the applied dose. Since the amount in the stratum corneum does not change over time (6 to 72 hours) it thus appears acceptable to conclude on set the dermal absorption on 2% for a 0.1% aqueous solution and 2.5% for in-use dilutions.

Acute toxicity

Oral, rats: N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine is harmful if swallowed due to the corrosive nature of the substance to mucosal surfaces.

Dermal: The substance was tested in the aqueous form marketed, which contains approximately 30% of the active substance. Due to the corrosive nature of the active substance, there is a danger of irreversible damage to the skin upon exposure to the undiluted substance. Therefore toxicity would be secondary to the local tissue damage rather than the result of percutaneously absorbed material.

No acute toxicity study by inhalation was required due to corrosive properties of a.s.

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine is classified as GHS06 Acute Tox. 3 H301: Toxic if swallowed, based on the oral LD50 in rats of 261 mg a.s./kg bw.

Skin irritation: The substance is corrosive to rabbit skin, 3 minutes after application.

Eye irritation: The substance is classified as corrosive and hence is considered to cause severe damage to eyes.

Because of the corrosive effects of the undiluted product, N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine is assigned GHS05, Skin Corr. 1B, H314: Causes severe skin burns and eye damage. The risk of severe damage to eyes is considered implicit.

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine is not a skin sensitizer under the conditions of the study.

Short-term toxicity

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine was tested by the oral route to rats and dogs and by dermal administration in a 90-day subchronic/immunotoxicity study in rats.

90-day oral, rat

[redacted]

For the 90-day oral rat study, test material was administered as a 29.8% aqueous solution, once daily, by oral gavage, to groups of 10 Wistar rats/sex at dose levels of 0 (purified water only), 5, 10, 30 and 90 mg/kg bw/day over 13 weeks (corresponding to groups I, II, III, IV and V respectively). For recovery observations, additional satellite groups of 10 rats/sex were included in the control and high dose groups. For baseline blood analyses, 5 rats/sex were used and designated as Group VI. These dose levels had to be corrected for the actual content of a.s. in dose to 0, 1.5, 3, 8.9 and 26.8 mg a.s./kg bw/day. As the contract research laboratory ceased trading soon after the completion of the study, the Applicant considered prudent to have the report and slides of the study reviewed by an independent consultant (1999). The histopathological review did not reveal any new of additional target organ toxicity, but considered that the original pathology report did not give a complete or conclusive interpretation of the renal and respiratory tract findings.

Groups II to V (all test groups) presented changes in the respiratory tract that were attributed to accidental instillation of test material into the lungs during oral gavage and related to the irritant effects of the substance (sanguineous salivation, respiratory sounds, defensive movements upon dosing and histopathological findings).

Groups IV and V: reduced body weight gain in both sexes, reduced MCV values, increased AST value and histopathological changes in the small intestine and mesenteric lymph node (foamy macrophages within the mucosa) derived from irritant properties of test material.

High dose Group V showed nephrotoxicity (moderate proximal tubular changes with evidence of degeneration, regeneration and hyperplasia) and minimal proximal tubular changes with active degeneration/regeneration, abnormal epithelial nuclei and peritubular fibrosis in recovery animals. A slight increase in the incidence of extramedullary haematopoiesis in the liver, increase ALT and decrease food consumption were also observed.

The NOAEL was found to be the Group III level corresponding to 3 mg a.s./kg bw/day based on reduced body weight gain and irritating effects on the gastrointestinal tract at the higher dose level of 8.9 mg a.s./kg bw/day.

It was noted that this study has a relatively poor reliability due to the gavage administration. This was unsuitable for testing animals due to undesirable inhalative exposure (through test material residues in respiratory tract) that produced marked irritation in the respiratory tract and unnecessary stress to the animals. The study is however considered acceptable, and no further testing is required, because enough information was obtained, and the worst case was considered.

The substance should be classified, as STOT RE 2, GHS08, H373: May cause damage to organs through prolonged or repeated oral exposure..

90-day oral, rat

[redacted]

[redacted] was given by dietary admixture to Sprague-Dawley rats at concentrations of 100, 300 and 900 ppm. Achieved dose of [redacted]
- Males: 7, 20 and 59 mg/kg/day
- Females: 8, 22 and 65 mg/kgBW/day

- at 100 ppm, the test item was well tolerated and there were no notable effects.

- at 300 ppm: pallor of the extremities for females. Slightly lower mean body weight gain. Higher ASAT activity. Slightly increased kidney weights. Tubular nephropathy together with foamy macrophages in the mesenteric lymph nodes.

- at 900 ppm (for both sexes): pallor of the extremities, piloerection, round back and slight decrease in motor activity. Markedly lower mean body weight gain together with a markedly lower food consumption. Pallor of the fundus (often associated with retinal hypovascularisation). Higher urea levels and ASAT activity, but no increase of ALAT. Pallor of the kidneys and higher weight (often associated with enlargement and higher weights) together with enlargement of the mesenteric lymph nodes. Tubular nephropathy together with foamy macrophages in the mesenteric lymph nodes. These effects on the mesenteric lymphnodes are characteristic for local irritating effect in gastro-intestinal system. Tubular nephropathy can be the result of local concentration accumulation caused by the rapid urinary excretion at a level just above cytotoxicity threshold. This is a fully reversible effect.

Following administration of the test substance (dodecyldipropylenetriamine) to rats for 13 weeks by diet admixture, the NOAEL was established at 100 ppm (corresponding to 7 and 8 mg/kg/day for males and females, respectively, as active ingredient) and a LOAEL of 300 ppm (corresponding to 20 and 22 mg/kg/day for males and females, respectively, as active ingredient).

LOAEL 300 ppm (corresponding to 20 and 22 mg/kg/day for males and females, respectively, as active ingredient).

Critical effects are tubular nephropathy with associated increased ASAT activity and also Urea nitrogen levels at the highest dose.

NOAEL 100 ppm (corresponding to 7 and 8 mg/kg/day for males and females, respectively, as active ingredient).

90-day oral, dog

[redacted]

In the 90-day dog study, [redacted] was administered orally via the diet to 4 Beagle dogs/sex/dose group at dose levels of 0 (control), 200, 500 and 1500 ppm (referred as active substance) daily for 90 days. Treatment with either 500 or 1500 ppm resulted in dose-related increased plasma activity of ALAT and ASAT. The high dose of 1500 ppm caused reduced food consumption, reduced body weight, and increased relative and absolute gall bladders weights.

In the absence of pathological changes and other signs of systemic toxicity, the increased ASAT and ALAT values were not considered as adverse and the NOAEL was found to be the 500 ppm dose level corresponding to 20 mg/kg bw/day.

90-day dermal/immunotoxicity, rat

[redacted]

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine was applied in aqueous solution to the shaved dorsal skin of Sprague-Dawley rats for 6 hours/day, 5 days/week at dose levels of 0, 5, 10 and 20 mg/kg bw/day. The high dose group was lowered to 15 mg/kg bw/day after 1 week of treatment due to severe skin irritation. The study was divided in 2 Cohorts:

Cohort I was used to evaluate immunotoxicity of the test substance by means of the antibody forming cell (AFC) assay and consisted of 8 rats/sex/group treated during 6-7 weeks, including a positive control group treated with the immunosuppressant cyclophosphamide.

Cohort II was used to evaluate systemic toxicity and consisted of 15 rats/sex/group treated during 13-14 weeks.

Overall mean body weight gain was decreased 12% and 14% in mid and high dose males respectively at the end of 13-14 weeks of dosing. Sporadic decreases in food consumption were observed in the high dose males, while statistically significant increases in food consumption were seen in mid and high dose females. Dermal irritation was observed at all dose levels in both males and females although in the low dose males, irritation was minimal. Increased white blood cell counts, associated with increases in neutrophils and eosinophils counts and decreased relative lymphocyte counts were observed in mid and/or high dose females. Treatment-related histopathological changes indicative of dermal irritation (hyperplasia, ulceration, scab formation and chronic inflammation in the dermis were seen in the application site skin of females at all dose levels and in mid and high dose males. Microscopic lesions were also seen in the axillary lymph nodes (follicular hyperplasia with accumulation of plasma cells and macrophages) and sternal bone marrow (hyperplasia) and were accounted as a response to the dermal irritation. No significant histopathological effects were seen in the low dose males and no microscopic evidence of any organ specific systemic toxicity was seen in males of females at any dose level.

No evidence of immunotoxicity was seen in the Cohort I immunotoxicity assay.

A NOAEL for systemic toxicity and local effects can be established at the low dose level of 5 mg/kg bw based on decreased body weight gain in males at 10 mg/kg bw.

Genotoxicity

In vitro

There is no evidence of genotoxicity potential of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine conducted to existing guidelines.

In vivo

No data available. The in vitro studies gave no indication of a mutagenic effect and no metabolites of concern have been identified, so no further testing for this end-point is required

Long-term toxicity and carcinogenicity

[redacted]

The aim of the experiment was to obtain information on the chronic toxicity of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine by dietary administration to rats for 52 weeks.

Eight high-dosed male animals treated with 20 mg N-(3-aminopropyl)-Ndodecylpropane-1,3-diamine/kg b.w./day died prematurely.

The body weight of the rats treated with 20 mg N-(3-aminopropyl)-Ndodecylpropane- 1,3-diamine/kg b.w./day was reduced by up to 34% from test week 15 onwards for the male animals and by up to 22% from test week 33 onwards for the female animals. The body weight gain and body weight at autopsy changed accordingly.

The food consumption of the animals treated with 20 mg N-(3-aminopropyl)-N-dodecylpropane- 1,3-diamine/kg b.w./day was increased by up to 18% for the male rats in test weeks 39 to 45 and by up to 20% for the females in test weeks 31 to 51 caused by the severely reduced body weight.

Changes in haematological and biochemical parameters were recorded for the animals treated with 20 mg N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine/kg b.w./day.

At necropsy, discoloured or reddened lungs were noted for the males and enlargement of the pituitary gland was noted for the females of the high dosed group.

Increased absolute kidney weights were noted for the females and decreased absolute liver weights were noted for the males treated with 20 mg N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine/kg b.w./day.

The myeloid:erythroid ratio of the male animals treated with 20 mg N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine/kg b.w./day was significantly increased (Control: 0.993 : 1, 20 mg/kg: 1.847 : 1).

The males treated with 8 mg/kg and animals of both sexes treated with 20 mg N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine/kg b.w./day showed a dose dependent increase of lympho-histiocytic myocarditis. This finding was associated with degenerative changes of the myofibers in the heart. The males treated with 8 or 20 mg N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine/kg and the females of the high dose group showed an increase of lympho-histiocytic infiltrations in the skeletal muscles. Degeneration of the skeletal muscles was noted in 2 intermediate dose males. Additionally, the animals treated with 8 or 20 mg N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine/kg b.w./day showed a minimal to moderate increase in basophilic tubular cells and lympho-histiocytic infiltration of the kidney.

Suppurative inflammation was observed in the prostate and mesenteric lymph nodes of the animals treated with 20 mg N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine/kg b.w./day compared to the controls animals and the other test item-treated groups. Granulomas with central neutrophilic granulocytes were only noted in the mesenteric lymph node of male and female rats of the high dose group.

A high percentage of animals in all substance-treated groups without dose-related pattern had large macrophages with cytoplasmatic vacuoles in the mesenteric lymph nodes. This was considered to reflect the exposure to the lipophilic test item via the diet. As there was no dose-dependency and loading of macrophages with lipophilic substances with a difficult absorption behaviour is a physiological reaction, this finding was not considered adverse.

Furthermore, the lungs of the male and female animals treated with 8 mg N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine/kg b.w./day showed an increased incidence of foci of foamy macrophages (alveolar histiocytosis) in the alveoles of the lungs.

No test item-related influences were noted on behaviour, external appearance or faeces, functional observations and urine parameters.

Based on the present results the no-observed-adverse-effect-level (NOAEL) was 4mg N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine/kg b.w/day 4

The test item N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine was tested for carcinogenic potential in male and female rats. The animals were treated with 4 or 8 mg N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine/kg b.w./day by dietary administration for 104 weeks or with 20/15/12 mg N-(3-aminopropyl)-N-dodecyl-propane-1,3-diamine/kg b.w./day by dietary administration for 61 weeks (high dosed male animals) or 81 weeks (high dosed female animals).

A dose-related systemic toxicity was noted. A MTD (maximum tolerated dose) as defined by the ICH guideline S1C(R2): 'Dose Selection for Carcinogenicity Studies of Pharmaceuticals' in form of e.g. no more than 10% decrease in body weight gain relative to controls, target organ toxicity and/or significant alterations in clinical pathological parameters was met by the 8 mg/kg dose level.

The body weight of the males and females treated with 8 mg N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine/kg b.w./day was below the body weight of the control group from approximately test week 53 onwards in males (by up to 14%, statistically significant at $p \leq 0.01$ in test weeks 59 to 91, 95 and 101) and from test week 75 onwards in females (by up to 12%, statistically not significant at $p \leq 0.01$). In addition, changes were noted for biochemical and haematological parameters and non-neoplastic changes were noted in the mesenteric lymph nodes, kidneys, heart, skeletal muscle of the leg and larynx.

Hence, the 8 mg/kg dose was considered to be suitable for histopathological evaluation for neoplastic changes according to the above MTD considerations.

All neoplastic lesions recorded in this study were commonly encountered in rats of this strain and age. Type, incidence, and severity of the lesions recorded were not increased in the test-item treated animals as compared to the control animals.

Developmental toxicity

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine was tested for developmental toxicity in rats and rabbits.

Rats

[redacted]

Maternal toxicity was indicated in the high and median dose level by reduced body weight gain and food consumption and by clinical reactions to treatment, which in two animals of the high dose level required premature sacrifice.

In the high dose level, there was an increased incidence of early embryonic deaths: the 3 females with the greatest number of early deaths were all among the 5

females showing weight loss between Days 9 and 13 of gestation, suggesting that the early deaths may have been secondary to maternal toxicity. Mean foetal weight at this level was slightly lower than control. At low and median dose level there were no obvious effects on pregnancy performance or foetal weight. The incidences of foetal malformations, anomalies and variants were essentially similar in all groups

Rabbits

[redacted]

Maternal toxicity was indicated at high dose level by the death of two dams, by marginally reduced body weight and food intake during the last days of pregnancy. Necropsy revealed an irritation of the gastrointestinal tract in 5 dams and an increased incidence of resorptions.

No test substance-related influence was detected on the prenatal foetal development. The incidences of foetal malformations, variations and retardations were similar in all groups.

Reproductive toxicity Rats

[redacted]

High dose level: Most animals showed dyspnoea, piloerection and hunched posture, with many animals also having episodes of post dosing salivation. On occasional animals the outline of the spine was prominent. There were up to 9 treatment-related deaths in the group. Animals had a marked reduction in bodyweight, for females, during pre-mating and gestation periods. Mean epididymides weights in both generations were lower than control, with the value for F0 animals attaining statistical significance, mean seminal vesicle weights were lower than the control and were considered to be a direct effect of the a.i.. Mean litter and pup weights of the F2 pups were lower than the control. Two pups showed body tremors in late lactation.
Median dose level: The only finding was of occasional animals with post-dosing salivation.
Low dose level: No significant effects noted.

Neurotoxicity
No data necessary. Study waived based on the absence of indications for neurotoxicity

Medical data
No data available.

A summary of NOAELs and LOAELs is presented below:

Type of study	**LOAEL (mg a.s/kg bw/day)**	**NOAEL (mg a.s./kg bw/day)**	**Reliability**	**Effects**
90-day oral, rat by gavage	8.9	3.0 Oral NOAEC 0.03%	2	Reduced body weight gain and irritating effects on the gastrointestinal tract at 9 mg a.s./kg bw/day
90-day oral rat Diet	22	8	1	High dose level: irritating effects in gastro-intestinal system. Mid dose: tubular nephropaty with foamy macrophages in the mesenteric lymph nodes.
90-day oral, dog Dietary	55.1 mg/kg bw/day	20 mg/kg bw/day	1	No pathological effects or adverse effects was found at the higher dose
90-day dermal, rat	~~5~~ 10 (0.5%)	5 (0.25%) NO(A)EC dermal 0.25%	2	Dermal irritation at all doses levels in both females and males. Decreased body weight gain in males at 10 mg a.s./kg bw/day
Teratogenicity, rabbit By gavage	20	9	1	Maternal toxicity (decreased body weight and food intake), irritation in the gastrointestinal tract.
2-generation, rat By gavage	27	9	1	High dose level, decreased body weight for females during pre-mating and gestation period. Mean epididymides weights in both generations were lower than control, with the value for F0 animals attaining statistical significance, mean seminal vesicle weights were lower than the control and were considered to be a direct effect of the a.s.
Combined chronic carcinogenicity 52 weeks Rat Sprague-dawley Diet	8	4	1	High dose males: eight died prematurely during the last week of the 12 month studyand reached 8/20 (40%). Body weight high dose rats was reduced up to 34%. At 8 mg7kg bw/day: increased ASAT by 122%.

Reference values to be used in risk characterisation

	Study	NOAEL/ LOAEL	Assessment Factor	Correction for oral absorption	Value
$AEL_{short-term}$	Prenatal developmental toxicity, rabbit	NOAEL: 9 mg/kg bw/day	100	2.5	0.0023 mg/kg bw/day
$AEL_{medium-term}$	90 days oral gavage, rat	NOAEL: 1.5 mg/kg bw/day	100	2.5	0.0004 mg/kg bw/day
$AEL_{long-term}$	52 weeks oral, rat	LOAEL: 4 mg/kg bw/day	400	2.5	0.00025 mg/kg bw/day
ARfD	Prenatal developmental toxicity, rabbit	NOAEL: 9 mg/kg bw/day	100		0.09 mg/kg bw
ADI	52 weeks oral, rat	LOAEL: 4 mg/kg bw/day	400		0.01 mg/kg bw/day
Dermal absorption	In vivo rat				2% for 0.1% aqueous solution 2.5% in-use solution
Oral absorption					2.5%
NOAEC, oral	90 days oral gavage, rat	NOAEC 0.03%			NOAEC 0.03%
NOAEC, dermal	90 days dermal, rat	LOAEC 0.25%			LOAEC 0.25%

2.2.1.2. Exposure assessment and risk characterisation

2.2.1.2.1. *Identification of main paths of human exposure towards active substance from its use in biocidal products*

Wood preservative products based on N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine are only used in industrial wood preservative facilities and will not be used by industrial/professional workers outside these facilities.

During and after pre-treatment of timber with the product [redacted] industrial/professional operator contamination could principally occur via the dermal, inhalation and oral routes. The primary exposure to industrial/professional users, working in industrial plants for the preventive treatment of wood preservatives, will be via the dermal route as a result of direct contact with the surface of treated timber and through contact with equipment, contaminated process plants as well as contaminated coveralls and gloves. As for the inhalation exposure, the a.s. is not volatile and does not vaporise from solutions. However, exposure to aerosol might occur following industrial vacuum pressure impregnation.

The potential for exposure of operators through ingestion of [redacted] during the industrial/professional uses is considered negligible.

Non-professional use of [redacted] is not intended and no calculations for such exposure have been made.

The secondary (indirect) exposure could occur after the actual use or application of the biocidal product. Secondary exposure to the general public could result from contact with treated timber/wood or adults laundering clothes; e.g. children being exposed indoors to treated wood via vapour and infants chewing preserved timber off-cuts.

The treated wood is not placed on the market until dried. Consequently, exposure through touching of treated wet surfaces is considered to be an unlikely exposure scenario.

Use of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine based products on wood, which is likely to come into prolonged contact with foodstuffs or feedstuffs, is not expected.

Indirect exposure via the environment is considered not relevant.

Use in Product type 8.01

Exposure path	Industrial use	General public	Via the environment
Inhalation	Yes (aerosol)	Yes (vapour)	No
Dermal	Yes	Yes (toddler)	No
Oral	No	Yes (toddler)	No

Primary and secondary exposure scenarios pertaining to the proposed use of the product [redacted] are detailed in the tables below.

Summary table: scenarios for [redacted]			
Scenario number	**Scenario**	**Primary or secondary exposure** **Description of scenario**	**Exposed group** (e.g. professionals, bystander)
1.	Automated short-term dipping application	Primary exposure – automated short-term dipping of wooden articles	Industrial users
2.	Automated dipping application	Primary exposure – automated dipping of wooden articles	Industrial users
3.	Vacuum pressure treatment application (HC 2 & 3)	Primary exposure – vacuum pressure treatment of wooden articles	Industrial users
4.	Vacuum pressure treatment application (HC 4a)	Primary exposure – vacuum pressure treatment of wooden articles	Industrial users
5.	Cleaning treatment equipment	Primary exposure – cleaning of treatment equipment	Industrial users
6.	Restacking fallen treated timber	Secondary exposure – restacking of fallen timber treated	Industrial users
7.	Laundering work clothing	Secondary exposure - adult launders contaminated clothing at home	Non-professionals (adults)
8.	Chewing treated wood off-cuts	Secondary exposure – a toddler ingests residues through mouthing treated wood off-cuts	General public (toddlers)
9.	Playing on (weathered) playground structures	Secondary exposure – dermal and ingestion exposure of a toddler playing on treated wood structures	General public (toddlers)

10.	Vapour released from wood used indoor	Secondary exposure – Inhalation exposure of a toddler playing on treated wood structures	General public (toddlers)

Production/formulation of the active substance and the biocidal product

The modelling of exposures and subsequent risk characterisation during production and formulation of the biocidal product [redacted] is addressed under other EU legislation (e.g. Directive 98/24/EC) and not repeated under Directive 98/8/EC (agreed at Biocides Technical meeting TMI 2006) [Directive 98/8/EC now replaced by BPR 528/2012]. It was agreed at TMII 2006 (Arona,19-22 June 2006) that these data should not be routinely considered as a core requirement for the purposes of Annex I inclusion [now called Approved List under BPR]

2.2.1.2.2. *Human exposure for professional (industrial users); primary and secondary*

[redacted] can be applied by industrial users of the product through automated dipping and vacuum pressure impregnation. Manual dipping is not foreseen for this product. The mixing/loading and application of the product may result in primary exposure, via skin contact or via aerosol inhalation after vacuum pressure impregnation. For industrial users oral ingestion is not expected to occur and oral exposure is not assessed further.

Mixing and loading stage

The active substance is supplied by tanker as a concentrate with approximately one delivery per week. It is delivered to the holding tank by transfer pipes via a closed system. The concentrate is then diluted as appropriate in the process plant to give a solution to be used for preservation of the wood. All workers wear gloves, coveralls, and foot protection to prevent dermal exposure and are trained in the use of the equipment.

Other than incidental exposure in connecting and disconnecting transfer lines is not foreseen.

In view of the automated nature of the industrial treatment process, it is unlikely that operators will routinely undertake manual mixing & loading activities. Any manual mixing & loading is therefore likely to be infrequent and represent a minor contribution to the overall level of exposure as predicted by the TNsG Handling Model 1.

Application via automated dipping

Dipping is a batch process with continuous treatment. A pack or single piece of wood is submerged into a dipping tank filled with a solution containing the wood preservative. Packs of wood are loaded on automatic equipment (e.g. hydraulic elevator) and lowered into a dipping tank. The period of time that the wood is

submerged varies from a few minutes to an hour depending on anticipated use of the wood. At the end of treatment, the wood is held over the dipping vat for up to an hour to allow draining of the excess preservative. Drips are collected and recycled. The treated wood is then removed for storage. The dipping facilities are closed, and equipped with vapour trapping and air emission control.

Scenario 1 and 2 - Primary exposure during automatic dipping of wooden articles in [redacted]

Industrial user exposure to N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine during the application of [redacted] through automatic dipping has been assessed using TNsG Handling Model 1 (TNsG 2002, part 2, p.160) as recommended in the Biocides Human Health Methodogy Document (2015, p.119) and the HEEG opinion 18 (2013)3. This model relates to professional intermittently handling water-wet or solvent-damp wood and associated equipment. The models are derived from data relating to industrial timber treatment using vacuum pressure plants and water-based (WB) or solvent–based (SB) liquid formulations and are thought to best represent automated dipping. HEEG opinion 84 informs us that 4 automatic dipping cycles per day are performed and that these cycles can last up to 60 minutes. However, the applicant informed that for **short-term dipping (Scenario 1)** 5 cycles per day (duration 0.25h) with 0.588% a.s. in-use concentration and **dipping (Scenario 2)** 1 cycle per day (duration 9h) with 0.294% a.s. in-use concentration can be assumed.

In view of the automated nature of industrial automated dipping, it is unlikely that operators will routinely undertake manual mix/loading activities. Any manual mix/loading is therefore likely to be infrequent and represent a minor contribution to the overall level of exposure as predicted by the TNsG Handling Model 1.

HEEG opinion 8[2] informs us that for water-based solutions for automated dipping, inhalation exposure can be consider negligible. As such inhalation exposure has not been considered for this product.

Description of Scenario 1		
Industrial user short-term dipping wooden articles using automated equipment. *Potential exposure for [redacted] is via the dermal route.*		
Tier 1	**Parameters**	**Value**
	In-use concentration of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in [redacted] for short-term dipping	0.588 % w/w

[3] HEEG opinion 18 (2013) - For exposure assessment for professional operators undertaking industrial treatment of wood by fully automated dipping

[4] HEEG opinion 8 (2009) - Defaults and appropiate models to assess human exposure for dipping processes (PT 8)

	Adult body weight	60 kg
	Dermal penetration of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in [redacted] (applicable to the in-use dilution)	2.5%
	Number of cycles/day	5
	Hand exposure (in gloves); indicative 75th percentile value	1080 mg/cycle*
	Potential body exposure; indicative 75th percentile value	8570 mg/cycle
Tier 2	PPE (coated coveralls)	90% protection (10% penetration)
Notes	* In view of the proposed industrial use of the product, PPE has been included in exposure assessments where appropriate, reflecting the underlying data.	

Tier 1 assessment

It is assumed that gloves are worn (reflecting the underlying data of the model used).

Tier 2 assessment

The 'Tier 1' exposure assessment is refined by including in the calculations: The protection afforded by coated coveralls. According to HEEG opinion 95 it is assumed that protective clothing for professionals (coated coveralls) would offer a protection of 90% (that is 10% penetration) where the main challenge is from contact with preservative wet wood.

Calculations for [redacted] for Scenario 1

Summary table for [redacted] estimated exposure to N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine from industrial uses, short-term dipping 5 cycles/day					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake** (mg a.s./day)	**Estimated dermal uptake** (mg a.s./person/day)	**Estimated oral uptake** (mg a.s./day)	**Estimated total uptake** (mg a.s./kg bw/day)

[5] HEEG opinion 9 (2010)- Default protection factors for protective clothing and gloves.

1	1	negligible	7.093	n.a.	0.118
1	2	negligible	1.424	n.a.	0.024

Description of Scenario 2		
Industrial user dipping wooden articles using automated equipment. *Potential exposure for [redacted] is via the dermal route.*		
Tier 1	**Parameters**	**Value**
	In-use concentration of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in [redacted] for short-term dipping	0.294 % w/w
	Adult body weight	60 kg
	Dermal penetration of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in [redacted] (applicable to the in-use dilution)	2.5%
	Number of cycles/day	1
	Hand exposure (in gloves); indicative 75th percentile value	1080 mg/cycle*
	Potential body exposure; indicative 75th percentile value	8570 mg/cycle
Tier 2	PPE (coated coveralls)	90% protection (10% penetration)
Notes	* In view of the proposed industrial use of the product, PPE has been included in exposure assessments where appropriate, reflecting the underlying data.	

Tier 1 assessment

It is assumed that gloves are worn (reflecting the underlying data of the model used).

Tier 2 assessment

The 'Tier 1' exposure assessment is refined by including in the calculations: The protection afforded by coated coveralls. According to HEEG opinion 96 it is assumed that protective clothing for professionals (coated coveralls) would offer a protection of 90% (that is 10% penetration) where the main challenge is from contact with preservative wet wood.

Calculations for [redacted] for Scenario 2

Summary table for [redacted] estimated exposure to N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine from industrial uses, dipping 1 cycle/day					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake (mg a.s./day)**	**Estimated dermal uptake (mg a.s./person/day)**	**Estimated oral uptake (mg a.s./day)**	**Estimated total uptake (mg a.s./kg bw/day)**
2	1	negligible	0.709	n.a.	0.0118
2	2	negligible	0.142	n.a.	0.0024

Application via vacuum pressure impregnation

Vacuum pressure is a process used to apply wood preservative by overcoming the resistance of the wood to deep penetration using pressure. The treatment is carried out in cylindrical airtight steel pressure/vacuum vessels. The operations are carried out on a cyclical basis.

The untreated wood is loaded onto small rails or tramcars that are pushed into the cylinder using forklifts or other mechanical means. The cylinder door is sealed via a pressure tight door, either manually with bolts or hydraulically, and a vacuum applied to remove most of the air from the cylinder and the wood cells. The preservative solution is then pumped into the cylinder and the pressure raised. The total treatment time varies depending on species of wood and the commodity being treated, but in all instances the treating process remains a closed system. At the end of the treatment time, the pressure is released and the excess solution removed, typically by pumping, and recycled. A final vacuum may be applied to remove excess preservative that would otherwise drip from the wood. The treated wood is then unloaded and stored.

[6] HEEG opinion 9 (2010)- Default protection factors for protective clothing and gloves.

Scenario 3 - Primary exposure during vacuum pressure treatment (HC 2 & 3) in [redacted]

Industrial user exposure to N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine during the application of [redacted] by vacuum pressure treatment (HC 2 & 3) has been assessed using the TNsG Handling Model 1 (User guidance, version 1, p.26). This model is derived from data relating to industrial timber treatment using vacuum/pressure plants applying water-based or solvent-based liquid formulations. Exposure values obtained from the model reflect the intermittent manual handling of water-wet or solvent-damp wood and associated equipment.

One cycle for a vacuum-pressure treatment (water-based products) has according to the applicant the typical cycle duration of 4 to 9 hours. This results in 1 to 2 cycles per day. Inhalation exposure time to the aerosol is assumed to be 20 minutes which is the time spent with the door open for 2 cycles (Biocides Human Health Methodology Document, 2015, p120). To use 1 or 2 cycles as a refinement option from the scientific point of view was not accepted; was decided to consider only the use of 3 cycles (HEEG opinion #6 indicates 3 cycles a day as the default value).

In view of the automated nature of the industrial vacuum pressure treatment process, it is unlikely that operators will routinely undertake manual mixing & loading activities. Any manual mixing & loading is therefore likely to be infrequent and represent a minor contribution to the overall level of exposure as predicted by the TNsG Handling Model 1.

Description of Scenario 3		
Industrial user vacuum pressure treatment (HC 2 & 3). *Potential exposure for [redacted] is via the dermal and inhalation route.*		
Tier 1	**Parameters**	**Value**
	In-use concentration of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in [redacted] for vacuum pressure treatment (HC 2 & 3)	0.025 % w/w
	Adult body weight	60 kg
	Dermal penetration of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in [redacted] (applicable to the in-use dilution)	2.5%
	Inhalation absorption of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in [redacted]	100%

	Number of cycles/day	3
	Hand exposure (in gloves); indicative 75th percentile value	1080 mg/cycle*
	Potential body exposure; indicative 75th percentile value	8570 mg/cycle
	Potential inhalation exposure: indicative 75th percentile value	1.9 mg/m^3
	Short-term inhalation rate, adult (based on recommendation in HEAdhoc Recommendation 14[7])	1.25 m^3/h
	Total inhalation time/day for 3 cycles	30 min
Notes	* In view of the proposed industrial use of the product, PPE has been included in exposure assessments where appropriate, reflecting the underlying data.	

The default number of vacuum cycles is 3; however, with default assumptions for PPE, the HHRA is not acceptable at default. Additional refinements at the product authorisation level, to improve the HHRA and potentially increase the acceptable number of cycles, could include:

- Product-specific dermal absorption data
- Lower in-use concentration of Diamine compared to 0.025%
- More appropriate exposure data
- Additional PPE

[7] HEAdhoc Recommendation 14 (2017) – Default human factor values for use in exposure assessments for biocidal products

Refined HHRA with higher level of PPE

Improving the protectiveness of the PPE alone improves the current HHRA.

- **Gloves:** Handling Model 1 used for PT8 provides a 75th percentile indicative actual hand exposure value of 1080 mg/cycle under gloves (p. 300 of HHEM), which is the default value used for risk assessment. However, new gloves at the beginning of each shift is considered to significantly reduce hand exposure.
    - By default, use of new gloves is considered to reduce exposure by half (p. 4 of HEEG Opinion 9); this would correspond to 540 mg/cycle.

.

- **Impermeable coveralls:** The standard assumption for PT8 is that penetration of coated coveralls is 10% (HEEG Opinion 9). The use of impermeable coveralls offers a higher level of protection (5% penetration, although the actual reported value is 4%). According to HEEG Opinion 9, the majority of the challenge during wood treatment is from contact with wet surfaces, limiting potential for contamination at wrists/neck (compared to spray applications).

The first tier scenario as well as one refined scenario (with 5% penetration of coveralls and both options for estimating hand exposure with new gloves) are provided below for 1 cycle, and extrapolated to 3 cycles**.**

Refined risk assessment

Vacuum/Pressure			
Model choice		Handling Model 1	
Dermal absorption		2.50%	
Long term AEL		0.00025	mg/kg bw/d
Content of a.i. in treatment solution		0.025	%
		Tier 1 (Doc IIB)	**Tier 2**
Hand exposure			
	Indicative value (in glove)	1080	540
	Task duration	1	1
	Glove penetration	100	100
	Actual deposit on hands (product)	1080	540

Rest of body exposure		
Indicative value	8570	8570
Task duration	1	1
Potential dermal deposit on body	8570	8570
Clothing penetration	10	5
Actual deposit on body (product)	857	428.5
Total actual dermal exposure		
In use product	1937.0	968.5
Active substance	0.48	0.24
Total dermal systemic exposure	0.01211	0.00605
Inhalation exposure		
Inhalation rate	1.25	1.25
Indicative value	1.9	1.9
Task duration	10	10
Volume of air inhaled	0.2083	0.2083
In-use product inhaled	0.3958	0.3958
Total inhalation systemic exposure	9.90E-05	9.90E-05
Body weight	60	60
Total systemic dose	0.0002034	0.0001025

3 cycles	**Percent long term AEL**	244.1%	123.0%

From the table above no safe uses could be reached for vaccum presure impregnation (3 cycles) even with the use of new gloves and impermeable coveralls.

Scenario 4 - Primary exposure during vacuum pressure treatment (HC 4a) in [redacted]

Scenario 4 is calculated for vacuum pressure treatment (HC 4a) in [redacted] with the N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in-use concentration of 0.05 % w/w which is twice as much as for scenario 3. All other parameters related to the exposure scenario are identical to scenario 3.

Calculations for [redacted] for Scenario 4

Summary table for [redacted] estimated exposure to N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine from industrial uses, vacuum pressure treatment (HC 4a).					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake** (mg a.s./day)	**Estimated dermal uptake** (mg a.s./person/day)	**Estimated oral uptake** (mg a.s./day)	**Estimated total uptake** (mg a.s./kg bw/day)
4	1	3.96×10^{-4}	0.242	n.a.	0.004
4	2	3.96×10^{-4}	0.048	n.a.	0.0008
4	3	1.97×10^{-4}	0.0284	n.a.	0.0005

Scenario 5 - Primary exposure during cleaning and maintenance of dipping tank and solution reservoir

The Applicant states that emptying, cleaning and maintenance of the solution reservoir or dipping tank is assumed to take place once or twice per year and for a duration of no more than 120 minutes. Due to the low frequency of this task this activity is considered as medium-term exposure.

There is no generic model in the TNsG for cleaning of internal surfaces of dipping tanks. To predict exposure for this primary exposure scenario, the indicative exposure values from Handling Model 1 (TNsG User Guidance 2002, p26) have been used. These values reflect professional workers working in a wet environment with intermittent handling of wet surfaces, i.e. treated wood and associated equipment. The exposure data in this model relate to industrial timber treatment using vacuum-pressure (User Guidance, 2002, p. 41). The duration of exposure assumed for this scenario is 120 min. Potential exposure is via the inhalation and dermal routes.

It is assumed that cleaning of internal surfaces of dipping tanks, as used for short-term dipping and of solution reservoir, as used for vacuum pressure treatment takes place. Exposure assessments are calculated by using the highest active substance in-use concentration of 0.588 % w/w a.s. for short-term dipping (Tier 1a and 2a), and the lowest in-use concentration of 0.025% w/w for vacuum pressure treatment HC 2 & 3 (Tier 1b and 2b).

Calculations for [redacted] for Scenario 5

Description of Scenario 5		
Cleaning and maintenance of dipping tank and solution reservoir *Potential exposure for [redacted] is via the dermal and inhalation route.*		
Tier 1	**Parameters**	**Value**
	Tier 1a: In-use concentration of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine for short-term dipping	0.588 % w/w
	Tier 1b: In-use concentration of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine for vacuum pressure treatment HC 2 & 3	0.025 % w/w
	Adult body weight	60 kg
	Dermal penetration of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in [redacted] (applicable to the in-use dilution)	2.5%
	Inhalation absorption of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in [redacted]	100%
	Number of cycles/day	1 cycles/day
	Hand exposure (in gloves); indicative 75th percentile value	1080 mg/cycle*
	Potential body exposure; indicative 75th percentile value	8570 mg/cycle
	Potential inhalation exposure: indicative 75th percentile value	1.9 mg/m^3
	Short-term inhalation rate, adult (based on recommendation in HEEG opinion 13)	1.25 m^3/h
	Total inhalation time/day for 1 cycle	120 min

Tier 2	PPE (coated coveralls)	90% protection (10% penetration)
Notes	* In view of the proposed industrial use of the product, PPE has been included in exposure assessments where appropriate, reflecting the underlying data.	

Tier 1 assessment

It is assumed that gloves are worn (reflecting the underlying data of the model used).

Tier 2 assessment

The 'Tier 1a and b' exposure assessments are refined by including in the calculations: The protection afforded by coated coveralls. According to HEEG opinion 9 it is assumed that protective clothing for professionals (coated coveralls) would offer a protection of 90% (that is 10% penetration) where the main challenge is from contact with preservative wet wood.

Calculations for [redacted] for Scenario 5

Summary table for [redacted] estimated exposure to N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine from industrial uses, cleaning and maintenance of dipping tank and solution reservoir

Exposure scenario	**Tier/PPE***	**Estimated inhalation uptake** (mg a.s./day)	**Estimated dermal uptake** (mg a.s./person/day)	**Estimated oral uptake** (mg a.s./day)	**Estimated total uptake** (mg a.s./kg bw/day)
5	1a	0,028	1.42	n.a.	0.024
5	1b	0,0012	0.06	n.a.	0.001
5	2a	0.028	0.28	n.a.	0.0052
5	2b	0.0012	0.012	n.a.	0.00022

* Tier 1a and 2a are calculated with 0.558% w/w a.s. in-use concentration. Tier 1b and 2b are calculated with 0.025% w/w a.s. in-use concentration.

Scenario 6 - Secondary exposure during restacking of treated timber

For fully automated dipping HEEG opinion 18 states that "at the drying/storage site, transfer of wet wood from the forklift truck might be undertaken manually or more likely, the forklift truck might drop the wet treated wood at the drying point. At some point in the drying cycle piles of wooden articles in the storage area could fall, particularly if the tension straps fail, and the wooden articles will need to be manually restacked. It could be anticipated that this would not be a frequent occurrence and it is assumed that in any day only one batch of timber from the dipping process will need to be manually re-stacked. In any particular day, these operations will normally be undertaken by a person other than the person who is undertaking the actual dipping of the wood."

HEEG opinion 18 further states that "as the exposure of the person actually carrying out the dipping has already been assessed and this exposure being chiefly from handling the wet treated wood (when fallen wooden articles need re-stacking/re-positioning) then, this same calculated exposure value can be used to define the exposure of the person re-stacking/re-positioning treated wood in the drying/storage area. It should be noted that, this exposure is for a person re-stacking wet wood and in the drying/storage area, in many instances the wood will be dry thus, dermal exposure could be much less. Taking this into account might allow the exposure assessment to be refined if necessary".

Based on the above information, refinement is proposed by concluding that secondary exposure during restacking of treated timber will be of the same magnitude or less than user exposure during one cycle vacuum pressure treatment (HC2 & 3) as more realistic worst case scenario. As such scenario 3, Tier 3 ((primary exposure during one cycle vacuum pressure treatment) forms a risk envelope for restacking treated timber and an additional estimate has not been carried out. Please refer to Scenario 3 above for the predicted systemic exposure.

2.2.1.2.3. *Combined exposure via [redacted] at industrial site*

For each industrial application method, it has been assumed that application of [redacted] and cleaning of the subsequent equipment (emptying, cleaning and maintenance of the solution reservoir or dipping tank) may be carried out by an individual on different days. Due to the duration of the single tasks it is assumed that application and cleaning tasks cannot be conducted at the same working day and combined exposure is considered as not relevant.

According to HEEG opinion 18 restacking of treated timber will normally be undertaken by a person other than the person who is undertaking the actual treatment of the wood. Therefore, also for this scenarios combined exposure is not foreseen and no specific exposure assessment is calculated.

2.2.1.2.4. *Secondary exposure assessment -non-professionals/general public*

Scenario 7 - Secondary exposure for an adult laundering contaminated

work clothing

At TM III08 it was decided that this scenario should be considered where there was a possibility of workers taking soiled workwear home to launder (e.g. for small-scale dipping processes), but that the exposure scenario was not required when wood preservatives were applied under industrial conditions. For industrial treatments, it was assumed the employer would employ professional means to launder contaminated workwear where contact with dirty clothes would be insignificant. Since [redacted] was applied under industrial conditions only, this scenario is not considered.

Scenario 8 - Secondary exposure (acute) for a toddler chewing a treated wood off-cut

Preserved timber is not placed on the market before it is dried. Timber treated with the product [redacted] can be used indoors and outdoors. Toddlers (10 kg bodyweight) might chew treated wood. For this scenario it is assumed that the active substance in the treated timber is located in the outer 1cm layer. It is also assumed that the toddler is chewing a 4 cm x 4 cm x 1 cm wood off-cut (volume of 16 cm^3) and in doing so extracts 10% of the active substance (TNsG 2002, part 3, p46). For dipping application (scenario 8a) as worst case scenario the retention rate is 0.3 kg a.s./m^3 for [redacted] (equivalent to 0.3 mg/cm^3) (Tier 1a) and for vacuum pressure treated timber (scenario 8b) with hazard class 2 for interior use the retention rate is 0.125 kg a.s./m^3 for [redacted] (equivalent to 0.125 mg/cm^3) (Tier 1b) assuming all of the product is absorbed to a depth of 1cm and penetrates no further. These values relate to the concentration in the treated zone.

Description of Scenario 8 a (dipping application) and b (vacuum pressure treatment)		
A toddler chewing on wood off-cut treated with [redacted] where exposure would be via the ingestion route. It is assumed that the active substance in the treated timber is located in the outer 1 cm layer.		
Tier 1	**Parameters**	**Value**
	Infants body weight	8 kg
	Toddler body weight	10 kg
	Volume of timber off-cut	4 cm x 4 cm x 1 cm (equivalent to 16 cm^3)
	Extraction rate from chewing	10 %

	Oral absorption of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine (a.s.)	2.5%
	Concentration of a.s. in timber treated with [redacted] via (a.s. retention rate): • dipping application • vacuum pressure treatment	 0.3 mg/cm^3 0.125 mg/cm^3
	Amount of a.s. in off-cut treated with [redacted] • dipping application • vacuum pressure treatment	 4.8 mg 2 mg
	Extracted amount of a.s. from off-cut treated with [redacted] • dipping application • vacuum pressure treatment	 0.48 mg 0.2 mg

Tier 1 assessment

In considering the frequency of this exposure scenario to the general public, the acute AEL (0.0023 mg/kg bw/day) is considered the most relevant endpoint.

Calculations for [redacted] for Scenario 8

Summary table: systemic exposure for the general public					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake** (mg a.s./kg bw/day)	**Estimated dermal uptake** (mg a.s./ kg bw/day)	**Estimated oral uptake** (mg a.s./day)	**Estimated total uptake** (mg a.s./kg bw/day)
Scenario 8a	dipping application				
	Infants	n.a.	n.a.	0.015	0.0015
	Toddler	n.a.	n.a.	0.012	0.0012
Scenario 8b	vacuum pressure treatment				

	Infants	n.a.	n.a.	0.006	0.0006
	Toddler	n.a.	n.a.	0.005	0.0005

Scenario 9 - Secondary exposure (chronic) for an toddlers playing on (weathered) playground structures and mouthing

Toddlers who play on treated wooden structures and have hand-to-mouth contact as they play may be exposed to N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine.

It is assumed that 20% of the hand is contaminated during long and repeated contact with the playground structure (TNsG 2002, Part 3, p.50 and TNsG User Guidance, p.57) and a toddler has a hand surface area of 230.4 cm² (HEEG opinion 17). The transfer efficiency from rough-sawn wood to the hands is 2% (TNsG 2002, Part 2, p. 204).

It is assumed that 100% ingestion of the calculated skin contamination of the hands (as described above) will occur.

In this exposure assessments two scenario are assessed. It is assumed that the timber is treated via dipping with total solution uptake of 500g/m^2 (0.147 mg a.s./cm^2 treated wood) and that timber is treated via vacuum/pressure process (HC 2&3) with total solution uptake of 500kg/m^3 (0.0625 mg/cm^2 treated wood). The assessment is based on the applicant's information that 1m^3 has an area of 200 m^2 and that therefore 30 g/m^2 corresponds to 6 kg/m^3.

Description of Scenario 9		
There is high risk for infants and toddlers who play on treated (weathered) wooden structures and have hand-to-mouth contact as they play. Potential exposure via dermal and ingestion routes is considered during this activity.		
Tier 1	**Parameters**	**Value**
	Concentration of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in timber treated with [redacted] via dipping application	0.147 mg/cm^2
	Concentration of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in timber treated with [redacted] via vacuum/pressure process (HC 2&3)	0.0625 mg/cm^2
	Infant body weight	8 kg
	Toddler body weight	10 kg

	Oral absorption	2.5 %
	Dermal absorption for N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine	2.5 %
	Hand surface area (infant)	196.8 cm^2
	Hand surface area (toddler)	230.4 cm^2
	Hand contamination	20 %
	Transfer efficiency of dried residue	2 %

Tier 1 assessment

Parameter/Active	**Dipping application**	**Vacuum/pressure process (HC 2&3)**
Concentration of a.s in the wood (mg a.s/cm^3)	0.147 mg/cm^2	0.0625 mg/cm^2
Oral Absorption (%)	2.5%	2.5%
Dermal Absorption (%)	2.5%	2.5%
Body weight Infant (kg)	8	8
Body Weight Todler (kg)	10	10
Hand surface area Infant (cm^2)	196.8	196.8
Hand surface area Todler(cm^2)	230.4	230.4
Hand contamination (%)	20.00%	20.00%
Transfer efficiency of dried residue (%)	2.00%	2.00%
Systemic dose (dermal Infant) (mg/kg bw/day)	3.6 E-04	1.54 E-04
Systemic dose (dermal Todler) (mg/kg bw/day)	3.4 E-04	1.5 E-04
Systemic dose (oral Infant) (mg/kg bw/day)	3.6 E-04	1.54 E-04
Systemic dose (oralTodler) (mg/kg bw/day)	3.4 E-04	1.5 E-04

Total systemic dose Infant (mg/kg bw/day) Total systemic dose Todler (mg/kg bw/day)		0.00072 0.00067	0.00031 0.0003
Notes	Systemic exposure via the dermal route = concentration of a.s. on the wood surface (mg/cm^2) x surface area of hand (cm^2) x area of hand contaminated (%) x transfer coefficient (%) x dermal absorption (%) ÷ bodyweight (kg)		
	Systemic exposure via the oral route = concentration of a.s. on the wood surface (mg/cm^2) x surface area of hand (cm^2) x area of hand contaminated (%) x transfer coefficient (%) x oral absorption (%) ÷ bodyweight (kg)		

Scenario 10 - Secondary exposure (chronic) for a toddler infant inhaling volatilised residue from treated timber indoors

The HEEG opinion 13 on the assessment of inhalation exposure to volatilised biocides provides the following screening tool to determine whether inhalation exposure can be considered not to be a potential risk:

This is a worse-case scenario based on the saturated vapour concentration of the active substance as is considered as Tier 1 assessment.

Where *m*w and *vp* denote the molecular weight (in g/mol) and the vapour pressure (in Pa), for a toddler (based on an inhalation rate of 8 m^3/24 hr and bw of 10 kg) and using an AEL expressed in mg a.s./kg bw/d, if

$$0.328 \cdot \frac{mw \cdot vp}{AEL_{long-term}} \leq 1$$

then the risk from inhalation exposure is considered negligible. The assessment assumes that the individual is exposed to the saturated vapour concentration of the active substance for 24 hours a day and therefore reflects a 'worst-case' scenario. The calculation of toddler inhalation exposure represents a 'worst case' scenario as stipulated in HEEG opinion 13 and as such forms the risk envelope for the assessment of an infant, child and/or adult.

N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine has a molecular weight of 299.54 g/mol and a vapour pressure of 5.45 x 10^{-5} Pa at 25°C. According to HEEG opinion 13 in case the vapour pressure is given for 25°C instead of 20°C the same formula can be applied. The AEL (long term) is 0.00025 mg/kg bw/d.

In the Tier 1 assessment applying the above equation results in the value of 21.42. This value can also be recalculated as systemic exposure dose resulting in 5.355 x 10^{-3} mg/kg bw/d.

This value of 21.42 is > 1 and therefore risk from inhalation exposure to N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine cannot be excluded. However, this result does not mean according to HEEG opinion 13 that there is a risk from

inhalation exposure. It is also pointed out that the assessment using the saturated vapour concentration approach gives a very worst-case inhalation exposure as, at a given ambient temperature, air cannot hold more than the saturated vapour concentration of a substance.

HEEG opinion 13 recommends as alternative approach the ConsExpo's evaporation model to identify a generic worst-case inhalation exposure over a possible scenario. In the extreme case of pure substance and using the very conservative Langmuir estimate for the mass transfer rate, the evaporation model gives the same result as the SVC approach. However, as Tier 2 the ConsExpo evaporation model is used under the assumption that the substance evaporates from a wooden floor of a representative 14 m^2 room with a 35 m^3 room volume (Bed room 1 General Fact Sheet; General default parameters for estimating consumer exposure - Updated version 2014 (RIVM Report 090013003/2014). The timber of the wooden floor had been treated via vacuum pressure application HC 2 & 3. In the table below default values used for the Tier 1 and Tier 2 assessments are listed.

Description of ConsExpo calculation **Exposure model: Exposure to vapour – Evaporation**		
Secondary exposure (chronic) for a toddler inhaling volatilised residue from treated timber indoors *Potential exposure for* [redacted] *is via the inhalation route.*		
Tier 1	**Parameters**	**Value**
	Molecular weight	299.54 g/mol
	Vapour pressure	0.0000545 Pa (at 25°C)
	Toddler body weight	10 kg
	Inhalation rate	8 m^3/24 hr
	Inhalation absorption of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in [redacted]	100%
Tier 2	Product amount (for 14 m^2 wooden floor)	175 g
	Weight fraction substance	0.025%
	Exposure duration	1 day

	Log Kow *	0
	Dilution of product (for vacuum pressure application HC 2 & 3)	200 x
	Molecular weight matrix **	18 g/mol
	Release area mode	constant
	Release area ***	14 m^2
	Room volume ***	35 m^3
	Ventilation rate	1/h
	Emission duration	1 day
	Mass transfer coefficient	131000 m/h
Notes	* calculated via SciFinder®, at pH 1 to 7, 25°C ** up to 80% water in frame formulation (information from applicant) *** Bed room 1, Table 4: Floor surface area and volume of rooms in Dutch homes; RIVM Report 090013003/2014	

The same values used for Tier 1 assessment have been used for Tier 2.

Calculations for [redacted] vapour absorption for Scenario 10

Summary table: systemic exposure for the general public					
Exposure scenario	**Tier**	**Estimated inhalation uptake** (mg a.s./kg bw/day)	**Estimated dermal uptake** (mg a.s./ kg bw/day)	**Estimated oral uptake** (mg a.s./day)	**Estimated total uptake** (mg a.s./kg bw/day)
Scenario 10	Tier 1	5.355×10^{-3}	n.a.	n.a.	5.355×10^{-3}
	Tier 2	3.92×10^{-10}	n.a.	n.a.	3.92×10^{-10}

2.2.1.2.5. *Human health risk from indirect exposure as a result of use (secondary exposure to treated wood)*

The secondary human exposure estimates consider the potential for the exposure of professional adults, infants and children in a number of possible scenarios in which they may come into contact with N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine treated timber.

The scenarios used in this assessment are described in the TNsG on Human Exposure to Biocidal Products Part 3, p.50-51 as revised by User Guidance p.50-54 (EC, 2002a)

Potential risk of industrial/large-scale joinery workers when handling treated timbers (OECD Hazard Class 3)

Indirect exposure occurs due to shaping of treated wood to form roof timbers and trusses, and cladding. Large industrial scale joinery uses engineering controls, i.e. sawdust pullers (vacuum) when cutting treated timber. The resultant sawdust and waste may be bagged up and sold to produce chipboard or MDF, or is more likely to be directly transferred by closed system through a cyclone to a storage hopper for automated feeding into a furnace.

The worst case indirect exposure is to timber which has been vacuum impregnated with the product (application rate: 0.25 kg/m^3) as the product will be present in all cut surfaces and sawdust. Dipped timber and that treated in open-tanks are only treated with the preservative on the outer surfaces, (application rate: 0.3 kg/m^3) so confining indirect exposure to workers handling the treated timber.

Workers are trained to use personal protective equipment such as goggles, gloves and dust masks when advisable.

Potential risk of small-scale joinery workers when handling treated timbers (OECD Hazard Class 3)

Indirect exposure occurs due to shaping of roof timbers and trusses, and cladding manufactured from treated wood. Normally there will be no engineering controls provided. Minimal shaping and cutting will mainly be performed in situ and hence in open air. Sawdust and cuttings will be collected where possible and sent to landfill or incineration.

The worst case indirect exposure is to timber which has been vacuum impregnated with the product (application rate: 0.25 kg/m^3) as the product will be present in all cut surfaces and sawdust. Dipped timber and that treated in open-tanks are only treated with the preservative on the outer surfaces, (application rate: 0.3 kg/m^3) so confining indirect exposure to workers handling the bulk treated timber. Gloves, goggles, and dust masks are advisable, but may not be worn; secondary exposure for the use and handling of wood by industrials/professionals is considered to require no further assessment.

2.2.1.2.6. *Secondary exposure model calculations – Acute Exposure (Systemic Exposure)*

Adult (non-professionals): sanding treated wood from vacuum/pressure impregnated timber.

Inhalation route

Assumptions: N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine in outer 1cm layer, 0.25kg/m^3 wood (equivalent to 0.25 mg/cm^3)

Task duration: 1 hour

Article size: 4 cm x 4 cm x 2.5 m treated posts (0.004 m^3 wood)

Adult body weight: 60 kg

Exposure (Occupational exposure limit for wood dust): 5 mg/m^3 dust for 60 minutes

Inhalation rate: 1.25m^3/hour, 60 kg adult

Inhalation exposure to the a.s.: 5 mg/m^3 x 1 hour/day x 1.25 m^3/hour = 6.25 mg (0.00625 g) wood dust that at a wood density of 0.4 g/cm^3 (as agreed at the TMIII08) is equivalent to 0.00625 /0.4 = 0.015625 cm^3 wood

Inhalation exposure to the a.s.: 0.015625 cm^3 x 0.25 mg/cm^3 = 0.0039 mg a.s.

Systemic inhalation exposure to the a.s.: 0.000065 mg/kg bw (60kg)

Dermal route

Assumptions: N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine in outer 1cm layer, 0.25kg/m3 wood (equivalent to 0.25 mg/cm3)

Task duration: 1 hour

Article size: 4 cm x 4 cm x 2.5 m treated posts (0.004 m^3 wood)

Adult body weight: 60 kg

Hand surface area: 420 cm^2

20% hand contamination = 84 cm^2

Transfer coefficient: 2%

Active substance residue on surface: 0.25 mg/cm^3 x 1 cm = 0.25 mg/cm^2

Dermal exposure to the a.s.: 0.25 mg/cm^2 x 84 cm^2 x 0.02 x 0.025 = 0.0105 mg a.s.

Systemic Dermal exposure to the a.s.: 0.000175 mg/kg bw

Total systemic exposure: 0.00024 mg/kg bw

Secondary exposure model calculations – Chronic Exposure

The refined risk assessment considers the lower HC2&3 use rate. Only chronic professional exposure is assessed; risks are considered acceptable.

Sanding treated wood (professional)

First tier: Assume all a.i./cm3 is present at the sanded surface. E.g., for HC2&3 application rate of 0.125 mg/cm3, the amount of ai at the sanded surface is 0.125 mg/cm2. Dermal absorption included

Second tier – use same calculations as in playstructure scenario, which relate volumetric application rate to surface area (1 m3; 200 m2) and assume that only 10% of a.i. per cm3 is available at surface

Third tier - use leaching data, which is a worst case estimate of release of a.i. compared to the conditions of dermal exposure during sanding

Fourth tier – apply inhalation absorption of 50% (assuming 2.5% absorption for about half of the inhaled mass, and 100% absorption for the remaining inhaled mass). This is still conservative

Inhalation

Application type	Vacuum HC2&3				
	1st tier	2nd tier	3rd tier	4th tier	
Application rate (volumetric)	0.125	0.125	0.125	0.125	kg ai/m3 or mg/cm3 wood
Density of wood	400	400	400	400	mg wood/cm3 wood
Wood dust in air	5	5	5	5	mg wood/m3 air
Inhalation rate	1.25	1.25	1.25	1.25	m3/hr
Hours per day - worker	6	6	6	6	hrs
Body weight	60	60	60	60	kg bw

Conc a.i. in wood	0.0003	0.0003	0.0003	0.0003	mg a.i./ mg wood
Conc a.i. in air	0.0016	0.0016	0.0016	0.0016	mg a.i./m3 air
Inhaled a.i. - worker	0.01172	0.01172	0.01172	0.01172	mg a.i.
Inhalation absorption	100%	100%	100%	50%	
Inhaled systemic dose - worker	**1.95E-04**	**1.95E-04**	**1.95E-04**	**9.77E-05**	**mg/kg bw**

Dermal					
	1st tier	2nd tier	3rd tier	4th tier	
Available active at surface	0.125	0.00625	7.40E-06	7.40E-06	mg a.i./cm2 wood
Surface area, both hands	410	410	410	410	cm2
Exposed area	20%	20%	20%	20%	
Transfer factor	2%	2%	100%	100%	
Dermal absorption	2.5%	2.5%	2.5%	2.5%	fraction
Body weight	60.00	60.00	60.00	60.00	kg bw
Dermal exposure	5.13E-03	2.56E-04	1.52E-05	1.52E-05	mg a.i.
Dermal systemic dose - worker	**8.54E-05**	**4.27E-06**	**2.53E-07**	**2.53E-07**	**mg/kg bw**
LT AEL	0.00025	0.00025	0.00025	0.00025	mg/kg bw
Total dose (inhaled + dermal)	**2.81E-04**	**2.00E-04**	**1.96E-04**	**9.79E-05**	**mg/kg bw**
Chronic exposure (worker), % LT AEL	**112 %**	**80%**	**78%**	**39%**	

2.2.1.2.7. *Toxicological profile of the biocidal product:*

The biocidal product [redacted] is a water-miscible wood preservative concentrate with an active substance concentration of 44.54 g/l (4.41% w/w), which will be diluted with large amounts of water to form an on-site treatment solution with an in-use a.s. concentration of 0.294% w/w to 0.588% w/w for dipping and 0.025% w/w to 0.05% w/w for treatment by vacuum-pressure impregnation

[redacted] is not classified for oral toxicity or dermal toxicity.

No inhalation study was submitted. The vapour pressure of the active substance is 5.45x10-5 Pa at 25◦C.

[redacted] is not irritant to skin and causes serious eye damage (H318).

No sensitizing study was performed, but based on the hazardous properties of propiconazole, [redacted] must be classified as skin sensitizer (H317). Because propiconazole classification with H360D, [redacted] must be classified with H360D.

2.2.1.2.8. *Industrial uses*

Systemic effects

Estimated Uptake and Risk Characterisation of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine from [redacted] for Industrial Users

The table below presents estimated uptake of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine for an industrial user for each relevant scenario from the use of [redacted] Exposure occurring during the application phases (Scenarios 1 to 4) is compared to the long-term AEL (0.00025 mg/kg bw/day).

Exposure occurring during cleaning and maintenance (Scenario 5) is compared to the medium-term AEL (0.0004 mg/kg bw/day) since it can be assumed that this task takes place only once or twice per year.

The exposure via timber treatment (application phase) is considered as primary exposure, whereas restacking fallen treated timber (scenario 6) will normally be undertaken by a person other than the person who is undertaking the actual dipping of the wood (HEEG opinion 18). This exposure is considered as secondary.

The exposure for an industrial user from the use of [redacted] during short-term dipping, dipping and vacuum pressure treatment application HC 4a are concluded to result in unacceptable risk also when appropriate PPE (coverall and gloves) is worn.

The exposure for an industrial user from the use of [redacted] during vacuum pressure treatment application HC 2 & 3 are concluded to result in unacceptable risk also when appropriate PPE is worn and three treatment cycles/day are performed. .

Industrial user can be exposed up to twice a year to [redacted] during cleaning and maintenance of dipping tanks as used for dipping treatment and of solution reservoir, as used for vacuum pressure treatment.

The exposure for an industrial user to [redacted] during cleaning of dipping tanks result in unacceptable risk also when appropriate PPE (coverall and gloves) are worn. However, for an industrial user exposed during cleaning and maintenance of solution reservoir, as used for vacuum pressure treatment the exposure result in acceptable risk when appropriate PPE

(coverall and gloves) are worn.

The exposure calculation for the scenario of restacking fallen treated timber (scenario 6) follows the risk envelope of scenario 3 Tier 3. Acceptable risk was identified for this task when appropriate PPE (coverall and gloves) is worn.

Combined exposure for treatment application and restacking fallen treated timber is not considered relevant since normally both tasks are undertaken by different persons.

Task/ Scenario	**Tier/PPE**	**Systemic NOAEL** mg/kg bw/d	**AEL** mg/kg bw/d	**Estimated uptake** mg/kg bw/d	**Estimated uptake/ AEL** (%)	**Acceptable** (yes/no)
Scenario 1 (Automated short-term dipping application) *Primary exposure*	1 (gloves)	0.025	0.00025	0.118	47200%	no
	2 (gloves & coveralls)			0.024	9600%	no
Scenario 2 (Automated dipping application) *Primary exposure*	1 (gloves)	0.025	0.00025	0.0118	4720%	no
	2 (gloves & coveralls)			0.0024	960%	no
Scenario 3 (Vacuum pressure treatment application HC 2 & 3) *Primary exposure*	1 (gloves) 2 cycles	0.025	0.00025	0.002	800%	no
	2 (gloves & coveralls) 2 cycles			0.0004	160%	no
	3 (gloves & coveralls) 1 cycle			0.0002	80%	yes
Scenario 3 (Vacuum pressure treatment application HC 2 & 3)	gloves & coveralls) 1 cycle	0.025	0.00025	0.0001025	41%	yes
	gloves & coveralls) 2	0.025	0.00025			yes

Primary exposure	cycles			0.000205	82%	
	gloves & coveralls) 3 cycles	0.025	0.00025	0.0003075	123%	no
Scenario 4 (Vacuum pressure treatment application HC 4a) *Primary exposure*	1 (gloves) 2 cycles	0.025	0.00025	0.004	1600%	no
	2 (gloves & coveralls) 2 cycles			0.0008	320%	no
	3 (gloves & coveralls) 1 cycle			0.0005	200%	no
Scenario 5 (Cleaning and maintenance) *Primary exposure*	1a (gloves)	0.0375	0.0004*	0.024	6000%	no
	1b (gloves)			0.001	250%	no
	2a (gloves & coveralls)			0.0052	1300%	no
	2b (gloves & coveralls)			0.00022	55%	yes
Scenario 6 (Restacking fallen treated timber) *Secondary exposure*	1 (gloves & coveralls)	0.025	0.00025	0.0002	80%	yes
Notes: Scenarios 6 is in the risk envelope of scenario 3 Tier 3. *medium-term AEL, task occurs only 2x/year						

2.2.1.2.9. *Local effects*

The classification of [redacted] with respect to local effects is as follows:

Eye Dam. 1, H318: Causes serious eye damage

On the basis of the classification alone it is recommended that for [redacted] industrial users wear protective clothing (coveralls), suitable protective gloves and face protection (faceshield) when handling the concentrate.

As such local effects are not considered relevant to the general public since the active substance in-use concentration is always below the generic concentration limits of ingredients, classified for skin corrosive hazard that trigger classification of the mixture as corrosive/irritant to skin according to EC 1272/2008.

In a subchronic dermal rat study the LOAEC of 0.25% was identified. This value is well above the [redacted] in-use concentration for vacuum pressure treatment HC 2 & 3 or HC 4a of 0.05 to 0.025% (w/w). However, the in-use concentration of short-term dipping and dipping is with 0.294% to 0.588% (w/w) above the LOAEC.

It is assumed that the general public will not have contact to freshly impregnated timber but only after it is dried. Following this a risk of local effects could only occur via dried timber. The transfer efficiency of 2% for dried residue is used in scenario 9. Considering this it can be assumed that dermal contact is only to very low active substance concentrations. Furthermore dermal contact is only transient and no contact for a longer period of time is anticipated. Due to this the risk of local effects can be regarded as negligible.

Conclusion

The risk for industrial users is demonstrated to be acceptable only for vacuum pressure treatment application HC 2 & 3 (Scenario 3 and Scenario 4) when appropriate PPE (coverall and gloves) is worn and one , two or three treatment cycle/day is performed.

2.2.1.2.10. *Secondary (indirect) exposure as a result of use*

Systemic effects

Estimated Uptake and Risk Characterisation of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine from [redacted] for the General Public

The table below presents estimated uptake of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine for the general public for each relevant scenario from the use of [redacted] Exposure is then compared to the appropriate AEL. All scenarios for the general public from the use of [redacted] are concluded to result in acceptable risk.

At TM III08 it was decided that the exposure scenario describing adults laundering contaminated work clothing (Scenario 7) is not required when wood preservatives were applied under industrial conditions. Therefore, no risk assessment has been performed.

Scenario 8 describes secondary (acute) exposure for an infant and a toddler chewing a treated wood off-cut. In consideration of the expected low frequency of this exposure scenario the short-term AEL (0.0023 mg/kg bw/day) is regarded the most appropriate limit value for risk assessment.

Scenario 9 describes infant and toddler playing on a weathered playground and have hand-to-mouth contact as they play. This scenario is considered to occur rather on summer days than during wintertime. Therefore, the log-term AEL (0.00025 mg/kg bw/day) is regarded as the most appropriate limit value for risk assessment.

As worse-case scenario inhalation exposure to volatilised biocides based on the saturated vapour concentration is calculated (scenario 10). It is noted that N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine is not considered as volatile substance. Nevertheless, the exposure was assessed according to HEEG opinion 13, assuming that a toddler (worst case assumption) is exposed to the saturated vapour concentration of the active substance for 24 hours a day. For this scenario the long-term AEL of 0.00025 mg/kg bw/d has been used for risk assessment. Tier 1 assessment results in non-safe exposure and refined Tier 2 exposure calculation based on the ConsExpo evaporation model was performed resulting in an acceptable risk.

Scenario	Tier	Systemic NOAEL mg/kg bw/d	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/AEL	Acceptable (yes/no)
Scenario 7 (adult laundering contaminated work clothing)	1	0.025	0.00025	n.a.	n.a.	n.a.
Scenario 8 (infant chewing on treated wood)	1a*	0.23	0.0023	0.0015	65%	yes
	1b**			0.0006	26%	yes
Scenario 8 (toddler chewing on treated wood)	1a*	0.23	0.0023	0.0012	52%	yes
	1b**			0.0005	22%	yes
Scenario 9 (infant playing on a weathered playground)	1a*	0.025	0.00025	0.00072	288%	no
	1b**			0.00031	124%	no
Scenario 9 (toddler playing on a weathered playground)	1a*	0.025	0.00025	0.00067	268%	no
	1b**			0.0003	120%	no
Scenario 10 (inhalation of volatilised residues)	1	0.025	0.00025	5.355×10^{-3}	2142%	no
	2**			3.92×10^{-10}	2.14×10^{-4}%	yes
* dipping application ** vacuum pressure treatment HC2 & 3						

Secondary exposure for professionals and non-professional sanding treated wood

	Systemic NOAEL mg/kg bw/d	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/AEL	Acceptable (yes/no)
Acute					
Non-professionals					

Adult sanding	0.23	0.0023	0.00024	10.43%	yes
Chronic					
Professionals					
Adult sanding	0.025	0.00025	1.96E-04	78%	yes

Combined Exposure - Estimated Uptake and Risk Characterisation of N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine from [redacted] for the General Public

There are no relevant combined exposure scenarios for the general public foreseen

2.2.1.2.11. *Local effects*

As such local effects are not considered relevant to the general public since the active substance in-use concentration is always below the generic concentration limits of ingredients, classified for skin corrosive hazard that trigger classification of the mixture as corrosive/irritant to skin according to EC 1272/2008.

In a subchronic dermal rat study the LOAEC of 0.25% was identified. This value is well above the [redacted] in-use concentration for vacuum pressure treatment HC 2 & 3 or HC 4a of 0.05 to 0.025% (w/w). However, the in-use concentration of short-term dipping and dipping is with 0.294% to 0.588% (w/w) above the LOAEC.

It is assumed that the general public will not have contact to freshly impregnated timber but only after it is dried. Following this a risk of local effects could only occur via dried timber. The transfer efficiency of 2% for dried residue is used in scenario 9. Considering this it can be assumed that dermal contact is only to very low active substance concentrations. Furthermore dermal contact is only transient and no contact for a longer period of time is anticipated. Due to this the risk of local effects can be regarded as negligible.

2.2.1.2.12. *Risk characterisation for human health based on the local effects*

Secondary Exposure

Derivation of Oral NOAEC

An oral NOAEC for local effects can be derived from the 90 day oral toxicity study in rats. A NOAEL of 3.0 mg a.i./kg bw/day was identified from this study based on local effects observed on the gastrointestinal mucosa at the immediately higher dose 9 mg a.i./kg bw/day. The concentration of the active substance in the vehicle was reported to be fixed at 10 ml/kg bw, thus the 3 mg a.i./kg bw/day is equivalent to a NOAEC of 0.3 mg/ml or 0.03%.

Child playing on weathered structure

Secondary exposure

Child playing on weathered structure and mouthing –ingestion (Local Exposure due to irritant effect)

Exposure to treated articles		
	Parameters	Value
Tier 1	application rate (vacuum impregnation)	0.25 kg/m3 equivalent to 0.25 mg/cm3
	Volume of timber chips	16 cm3 (4 cm x 4 cm x 1 cm) TNsG, Part 3, p. 50 and User Guidance, p. 52
	Active substance on surface	0.3 mg/cm2/day
	Amount of saliva produced	3.6 ml/minute
	maximum absorption a.s	0.3 mg/m3
	Fraction a.s. extracted by chewing	0.1
	Event duration	1 min

1 Include generic parameters (e.g. respiration rates, exposed skin areas, exposure times) and protection/penetration rates for PPE. Use footnotes for references and justifications.2 Only include the parameters changed with respect to the previous Tier.

Calculations for Scenario

Maximum absorption of product is 0.3 mg/cm3. (worst case concentration)

The volume of the timber chips is 16 cm3 (4 cm x 4 cm x 1 cm) as reported in the TNsG, Part 3, p. 50 and User Guidance, p. 52.

The fraction extracted by chewing is 10% as reported in User Guidance, p. 52.

The amount of saliva produced is 3.6 ml/min median value reported for stimulated saliva production.

A	maximum absorption a.s	mg/cm3	0.3
B	size of chewed timber cut-off (chip)	cm2	16
C	depth of chewed timber cut-off (chip)	cm	1
D = B x C	volume of chip	cm3	16
E	a.s. extracted by chewing	fraction	0.1

F = A x D x E	a.s. in the mouth	mg	0.48
G	Amount of saliva produced	ml/min	3.6
H	Event duration	min	1

The event duration has been conservatively assumed to be of 1 min. Any increase in duration time is associated with an higher production of saliva and consequently with an higher dilution. Anyhow this has to be considered a very worst case scenario, as the release of the 10% of the active substance in a very short time (i.e. 1 min) has to be considered unrealistic.

The estimate of the concentration in the mouth has been derived with the above reported parameters revealing the following exposure calculation:

Amount of active substance in the mouth:

F. = A x D x E = 0.48 mg

Concentration in the mouth = F/(G x H) = 0.133 mg a.s./ml

Conclusion:

The maximum oral exposure to diamine for this scenario is predicted to be 0.133 mg a.s./ml. This is below the oral NOAEC value of 0.3 mg/ml and therefore, the risk of exposure to diamine in this scenario is considered acceptable.

This scenario is considered acceptable. Additional reassurance is provided by the fact that scenario is considered uncommon occurrence.

Dermal exposure

The handling of treated wet wood, where exposure was to diluted product, posed only a "Medium" hazard. When the treated wood was dried, the release of the active substance is not expected to reach a concentration that could lead to irritative effects during dermal exposure. Therefore, the potential of local effects during child playing on weathered structure is negligible. No risk to the child playing on weathered structure is identified.

Conclusion

The risk to the general public is demonstrated to be not acceptable, but no safe uses could be reached for infant and toddlers playing in a weathered playground.

2.2.1.2.13. *Combined exposure*

Combined exposure estimates will be applicable for further product types.

2.2.2. Environmental Risk Assessment

2.2.2.1. Hazard identification and effects assessment

Hazard Identification

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine has low tendency to volatilize, due to very low pressure (5.45 x 10-5 Pa at 25ºC) and is stable to photolysis. It is very soluble in water and hydrolytically stable under relevant environmental conditions and also completely soluble in organic solvents with an estimated partition coefficient n-octanol/water Pow of 0.7 that suggests that N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine does not have a tendency to bioaccumulate. The active substance shows irreversible binding or interaction with organic matter, supported by the soil adsorption studies with an estimated Koc of 254600 cm^3/L indicative that the substance is non-mobile in soil. N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine is readily biodegradable as evidenced in available biodegradability tests and also aerobically degraded under the test conditions of a sewage treatment plant aerobic degradation test conducted with activated sludge. No additional data is available on the aerobic/anaerobic degradation of the a.s. in soil or aquatic systems.

Effects assessment

The estimated EC50 (3h) for activated sludge was 18 mg/l.

The acute toxicity tests show that the substance is very toxic to aquatic organisms and algae represent the most sensitive taxonomic group, since EbC50 (72h) of 0.012 mg/l and ErC50 of 0.02 mg/l were obtained.

Acute toxicity tests on *Daphnia magna*, showed this substance to be very toxic to aquatic invertebrates, with a measured EC50 (static, 48h) of 0.073 mg a.s./l. Reproduction and growth rate tests performed with the same species confirm it is highly toxic to aquatic invertebrates during chronic exposure, since a NOEC (21d, static) of 0.024 mg a.s./l was determined. For sediment dwelling organisms a test conducted with *Chironomus riparius* resulted in an estimated NOEC (28d) of 320 mg/kg dwt in the sediment.

For fish, acute toxicity tests resulted in the most critical EC50 (96h, flow-through) of 0.45 mg/l showing this group of aquatic organisms is not the most sensitive to N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine. No chronic tests were conducted with fish and were not considered necessary on that basis.

The results of the acute toxicity tests conducted with the biocidal product [redacted] to the standard aquatic organisms (fish, *D. magna* and algae) are similar to the results of the active substance, indicating that the biocide product is very toxic to aquatic organisms.

For terrestrial organisms toxicity tests were conducted with *Eisenia foetida* that resulted in a LC50 (14 d) > 1000 mg a.s./kg soil based on no mortalities or sub-lethal effects observed at the end of the study and also no adverse effects on nitrogen transformation by soil micro-organisms was observed in the Nitrogen Transformation Test and resulted in an EC50 (28d) greater that 1000 mg a.s./kg soil.

The a.s. was tested for effects on germination, survival and plant growth, for a number of plant species. The estimated EC50 was> 1000 mg a.s./kg dry soil and the NOEC was 1000 mg a.s./kg dry soil for all species tested.

2.2.2.2. Exposure assessment and risk characterisation

Exposure assessment in air:

Emissions of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine can occur to air during the industrial treatment process. The estimated **PECair** range between 1.43E-09 mg/m^3 and 3.05 mg/m^3 indicating that risk to the air compartment could be considered negligible.

Exposure assessment in water:

As result of the industrial treatment and wood in service (noise barrier) emissions to Sewage Treatment Plants may occur, and indirectly the substance can be released to the surface water and sediment. As result of the use of treated wood in service (jetty lake and sheet piling waterway) direct emissions to surface water are predicted.

The estimated **PECstp** range between 2.5x10-05 and 0.19 mg/l.

The estimated **PECsurface water** range between 8.14x10-05 and 0.019 mg/l and the estimated **PECsediment** range between 4.61x10-04 and 10.8 kg/l.

No models were used to estimate **PECgroundwater**, however, the a.s. presents high potential of non-mobility in soil, i.e., has low potential to leach in soil. Therefore a negligible risk of contamination of groundwater is expected.

Fate and behaviour in soil:

No aerobic or anaerobic soil degradation studies were conducted with the active substance. On the basis of soil adsorption studies the a.s. can be considered as non-mobile in soil (Koc 254600 cm^3/l).

As result of intended uses of the active substance emission to soil may occur as result of the industrial process and from wood in service

The **PECsoil** estimations ranged from 0.038 to 220.6 mg/kg, where the house end-use scenario represents the major source of emission of the a.s. to soil.

Based on the fact that the Koc of the a.s. is very high (Koc values of 26000 to 551000 cm3/g), indicative that once adsorbed it will be relatively immobile in soil, and that the available proposed model in the TDG (2003) for calculation of PEC ground water is not fully appropriate to address groundwater contamination as it does not consider the transformation and dilution in deeper soil layers, it was considered that this was not investigated further. Thus it was considered that **no groundwater assessment** was required.

Risk characterisation:

The risks to the environment were addressed according to the ESD and TGD. In general all PEC values are overestimated, since no a.s. degradation was considered for PEC calculations. The consequence of this was, in some cases, PEC/PNEC values above the trigger value (1).

Risk was identified to **aquatic organisms** as a result of the industrial processes, open tank, dipping and vacuum pressure. The calculated **PEC/PNEC ratios ranged from 1.5 to 15.9.**

Risk to **sediment organisms** was only identified in one of the industrial processes, vacuum pressure (B), with a **PEC/PNEC ratio of 1.65 to 8.78**.

Unacceptable risk was also identified to the aquatic environment as result of the use of **treated wood in contact with water**, for the jetty lake and sheet piling waterway scenarios. The **PEC/PNEC ratios were above the trigger of 1.** The worst case was estimated for the sheet piling waterway, TIME2, with PEC/PNEC ratio of 1.49. The calculations can be considered as a worst case (TIER 1), since no risk refinement measures were considered appropriate. However, considering the properties of the a.s. (biodegradability) it is expected that under realistic conditions the use of treated wood in water will not pose an unacceptable risk to the aquatic environment.

For the **industrial processes**, in all industrial scenarios, unacceptable risk was estimated to the **soil compartment**. The **PEC/PNEC ratio ranged between 2.3 and 6.4.** The application

of the risk refinement measure, of increasing the size of the receiving soil compartment to 50cm x 50cm was not enough to exclude the risk to the terrestrial compartment for the open tank and dipping scenarios.

For **treated wood in service** unacceptable risk was estimated for all the end-use scenarios at long term (15 to 20 years), the **PEC/PNEC ratio ranged between 1.38 and 24.9.** For all the end use scenarios the increase of soil size to 50 cm x 50 cm was sufficient to refine the risk.

2.2.2.3. Fate and distribution in the environment

Fate and behaviour in air:

The very low pressure (5.45 x 10-5 Pa at 25ºC) indicates that N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine has low tendency to volatilize, therefore air has not been considered as a compartment of concern.

Fate and behaviour in water:

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine is very soluble in water and hydrolytically stable under relevant environmental conditions.

Fate and behaviour in soil:

No aerobic or anaerobic soil degradation studies were conducted with the active substance. On the basis on soil adsorption studies the a.s. can be considered as non-mobile in soil (Koc 254600 cm^3/l). N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine is readily biodegradable.

2.2.2.4. PBT and POP assessment

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine does not have potential for PBT or POP classification as it is not expected to be persistent in the environment, is non-volatile and will not be subject to long distance transport and does not have a bioaccumulation potential, despite compliance with the toxicity criteria as it may be considered Very Toxic to aquatic organisms

2.2.3. Assessment of endocrine disruptor properties

Human health

At the time of submission of the dossier no rules were set for the assessment of potential ED properties. Nevertheless, an assessment according to the «Guidance for the identification of endocrine disruptors in the context of Regulations (EU) nº 528/2012 and (EC) Nº 1107/2009 was requested form the applicant.

The following scientific data were generated and/or identified to assess the potential endocrine-mediated adversity of Triamine /Diamine:

BPR/REACH registration file(s)	- *In vivo* studies (guideline-compliant; corresponding to OECD Conceptual Framework Levels 4 and 5)
Newly generated information	- *In silico* modelling (conducted by applicants; corresponding to OECD Conceptual Framework Level 2)
Systematic literature search	- *In vitro* mechanistic studies (academic

	investigations; non-guideline) - *In vivo* studies (academic investigations; non-guideline) - Databases of compiled data (i.e. US ToxCast) (corresponding to OECD Conceptual Framework Level 1)

In vivo assays providing data on adverse effects on ED related endpoints (OECD Conceptual Framework Levels 4 and 5)

Repeated dose toxicity and carcinogenicity

A number of guideline-compliant repeated dose, carcinogenicity, reproductive and developmental toxicity studies have been conducted with Diamine. The repeat dose oral studies did not specifically evaluate ED-related endpoints. The most significant treatment-related changes in all studies performed on Diamine are effects on the mesenteric lymph nodes, alveoli of the lungs, kidney, skeletal muscle and heart and are mostly related to the action on the cell membranes and phospholipidosis in the cells. The NOAELs do not change with increasing duration of the study (especially based on concentration in the diet when compensated for allometric scaling and metabolic changes with age).

Originally, the OECD protocols for the repeat dose toxicity studies conducted in various species for the purpose of registering Diamine under the BPR were not specifically designed to detect endocrine-mediated adverse effects. However, the significant amount of repeat dose toxicity data which also include a whole range of EATS-sensitive parameters provide the coherent picture that exposure to Triamine/Diamine neither causes endocrine-mediated adverse effects nor any other type of systemic toxicity that is not secondary to the corrosive nature of the substance.

Reproductive / development toxicity

The reproductive and prenatal developmental toxicity of Diamine can be assessed based on a range-finding study, two pre-natal developmental toxicity studies and two 2-generation reproductive toxicity studies in rats and/or rabbits. The main studies were conducted in compliance with the testing guidelines at the time of conduct and rated to be reliable (i.e. Klimisch 1). The rabbit prenatal developmental toxicity study (Leuschner, 2005) showed maternal toxicity from gastrointestinal irritation, along with resorptions at the top dose (20 mg a.i./kg bw/day). No signs of toxicity were observed at the mid and low doses. Since effects on litters at top dose were secondary to maternal toxicity, Diamine is not considered as a developmental toxicant.

The 2-generation reproductive toxicity studies included a number of EATS-mediated and EATS–sensitive parameters allowing the preliminary identification of effects from (anti-)estrogenic, (anti-) androgenic, thyroid and steroidogenic modalities. In none of the studies did exposure to Diamine result in any reproductive or developmental adverse effects in the experimental animals. These findings therefore validate the large body of evidence showing that Diamine has no adverse effects on reproduction / development.

In vitro assays providing data about selected ED mechanisms / pathways (OECD Conceptual Framework Level 2)

(Q)SAR modelling

Overall, there was no consistent (Q)SAR-based evidence for strong binding to any of the evaluated ED receptors (models run: OECD (Q)SAR Toolbox v.4.2, DEREK Nexus, Endocrine Disruptome, Danish (Q)SAR database and Vega). Most results were negative, apart from

medium probability to bind to the AR receptor as antagonist (Endocrine Disruptome).

High throughput screening and ToxCast modelling predictions

Diamine has not been evaluated in any high throughput screening assay under this program to date.

The ToxCast modelling predictions, derived from the EDSP21 dashboard and based on CERAPP (Collaborative Estrogen Receptor Activity Prediction Project) potency levels are in line with those obtained using the EFSA/ECHA guidance (2018)-recommended models, i.e. no consistent evidence of strong interaction with ER or AR receptors.

In vitro mechanistic studies

No *in vitro* or *in vivo* mechanistic studies with Diamine could be identified.

In conclusion, none of the aforementioned evidence points to an endocrine-mediated mode of action.

Existing data and existing or new non-test information (OECD Conceptual Framework Level 1)

Published repeated dose, carcinogenicity and reproductive / developmental studies

Apart from the above-mentioned studies, no published repeated dose toxicity or reproductive-developmental toxicity study could be identified for Diamine.

Overall conclusions

Available data are sufficient to conclude and diamine does not meet the ED criteria for T modality. The EAS mediated parameters have not been sufficiently investigated.

No conclusion could be reached on the ED properties with respect to humans

Environment

Environmental endpoints:

At the time of submission of the dossier no rules were set for the assessment of potential ED properties. Nevertheless, an assessment according to the «Guidance for the identification of endocrine disruptors in the context of Regulations (EU) nº 528/2012 and (EC) Nº 1107/2009» was requested form the applicant.

The assessment of the potential ED properties followed the assessment strategy as foreseen in the Guidance document and was carried out considering the available data from the dossier.

For the lines of evidence and ED assessment through the EAS modality for non-target organisms other than mammals no level 3 studies are available with Diamine.

Studies considered to fit into Level 4, were available in the dossier, namely results from the 21 d semi-static *Daphnia magna* study conducted according to the OECD Guideline 211 and EU Method C.20, and of the OECD Guideline 218, 28d toxicity test to midge larvae *Chironomus riparius*. Although the tests were looking into the effects of diamine on reproductive and/or growth-related endpoints it is considered that these endpoints are sensitive to, but not diagnostic of, EATS parameters and therefore not sufficient to address the ED properties.

No specific studies have been conducted to address the potential of Endocrine disruption of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine.

(Q)SAR modelling:

An overview of the (Q)SAR modelling is included in the following Table:

QSAR model	**Indicative of**	**Results**
OECD QSAR Toolbox v.4.3	E and N (DART)	No alerts
Derek Nexus v.6.0.1	E, A, S, T and N (developmental toxicity)	No alerts
Endocrine Disruptome	E, A, S and T	Potential binding to AR as antagonist; low binding to the other nuclear receptors
Danish QSAR database	E, A, T and N	Not involved in AR antagonism No inhibition of TPO No activation of AhR and PXR No induction of CYP3A4
VEGA	E	No conclusive results
ToxCast: Models	E and A	Inactive

E = (E)strogen-; A = (A)ndrogen-; S = (S)teroidogenesis-; T = (T)hyroid modalities; N = (N)ot assignable to a specific modality.

In vitro high throughput screening (HTS) assays from the US EPA ToxCast program

Diamine was not evaluated in EDSP21 in any in vitro assays so far.

Conclusion:

The assessment was inconclusive as to whether the a.s. has endocrine disrupting properties for both T and EAS modalities on non-target organisms and further consideration of this issue is needed.

2.3. Overall conclusions[8].

The outcome of the assessment for N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine in product-type 08 is specified in the BPC opinion following discussions at the BPC 37 meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA website.

2.3.1. Overall conclusion of the evaluation including need for risk management measures

Human health

N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine, has a rate and extent of oral absorption of 2.5% based on excretion via urine, and limited metabolism, the rate and extent of dermal absorption was 2% for a aqueous solution (0.1% w/w active substance in aqueous solution) and 2.5% for in-use dilution (0.025 % w/w active substances in use dilutions). The distribution was mainly in kidney, lung, pancreas, salivary gland, small intestine mucosa, spleen and stomach mucosa. A potential for accumulation in the renal tubule was identified. The rate and extent of excretion was >90% of the radiolabelled substance and was excreted in faeces, 0.2% in urine, 0.3% in CO_2 (5 days after dosing). Acute toxicity studies resulted in a LD50 of 261mg/kg bw/day and N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine was corrosive (3-minutes application). Repeated dose toxicity studies in rats showed histopathological changes in the small intestine and mesenteric lymph node and nephrotoxicity (the latter at highest tested doses). In the combined long term carcinogencity study the No Observed Adverse Effect Level (NOAEL) could not be identified based on adverse effects at lowest doses tested in the mesenteric lymph node and in kidneys).

N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine was nNot mutagenic or clastogenic in in vivo studies, no carcinogenic potential. For reproductive toxicity, was found for rats a lower mean epidimydes weight, lower seminal vesicle weights and mean absolute testes weight at both generations at the maximum dose tested was found. For rabbits at the highest dose tested was found an increased incidence for early, late and total resorptions was found.

Accumulation of macrophages with vacuolized (foamy) cytoplasm in the mesenteric lymph node was considered as primary adverse N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine, has a rate and extent of oral absorption of 2.5% effect, occurring at different doses with a dose response relationship, and seen in several studies of different duration (repeated dose studies and combined long term carcinogenicity study). The histopathological changes in the mesenteric lymph node were considered relevant for humans and thus, they have been identified as the critical effect for the derivation of the Acceptable Exposure Level for the long-term and medium-term time frame (AEL long-term: 0.00025 mg/kg bw/day; AEL medium-term: 0.0004 mg/kg bw/day). The effects occurring in the developmental toxicity study in rabbit were considered relevant for the derivation of the Acceptable Exposure Level for the short term time frame (AEL short-term: 0.0023 mg/kg bw/day).

Due to the corrosive effects of the substance occurring via the oral route and dermal route a No Observed Adverse Effect Concentration (NOAEC) for oral route (NOAEC oral 0.03%) and a Lowest Observed Adverse Effect Concentration (LOAEC) for the dermal route (LOAEC dermal 0.25%) were derived and used, where relevant, in the risk assessment to account for local effects.

[8] Sections 2.3.1- 2.3.4 for the BPC shall be included in the opinion and in the AR should be replaced by the following text:

The outcome of the assessment for [name active substance] in product-type [PT] is specified in the BPC opinion following discussions at the [number of BPC meeting] meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA website.

The exposure estimations have been conducted according to the exposure scenario available in biocides guidance documents based on pattern of uses considered to be a reasonablistic worst case.

The exposure estimations of industrial users are compared with the long-term AEL, assuming a chronic exposure of the workers, who would perform their task on daily basis.

Exposure occurring during cleaning and maintenance (Scenario 5) is compared to the medium-term AEL (0.0004 mg/kg bw/day) since it can be assumed that this task takes place only once or twice per year.

The exposure via timber treatment (application phase) is considered as primary exposure, whereas restacking fallen treated timber (scenario 6) will normally be undertaken by a person other than the person who is undertaking the actual dipping of the wood (HEEG opinion 18). This exposure is considered as secondary.

The exposure for an industrial user from the use of the product during short-term dipping, dipping and vacuum pressure treatment application use class 4a are concluded to result in unacceptable risk also when appropriate PPE (coverall and gloves) is worn.

The exposure for an industrial user from the use of the product during vacuum pressure treatment application HCuse classes 2 and 3 are concluded to result in unacceptable risk also when appropriate PPE is worn and three treatment cycles/day are performed.

Industrial users can be exposed up to twice a year to the product during cleaning and maintenance of dipping tanks as used for dipping treatment and of solution reservoir, as used for vacuum pressure treatment.

The exposure for an industrial user to the product during cleaning of dipping tanks result in unacceptable risk also when appropriate PPE (coverall and gloves) are worn. However, for an industrial user exposed during cleaning and maintenance of solution reservoir, as used for vacuum pressure treatment the exposure result in acceptable risk when appropriate PPE (coverall and gloves) are worn.

The exposure calculation for the scenario of restacking fallen treated timber (scenario 6) follows the risk envelope of scenario 3 Tier 3 leads to an acceptable risk was identified for this task when appropriate PPE (coverall and gloves) is worn.

Combined exposure for treatment application and restacking fallen treated timber is not considered relevant since normally both tasks are undertaken by different persons.

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**
Automated short-term dipping application	Primary exposure - Automated short-term dipping application). PPE: gloves and coveralls.	Industrial users	Not acceptable

Automated dipping application	Primary exposure - Automated dipping application. PPE: gloves and coveralls.	Industrial users	Not acceptable
Vacuum pressure treatment application HC 2 & 3)	Primary exposure – vacuum pressure treatment of wooden articles PPE: gloves and coveralls.	Industrial users	Not acceptable
Vacuum pressure treatment application HC 4a)	Primary exposure – vacuum pressure treatment of wooden articles. PPE: gloves and coveralls.	Industrial users	Not acceptable
Cleaning and maintenance-dipping application	Primary exposure – cleaning of treatment equipment PPE: gloves and coveralls.	Industrial users	Not acceptable
Cleaning and maintenance-vacuum pressure treatment	Primary exposure – cleaning and maintenance of treatment equipment PPE: gloves and coveralls.	Industrial users	Acceptable with PPE
Restacking fallen treated timber	Secondary exposure – restacking of fallen timber treated PPE: gloves and coveralls.	Industrial users	Acceptable with PPE
Chewing treated wood off-cuts	Secondary exposure – a toddler or an infant ingests residues through mouthing treated wood off-cuts	General public (toddlers)	Acceptable
		General public (infants)	Acceptable
Playing on (weathered)	Secondary exposure – dermal and ingestion exposure of a toddler or an infant	General public (toddlers)	Not acceptable

playground structures	playing on treated wood structures	General public (infants)	Not acceptable
Vapour release from wood use indoor	Secondary exposure – inhalation exposure of a toddler playing on treated wood structures	General public (toddlers)	Acceptable
Sanding treated wood from vacuum pressure impregnated timber	Secondary exposue – Adults (non-professionls): sanding treated wood (inhalation and dermal exposure) from vacuum pressure impregnated timber (acute exposure) Adults (professionals): sanding treated wood (inhalation and dermal exposure) from vacuum pressure impregnated timber (chronic exposure)	General public (non professionals-adults)	Acceptable
		General public (professionals – adults)	Acceptable

An unacceptable risk has been identified for industrial users, short term dipping application/ surface treatment, dipping application and vacuum pressure treatment, even when gloves and coveralls are worn.

With respect to secondary exposure for the scenario playing on (weathered) playground structures for infants and toddlers, an unacceptable risk was identified. This scenario may be refined at product authorisation.

Environment

The proposed intended uses are restricted to industrial preventive treatments, conducted by the following process: open tank, dipping surface, dipping and vacuum/pressure. Environmental exposure has been addressed through industrial use emissions and emissions from wood in service. Applicable exposure routes have been considered (see summary table).

As a result of the industrial treatment and wood in service (noise barrier) emissions to the Sewage Treatment Plants may occur, and indirectly the substance can be released to the surface water and sediment. As result of the use of treated wood in service (jetty lake and sheet piling waterway) direct emissions to surface water may occur.

As result of intended uses of the industrial process and from wood in service a.s. emission to soil may occur.

The table below summarises the exposure scenarios assessed and conclusions on the acceptability of the risks identified.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusion**

Industrial Immersion treatment - Dipping	Industrial preventive treatment; exposure of sewage treatment plant (STP) and surface waters from draining facilities after application and during storage	Unacceptable risk identified for the soil compartment (long term), STP and aquatic environment. Acceptable if application process is carried out within a contained area, not connected to the surface water drainage or to STP, situated on impermeable hard standing, with bonding to prevent run-off; storage place must be paved with impermeable material and covered.
Industrial Immersion treatment - Open tank	Industrial preventive treatment; exposure of STP and surface waters from draining facilities after application and during storage.	Unacceptable risk identified for the soil compartment (long term), STP and aquatic environment. Acceptable if application process is carried out within a contained area, not connected to the surface water drainage or to STP, situated on impermeable hard standing, with bonding to prevent run-off; storage place must be paved with impermeable material and covered.
Industrial -Vacuum pressure	Industrial preventive treatment; exposure of STP and surface waters from draining facilities after application and during storage.	Unacceptable risks identified for the soil compartment (long term), STP and aquatic environment (except sediment organisms). Acceptable if application process is carried out within a contained area, not connected to the surface water drainage or to STP, situated on impermeable hard standing, with bonding to prevent run-off; storage place must be paved with impermeable material and covered.
Wood in service - Noise barrier – Use class 3	Wood in service. Noise barriers located in roadsides; exposure to soil and to STP via drainage systems and the aquatic environment	Un acceptable risks identified for the soil compartment (long term); after refinement of exposure by consideration of extended size of the receiving soil compartment no unacceptable risks were identified. No unacceptable risks for STP or aquatic environment identified.

Wood in service - House – Use class 3	Wood in service. Possible exposure to soil via leaching from wood in place; permanently exposed to wetting.	Unacceptable risks identified for the soil compartment (long term); after refinement of exposure by consideration of extended size receiving soil the use will not pose unacceptable risks to the soil compartment;
Wood in service - Transmission pole – Use class 3	Wood in service. Possible exposure to soil via leaching from wood in place permanently exposed to wetting	No unacceptable risks identified for the soil compartment.
Wood in service - Fence post – Use class 3	Wood in service. Possible exposure to soil via leaching from wood in place permanently exposed to wetting	No unacceptable risks identified for the soil compartment.
Wood in service - jetty in lake – Use class 4a	Wood in service. Exposure to surface waters	Considering the minor exceedance of the predicted no-effect concentration (PNEC) value and taking into account N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine is readily biodegradable risks were considered acceptable.
Wood in service -sheet piling waterway – Use class 4b	Wood in service. Exposure to surface waters and sediment	. Considering the minor exceedance of the PNEC value and taking into account N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine is readily biodegradable, risks were considered acceptable.

Unacceptable risks were identified for STP, aquatic organisms, sediment organisms and the terrestrial compartment for all treatments at industrial level. However, these can be addressed with appropriate risk management measures, as follows:

- Emissions can be avoided if the application process is carried out within a contained area, not connected to the surface water drainage or to STP. It should be situated on impermeable hard standing, with bonding to prevent run-off and a recovery system should be used. The storage place must be paved with impermeable material and covered. For the terrestrial compartment the exposure was further refined by considering an extended size of receiving soil and resulted in acceptable risk. No risk management measures are needed.

Unacceptable risks (long term) were identified for the terrestrial (soil) compartment for treated wood in service in the modalities noise barrier and house. However, after refinement of exposure the risk was considered acceptable. No risk management measures are needed.

Unacceptable risks were identified for the surface waters for treated wood in service in permanent contact with water – jetty lake and sheet piling waterway modalities. However, as PEC/PNEC values were close to 1 and N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine is readily biodegradable and dissipating from the aquatic environment the risk was considered acceptable. No risk management measures are needed. No risk was identified for the sediment

organisms from the jetty lake and sheet piling waterway scenarios.

Acceptable risks were identified for the terrestrial compartment (soil) as the only relevant exposure scenario for treated wood in service used as transmission posts or fence poles. No risk management measures are needed.

Overall conclusion

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine is proposed to be non-approved as unacceptable risks for N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine have been identified for industrial users, short term dipping application/ surface treatment, dipping application and vacuum pressure treatment, even when gloves and coveralls are worn.

For the environment it is expected that under realistic conditions of use of the a.s. as a wood preservative for industrial processes (open tank, dipping and vacuum pressure treatment) the use of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine will not pose unacceptable risks for the environmental compartments as long as appropriate Risk Management measures are considered namely, if the application process is carried out within a contained area, not connected to the surface water drainage or to a STP. The treatment area and equipments should be situated on impermeable hard standing, with bonding to prevent run-off and a recovery system should be used. The storage place must be paved with impermeable material and covered. The treated wood in service for all use classes (considering the scenarios for fence, house, noise barrier, transmission pole, fence post, jetty lake and sheet piling waterway) will not pose unacceptable risks for the environment (STP, aquatic and organisms, sediment organisms and the terrestrial compartment) under realistic use conditions.

2.3.2. Exclusion, substitution and POP criteria

2.3.2.1. 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	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine 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 and not vP	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine does not fulfil criterion (e) of Article 5(1) and does not fulfil criterion (d) of Article 10(1)
	Bioaccumulative (B) or very Bioaccumulative (vB)	Not B and not vB	
	Toxic (T)	T	
Endocrine disrupting properties	Section A of Regulation (EU) 2017/2100: ED	No conclusion can be drawn based on the	No conclusion can be drawn whether N-(3-

	properties with respect to humans	available data.	aminopropyl)-N-dodecylpropane-1,3-diamine fulfils criterion (d) of Article 5(1) and/or criterion (e) of Article 10(1)
	Section B of Regulation (EU) 2017/2100: ED properties with respect to non-target organisms	No conclusion can be drawn based on the available data.	
	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.		
Concerns linked to critical effects other than those related to endocrine disrupting properties	For N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine no concerns regarding critical effects according to Article 10(1)(e) are identified.		
Proportion of non-active isomers or impurities	Not applicable as N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine does not have isomers or relevant impurities.		

Consequently, the following is concluded:

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine does not meet the exclusion criteria laid down in Article 5 of Regulation (EU) No 528/2012.

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine 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"[9], "Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR"[10] and "Implementation of scientific criteria to determine the endocrine –disrupting properties of active substances currently under assessment[11]" 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).

[9] 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)

[10] 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)

[11] 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).

For the endocrine-disrupting properties as defined in Regulation (EU) No 2017/2100, no conclusion can be drawn on the available data: N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine does not meet the ED criteria for T modality, however the EAS mediated parameters have not been sufficiently investigated; hence, no conclusion on the ED properties can be drawn for human health and non-target organisms according to the criteria laid down in Regulation (EU) 2017/2100. For reports submitted before 1 September 2013, it is mentioned in the CA meeting note mentioned above that the evaluating Competent Authority has to conclude based on the already available data and/or the data provided by the applicant and, in case the data is insufficient to reach a conclusion, the BPC may conclude in its opinion that no conclusion could be drawn. It is noted that the evaluation of diamine for PT 8 was submitted before 1 September 2013.

2.3.2.2. POP criteria

N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine does not fulfil the criteria for being considered as a POP substance as it is not persistent, non-volatile with low affinity to be air born or transported to long distances and does not have a bioaccumulation potential.

2.3.3. Proposal for approval of the active substance N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine in product-type 08

In view of the evaluation, it is concluded that biocidal products containing N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine used for wood preservation may not be expected to meet the criteria laid down in point (b)(iii) of Article 19(1) of Regulation (EU) 528/2012. Consequently, it is proposed that N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine shall not be approved and included in the Union list of approved active substances.

2.3.4. Elements to be taken into account when authorising products[12]

Not applicable.

2.3.5. Requirement for further information[12]

Not applicable.

2.4. Requirement for further information related to the reference biocidal product[3]

Not applicable.

2.5. List of endpoints

The most important endpoints, as identified during the evaluation process, are listed in Appendix I.

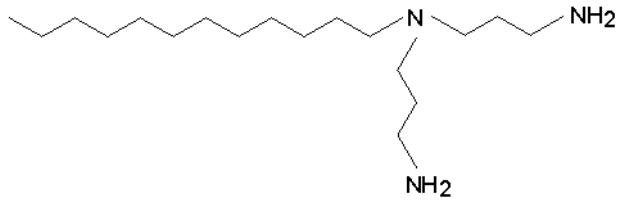
[12] Delete this section if non-approval is proposed.

Appendix I: List of endpoints

Chapter 1:Identity, Physical and Chemical Properties, Classification and Labelling

Active substance (ISO Name)	N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine
Product-type	Wood preservative

Identity

Chemical name (IUPAC)	N-(3-Aminopropyl)-N-dodecylpropane-1,3-diamine
Chemical name (CA)	1,3-Propanediamine, N-(3-aminopropyl)-N-dodecyl-
CAS No	2372-82-9
EC No	219-145-8
Other substance No.	---
Minimum purity of the active substance as manufactured (g/kg or g/l)	880 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	None of the impurities is of concern.
Molecular formula	$C_{18}H_{41}N_3$
Molecular mass	299.54 g/mol
Structural formula	

Physical and chemical properties

Melting point (state purity)	284 ± 0.5 K (10.9ºC) (≥98% w/w)
Boiling point (state purity)	639 ± 0.5 K (366ºC at 101.7 kPa) (≥98% w/w)
Thermal stability / Temperature of decomposition	Below boiling point (91.2% w/w)
Appearance (state purity)	Colourless liquid (≥98% w/w)
Relative density (state purity)	0.864 (≥98% w/w)
Surface tension (state temperature and concentration of the test solution)	35.8 mN/m at 20ºC (concentration 0.98 g/L)
Vapour pressure (in Pa, state temperature)	5.45 x 10-5 Pa at 25ºC (extrapolated from vapour pressure curve)
Henry's law constant (Pa m^3 mol^{-1})	5.95 x 10-07 Pa m3/mol (calculated v3.10 EPI Suite)
Solubility in water (g/l or mg/l, state temperature)	822 g/L at 20ºC pH not measured, extremely basic.

Solubility in organic solvents (in g/l or mg/l, state temperature)	Methanol -814 g/L acetone –813 g/L ethyl acetate – 819 g/L n-octanol: 60.0-66.0% w/w 10ºC – 543 g/L 20ºC – 560 g/L 30ºC – 782 g/L
Stability in organic solvents used in biocidal products including relevant breakdown products	Not applicable
Partition coefficient (log P_{OW}) (state temperature)	Pow = 0.7 (by estimation, based on bioaccumulation potential in terrestrial species)
Dissociation constant	pKa: 9.5, 8.8 and 6.9 at 19.5ºC
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	No molar absorption coefficients could be calculated.
Flammability or flash point	Not extremely flammable Not highly flammable Not flammable Auto-ignition temperature: 288ºC
Explosive properties	Not explosive
Oxidising properties	Not oxidising
Auto-ignition or relative self ignition temperature	288ºC

Classification and proposed labelling

with regard to physical hazards	none
with regard to human health hazards	H314 H301 H373
with regard to environmental hazards	H400

Chapter 2:Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	HPLC-MS/MS

Impurities in technical active substance (principle of method)	Titration (Karl Fischer) HPLC-MS/MS Titration (Karl Fischer)

Analytical methods for residues

Soil (principle of method and LOQ)	Soil samples were extracted with methanol:water: ammonia solution (90:10:1 v:v:v) containing 0.5M ammonium formate. An aliquot of the sample extracts was evaporated under nitrogen to a small volume, prior to reconstitution in methanol:water.formic acid (50:50:0.2 v:v:v) LC-MS/MS (m/z 300.5 > 226) LOQ: 0.01 mg/kg.
Air (principle of method and LOQ)	Not required (a.s. is not volatile and it will not be used by spraying application)
Water (principle of method and LOQ)	The fortified samples was mixed with an aliquot of methanol:water:formic acid (90:10:0.5 v:v:v) containing 0.5M ammonium formate. The analyte was removed from water samples using Strata-X SPE cartridges LC-MS/MS (m/z 300.5 > 226) LOQ: 0.1 µg/l in ground water ; 1.0 µg/l in surface water and > 1.0 µg/l in drinking water Due to the matrix (presence of chlorine) it was not possible to validate the analytical method in drinking water at the required limit of detection.
Body fluids and tissues (principle of method and LOQ)	Not required (a.s. is not classified as toxic or highly toxic)
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Not required (a.s. is not intended for use in areas where food and feeding stuffs are prepared, consumed or stored)
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required (a.s. in a b.p. is not intended for use in areas where food and feeding stuffs are prepared, consumed or stored)

Chapter 3:Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	2.5% (based on excretion via urine, and limited metabolism),
Rate and extent of dermal absorption*:	2% for a 0.1% aqueous solution and 2.5% for in-use dilution.
Distribution:	Mainly in the following organs: Kidney, lung, pancreas, salivary gland, small intestine mucosa, spleen and stomach mucosa.

Potential for accumulation:	In the renal tubule.
Rate and extent of excretion:	>90% of applied radiolabelled substance was excreted in faeces, 0.2% in urine, 0.3% in CO2 (5 days after dosing)
Toxicologically significant metabolite(s)	none

* the dermal absorption value is applicable for the active substance and might not be usable in product authorization

Acute toxicity

Rat LD_{50} oral	261 mg/kg bw, due to irritancy; **H301**
Rat LD_{50} dermal	> 594 mg/kg bw (no lethal effect at maximum dose)
Rat LC_{50} inhalation	Study not conducted due to corrosive properties of a.s.

Skin corrosion/irritation	Corrosive (3-minute application); **H314**
Eye irritation	Due to corrosive effect, risk of serious damage to eyes is considered implicit; H318 implicit on H314
Respiratory tract irritation	No data available
Skin sensitisation (test method used and result)	Not sensitising (0%) in a Buehler test
Respiratory sensitisation (test method used and result)	No data available

Repeated dose toxicity

Short term

Species / target / critical effect	No data available
Relevant oral NOAEL / LOAEL	No data available
Relevant dermal NOAEL / LOAEL	No data available
Relevant inhalation NOAEL / LOAEL	No data available

Subchronic

Species/ target / critical effect	Irritating effects on the gastrointestinal tract, rats
Relevant oral NOAEL / LOAEL	NOAEL 3 mg/kg bw/day/LOAEL 8.9 mg/kg bw/day
Relevant dermal NOAEL / LOAEL	NOAEL 5 mg/kg bw/day/LOAEL 10 mg/kg bw/day
Relevant inhalation NOAEL / LOAEL	No data available

Long term

Species/ target / critical effect	Rats, dose related of large macrophages with cytoplasmatic vacuoles in mesenteric lymph nodes.
Relevant oral NOAEL / LOAEL	NOAEL 4 mg/kg bw/day/LOAEL 8 mg/kg bw/day
Relevant dermal NOAEL / LOAEL	No data available
Relevant inhalation NOAEL / LOAEL	No data available

Genotoxicity	Not mutagenic or clastogenic in in vitro studies

Carcinogenicity

Species/type of tumour	Rats, Not carcinogenic
Relevant NOAEL/LOAEL	NOAEL 4 mg ./kg bw/day/LOAEL 8 mg/kg bw/day

Reproductive toxicity

Developmental toxicity

Species/ Developmental target / critical effect	Rabbits, reduced body weight statistical reduced uterus weight at high dose.
Relevant maternal NOAEL	9 mg/kg bw/day
Relevant developmental NOAEL	9 mg/kg bw/day

Fertility

Species/critical effect	Rats, rabbits
Relevant parental NOAEL	9 mg/kg bw/day
Relevant offspring NOAEL	9 mg/kg bw/day
Relevant fertility NOAEL	9 mg/kg bw/day

Neurotoxicity

Species/ target/critical effect	No data available

Developmental Neurotoxicity

Species/ target/critical effect	No data available

Immunotoxicity

Species/ target/critical effect	No data available

Developmental Immunotoxicity

Species/ target/critical effect	No data available

Other toxicological studies

No data available.

Medical data

No specific effects have been noted

Summary

	Value	Study	Safety factor
$AEL_{long\text{-}term}$	0.00025 mg/kg bw/day	52 weeks oral,rat	400
$AEL_{medium\text{-}term}$	0.0004 mg/kg bw/day	90 days oral gavage, rats	100
$AEL_{short\text{-}term}$	0.0023 mg/kg bw/day	Prenatal develçopmental toxicity, rabbit	100
ADI[13]	0.01 mg/kg bw/day	52 weeks oral,rat	400
ARfD[13]	0.09 mg/kg bw/day	Prenatal develçopmental toxicity, rabbit	100
$NOAEC_{dermal}$	LOAEC 0.25%	90 days dermal, rat	-
$AEC_{inhalation}$	-	-	-

MRLs

Relevant commodities	-

Reference value for groundwater

According to BPR Annex VI, point 68	0.1 ug/L

Dermal absorption

Study (*in vitro/vivo*), species tested	Study in vitro human skin/in vivo rat
Formulation (formulation type and including concentration(s) tested, vehicle)	In vitro study: 14C-Lonzabac12, 1%w/v aqueous solution. In vivo: 14C-Lonzabac12, 0.1%w/v aqueous solution
Dermal absorption values used in risk assessment	2% for a 0.1% aquous solution (in vivo rat study) 2.5% for in-use dilutions

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	No data available
pH 5	pH 5: > 1 year (25 ºC)

[13] If residues in food or feed.

pH 9	pH 9: >1 year (25 ºC)
Other pH: *[indicate the value]*	pH 7: > 1 year (25ºC)
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Not expected to degrade under exposure to light
Readily biodegradable (yes/no)	Yes
Inherent biodegradable (yes/no)	No data available
Biodegradation in freshwater	No data available
Biodegradation in seawater	No data available
Non-extractable residues	No data available
Distribution in water / sediment systems (active substance)	Substance is very soluble in water and hydrolytically stable. On the basis of calculated Koc values, the substance would be considered non-mobile in soil. Partitioning to sewage sludge in an inherent biodegradability study indicated a high absorption to organic matter.
Distribution in water / sediment systems (metabolites)	No data available

Route and rate of degradation in soil

Mineralization (aerobic)	No data available
Laboratory studies (range or median, with number of measurements, with regression coefficient)	No data available
DT_{50lab} (20°C, aerobic):	No data available
DT_{90lab} (20°C, aerobic):	No data available
DT_{50lab} (10°C, aerobic):	No data available
DT_{50lab} (20°C, anaerobic):	No data available
degradation in the saturated zone:	No data available
Field studies (state location, range or median with number of measurements)	No data available
DT_{50f}:	No data available
DT_{90f}:	No data available
Anaerobic degradation	No data available
Soil photolysis	No data available
Non-extractable residues	No data available
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	No data available
Soil accumulation and plateau concentration	No data available

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	Kd values of 2970 to 10500 cm3/g Koc values of 26000 to 551000 cm^3/g

Fate and behaviour in air

Direct photolysis in air	DT50 of 0.72h
Quantum yield of direct photolysis	No data available
Photo-oxidative degradation in air	Latitude: ..... Season: ..... DT_{50} .....
Volatilization	No data available

Reference value for groundwater

According to BPR Annex VI, point 68	0.1ug/L

Monitoring data, if available

Soil (indicate location and type of study)	No data available
Surface water (indicate location and type of study)	No data available
Ground water (indicate location and type of study)	No data available
Air (indicate location and type of study)	No data available

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group)

Species	Time-scale	Endpoint	Toxicity
Fish			
Lepomis macrochirus	96 h	LC50	0.45 mg/l
Invertebrates			
Daphnia magna	48 h	LC0 LC50	0.025 mg/l 0.073 mg/l
Daphnia magna	21 d	NOEC	0.024 mg/l
Algae			
Scenedesmus subspicatus	72 h	E_bC_{50} E_rC_{50} NOEC	0.012 mg/l 0.020 mg/l 0.0069 mg/
Microorganisms			
Activated sludge, domestic	3 h	EC50	18 mg/l

Effects on earthworms or other soil non-target organisms

Acute toxicity to ……..	14 day, EC50 > 1000 mg/kg; NOEC 1000 mg/kg
Reproductive toxicity to ……	No data available

Effects on soil micro-organisms

Nitrogen mineralization	Soil microorganisms (28 day) EC50 >1000 mg/kg; NOEC ≥ 1000 mg/kg
Carbon mineralization	No data available

Effects on terrestrial vertebrates

Acute toxicity to mammals	No data available
Acute toxicity to birds	No data available
Dietary toxicity to birds	No data available
Reproductive toxicity to birds	No data available

Effects on honeybees

Acute oral toxicity	No data available
Acute contact toxicity	No data available

Effects on other beneficial arthropods

Acute oral toxicity	No data available
Acute contact toxicity	No data available
Acute toxicity to ……..	No data available

Bioconcentration

Bioconcentration factor (BCF)	log BCFfish < 10 (estimate) BCFearthworm = 0.85 (estimate).
Depuration time (DT_{50})	No data available
Depuration time (DT_{90})	No data available
Level of metabolites (%) in organisms accounting for > 10 % of residues	No data available

Chapter 6: Other End Points

Endocrine disruptor properties

TOX	Sufficient data to conclude on T modality. Diamine does not meet the ED criteria for T modality.
ECO	For EAS mediated parameters, based on the available information it is not possible to

conclude on either EAS-mediated activity or EAS-mediated adversity. Unsufficient data to conclude on ED properties for non-target organisms both for the T and EAS modalities

Appendix II: List of Intended Uses

Object and/or situation	Product name	Organisms controlled (a)	Formulation		Application			Applied amount per treatment			Remarks:
			Type	Conc. of as (w/w)	Method kind	Number min max	interval between applications (min)	g as/L application solution	solution L/m^2	g as/m^2 * or g as/m^3 **(b)	
Wood, use classes 1- 2	[redacted]	Wood destroying fungi	Liquid water miscible wood preservative concentrate	4.41 %	Short-term dipping	1	-	4.932	0.25	1.233 *	Preventive treatment
Wood, use class 1 - 2	[redacted]	Wood destroying fungi		4.41 %	dipping	1	-	2.466	0.50	1.233 *	
Wood, use classes 1 - 3	[redacted]	Wood destroying fungi		4.41 %	Open tank	1	-	1.644	1.00	1.644 *	
Wood, use classes 2 - 3	[redacted]	Wood destroying fungi		4.41 %	Vacuum pressure	1	-	0.205	2.5	0.512 **	
Wood, use class 4a	[redacted]	Wood destroying fungi		4.41 %	Vacuum pressure	1	-		2.1	0.670**	

(a)*Basidiomycetes:Coniophora puteana, Gloeophyllum trabeum, Poria placenta*

(b) Assumption : 1m^3 has an area of 200 m^2 , therefore 30g /m^2 corresponds to 6 kg /m^3 (Doc.III-B5.3)

Appendix III: List of studies

Data protection is claimed by the applicant in accordance with Article 60 of Regulation (EU) No 528/2012.

Section No / in Doc.III A	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
A3.1.1(1)	[redacted]	2001	[redacted] (Dodecylaminodipropylenetriamine): Determination of Melting/Freezing Temperature. [redacted]. GLP; Unpublished	Y	Lonza
A3.1.1(2) / 3.1.2 (2) / 3.1.3 (2) 3.3 (2) 3.4 (1,2, 3,4)	[redacted]	2004	Determination of general physico-chemical properties. [redacted] GLP; Unpublished	Y	Lonza
A3.1.2(1) / 3.10(1)	[redacted]	1999	Boiling Point Determination of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine. [redacted] GLP; Unpublished	Y	Lonza
A3.1.3(1) / 3.4(1) / 3.5(2) / 3.12(1)/ 3.14(1)	[redacted]	2000	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine- Physical and Chemical Properties. [redacted] GLP; Unpublished	Y	Lonza
A3.2(1) / 3.5(1)	[redacted]	1996	[redacted] Physicochemical Properties. [redacted] GLP; Unpublished	Y	Lonza
A3.2.1(1)	US EPA, EPIWIN v3.10, EPI Suite Software, 2000	2000	Henry's Law Constant, HENRYWIN v3.04	Y	Lonza

Section No / in Doc.III A	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
A3.2.1(2)	[redacted]	2002	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: QSAR estimation of Henry's constant. [redacted] GLP; Unpublished	Y	Lonza
A3.3.(1) / 3.15(1) / 3.16(1)	[redacted]	2000	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Product Chemistry: Discussion of Physical and Chemical Properties. [redacted] GLP; Unpublished	Y	Lonza
A3.4(2) /3.4(3)	[redacted]	2001	[redacted] (Dodecylaminodipropylenetriamine): Spectra. [redacted] GLP; Unpublished	Y	Lonza
A3.4(4) / A3.13(1)	[redacted]	2004	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Determination of Mass Spectra and Surface Tension. [redacted] GLP; Unpublished	Y	Lonza
A3.5(2)	[redacted]	1999	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine – Physical and Chemical Properties. [redacted] GLP; Unpublished	Y	Lonza
A3.6(1)	[redacted]	2000	Determination of the dissociation constant of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine. [redacted] GLP; Unpublished	Y	Lonza
A3.7(1)	[redacted]	1996	[redacted] Solubility in polar organic solvents. [redacted]	Y	Lonza

Section No / in Doc.III A	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
			GLP; Unpublished		
A3.7(2)	[redacted]	2004	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: determination of solubility in n-octanol. [redacted] GLP; Unpublished	Y	Lonza
A3.9(1)	US EPA, EPIWIN v3.10, EPI Suite Software, 2000	2000	Partition coefficient n-octanol/water, KOWWIN v1.65	Y	Lonza
A3.11(1)	[redacted]	2003	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Determination of Auto-Ignition Temperature (Liquids and Gases). [redacted] GLP; Unpublished	Y	Lonza
A4.1(1)	[redacted]	2004	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Validation of Methods for Detection and Indentification. [redacted] GLP; Unpublished	Y	Lonza
A4.1(2)	[redacted]	2000	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Data requirements. [redacted] GLP; Unpublished	Y	Lonza
A4.1(3)	[redacted]	2008	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine (technical material): Determination of the content of the active ingredient and impurities. [redacted] [redacted]	Y	Lonza

Section No / in Doc.III A	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
			GLP; Unpublished		
A4.2a(1)	[redacted]	2004	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Validation of Analytical Procedure in Soil. [redacted] GLP; Unpublished	Y	Lonza
A4.2a(2)	[redacted]	2007	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine (N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine): Validation of methodology for the determination of residues in soil. [redacted] GLP; Unpublished	Y	Lonza
A4.2c(1)	[redacted]	2004	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Validation of Analytical Procedure- water. [redacted] GLP; Unpublished	Y	Lonza
A4.2c(2)	[redacted]	2007	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine (N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine): Validation of methodology for the determination of residues in drinking water, ground and surface water. [redacted] GLP; Unpublished	Y	Lonza
A.5.3.2	[redacted]	2003	[redacted] Certificate [redacted]	Y	Lonza
A.5.3.2	[redacted]	2003	[redacted] Certificate [redacted]	Y	Lonza

Section No / in Doc.III A	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
A.5.3.2	[redacted]	2006	[redacted] test report [redacted]	Y	Lonza
A6.1.1	[redacted]	1988	[redacted] Acute Oral Toxicity Test in the Rat. [redacted]. GLP; Unpublished	Y	Lonza
A6.1.2	[redacted]	1989	[redacted] Acute Dermal Toxicity (Limit Test) in the Rat. [redacted] GLP; Unpublished	Y	Lonza
A6.1.4(1)	[redacted]	1994	[redacted] Acute Dermal Irritation Test in the Rabbit. [redacted] GLP; Unpublished	Y	Lonza
A6.1.5	[redacted]	1996	[redacted] Skin Sensitisation in the Guinea-pig. [redacted] GLP; Unpublished	Y	Lonza
A6.2(1)	[redacted]	1996	[redacted] Toxicokinetic Study in the Rat. [redacted] GLP; Unpublished.	Y	Lonza
A6.2(3)	[redacted]	2003	The *In Vitro* Percutaneous Absorption of [^{14}C]-N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine Through Human Skin at an Incorporation Rate of 1% (w/v) in Water. [redacted] GLP; Unpublished.	Y	Lonza
A6.2(5)	[redacted]	2011	Study on the dermal penetration of ^{14}C-N-(3-aminopropyl)-N-	Y	Lonza

Section No / in Doc.III A	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
			dodecylpropane-1,3-diamine in rats. [redacted] GLP; Unpublished.		
A6.2(6)	[redacted]	2011	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Tissue Distribution and Depletion Kinetics of ^{14}C-N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine in Male Rats After Single Oral Administration . [redacted] GLP; Unpublished.	Y	Lonza
A6.2(7)	[redacted]	2011	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Absorption, Distribution, Excretion and Metabolism of ^{14}C-N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine in Bile Duct Cannulated Male Rats After Single Oral Administration. [redacted] GLP; Unpublished.	Y	Lonza
A6.4.1(1) Part I	[redacted]	1992	90-day Oral Toxicity Study with "[redacted] in Rats followed by a four week Recovery Period. [redacted]	Y	Lonza
A6.4.1(1) Part II	[redacted]	1999	90-day Oral Toxicity Study with "[redacted] in rats followed by a 4-week recovery Period; A Histopathological Review and Expert Opinion. Preclinical Safety Consultants. [redacted]	Y	Lonza
A6.4.1(2)	[redacted]	2003	13-week dietary toxicity in rats. [redacted]	Y	Akzo Nobel Surface

Section No / in Doc.III A	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
			[redacted] GLP, Unpublished		Chemistry AB
A6.4.1(3)	[redacted]	2004	90-day Subchronic Toxicity Study of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine by Repeated Oral Administration via the Diet to Beagle Dogs. [redacted] GLP; Unpublished	Y	Lonza
A6.4.2	[redacted]	2000	Sub-chronic Dermal Toxicity / Immunotoxicity Study with N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine in Rats. [redacted]. GLP; Unpublished	Y	Lonza
A6.5	[redacted]	2010	Combined Chronic Toxicity and Carcinogenicity Study of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine by Dietary Administration to CD® Rats – Part II: 12 month Chronic Toxicity Study. [redacted] GLP; Unpublished	Y	Lonza
A6.6.1	[redacted]	1988	Study to Determine the Ability of [redacted] to Induce Point Mutations in Five Histidine-Requiring Strains of *Salmonella typhimurium*. [redacted] GLP; Unpublished	Y	Lonza
A6.6.2	[redacted]	1991	*In vitro* Mammalian Cytogenetic Test with [redacted] International Bioresearch (IBR) [redacted] GLP; Unpublished	Y	Lonza

Section No / in Doc.III A	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
A6.6.3	[redacted]	1991	*In vitro* mammalian cell gene mutation test with [redacted] GLP; Unpublished	Y	Lonza
A6.7	[redacted]	2011	Combined Chronic Toxicity and Carcinogenicity Study of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine by Dietary Administration to CD® Rats-104 Week Carcinogenicity Study. [redacted] GLP; Unpublished	Y	Lonza
A6.8.1(1)	[redacted]	1994	[redacted] Developmental Toxicity Study in Rats. [redacted] GLP; Unpublished	Y	Lonza
A6.8.1(2)	[redacted]	2005	Study of embryo-fetal development in rabbits with N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine by oral administration. [redacted] GLP; Unpublished.	Y	Lonza
A6.8.2	[redacted]	1995	[redacted] Two-Generation Reproduction Study in Rats. GLP; Unpublished	Y	Lonza
A7.1.1.1.1 (1)	[redacted]	1996	[redacted] Abiotic Degradation: Hydrolysis as a Function of pH. 	Y	Lonza

Section No / in Doc.III A	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
			GLP; Unpublished		
A7.1.1.1.2 (1)	[redacted]	2003	UV/visible Absorption Spectra-Estimation of Aqueous Photolysis of N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine. [redacted] GLP; Unpublished	Y	Lonza
A7.1.1.2.1 (1)	[redacted]	2002	Biodegradability of Triamine Y12D in the Closed Bottle Test. [redacted] GLP; Unpublished	Y	Lonza
A7.1.1.2.2 (1)	[redacted]	1997	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine. DOC Die-Away Test OECD 301A with Pre-adapted Inoculum. [redacted] GLP; Unpublished	Y	Lonza
A7.1.2.1.1 (1) Part I A7.1.2.1.1 (1) Part II A7.1.2.1.1 (1) Part III	[redacted]	2003	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine.100: Dieaway in Activated Sludge. [redacted] GLP; Unpublished. N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine.100: Mini-Aerobic Die-Away Procedure, Letter Report. [redacted] N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine.100: Porous Pot Acclimation Procedure, Letter Report. [redacted]	Y	Lonza
A7.2.3.1	[redacted]	2007	Determination of adsorption coefficient. [redacted]	Y	Lonza

Section No / in Doc.III A	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
	[redacted]		[redacted] GLP; Unpublished		
A7.3.1(1)	[redacted]	2004	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Estimation of Photodegradation Using the Atmospheric Oxidation Program (AOPWIN). [redacted]	Y	Lonza
A7.4.1.1(1)	[redacted]	1989	[redacted] 96-Hour Acute Toxicity Study (LC_{50}) in the Rainbow Trout. [redacted] GLP; Unpublished	Y	Lonza
A7.4.1.1(2)	[redacted]	2000	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: A-96 Hour Flow-Through Acute Toxicity Test with the Bluegill (*Lepomis macrochirus*). [redacted] GLP; Unpublished	Y	Lonza
A7.4.1.1(3)	[redacted]	1992	96-Hour Static Acute Toxicity Test with N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine.100 in Rainbow Trout. [redacted] GLP; Unpublished	Y	Lonza
A7.4.1.1(4)	[redacted]	1992	96-Hour Static Acute Toxicity Test with N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine.100 in Rainbow Trout, mitigated by dissolved organic carbon - 10 mg humic acid/l. [redacted] GLP; Unpublished	Y	Lonza
A7.4.1.1(	[redacted]	1992	96-Hour Static Acute Toxicity Test with N-(3-aminopropyl)-N-	Y	Lonza

Section No / in Doc.III A	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
5)	[redacted]		dodecylpropane-1,3-diamine.100 in Rainbow Trout, mitigated by dissolved organic carbon - 20 mg humic acid/l. [redacted] GLP; Unpublished		
A7.4.1.2(1)	[redacted]	2000	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: A 48-Hour Flow-Through Acute Toxicity Test with the Cladoceran (*Daphnia magna).* [redacted] GLP; Unpublished	Y	Lonza
A7.4.1.2(2)	[redacted]	1989	24-Hour Acute Toxicity Study of [redacted] to *Daphnia magna*. [redacted] GLP; Unpublished	Y	Lonza
A7.4.1.3(1)	[redacted]	2001	[redacted] (Dodecylaminodipropylenetrimaine): Algal Inhibition Test. [redacted] GLP; Unpublished	Y	Lonza
A7.4.1.3(2)	[redacted]	1992	96-Hour Toxicity Test with N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine.100 in fresh water alga (*Selenastrum capricornutum*). [redacted] GLP; Unpublished	Y	Lonza
A7.4.1.4(1)	[redacted]	1996	[redacted] Inhibitory Effect on the Respiration of Activated Sewage Sludge. [redacted]	Y	Lonza

Section No / in Doc.III A	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
			GLP; Unpublished		
A7.4.3.4(1)	[redacted]	2004	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: *Daphnia magna* Reproduction Test. [redacted] GLP; Unpublished	Y	Lonza
A7.4.3.5.1 (1)	[redacted]	2003	Protocol N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Sediment-Water Chironomid Toxicity Test using Spiked Sediment. [redacted].	Y	Lonza
A7.5.1.1(1)	[redacted]	2003	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Soil Microorganisms: Nitrogen Transformation Test. [redacted]. GLP; Unpublished	Y	Lonza
A7.5.1.2(1)	[redacted]	2003	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine: Acute Toxicity to Earthworms. [redacted] GLP; Unpublished	Y	Lonza
A7.5.1.3 (1)	[redacted]	2007	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine - Toxicity to Terrestrial Plants. [redacted] GLP; Unpublished	Y	Lonza

Section No / in Doc.III B	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
B3.1(1) 3.5 (1) 3.7(1) 3.8(1)	[redacted]	2004	[redacted] Determination of accelerated storage stability and physico-chemical characteristics. [redacted] GLP; Unpublished	Y	Lonza
B.3.6(1) 3.10.1(1) 3.10.2(1)	[redacted]	2004	[redacted] Determination of general physico-chemical properties. [redacted] GLP; Unpublished	Y	Lonza
B.3.7(1)	[redacted]	2005	[redacted] Determination of Long-term storage stability and physico-chemical characteristics. [redacted] GLP; Unpublished	Y	Lonza
B.3.7(2)	[redacted]	2006	Final report of shelf life of test item [redacted] at ambient temperature. [redacted]	Y	Lonza
B.3.7(3)	[redacted]	2006	[redacted] Determination of Low temperature stability. [redacted] GLP; Unpublished	Y	Lonza
B4.1(1)	[redacted]	2003	[redacted] Analytical method validation. [redacted]	Y	Lonza
B4.1(2)	[redacted]	2004	[redacted] Analytical method validation and active ingredient assay. [redacted]	Y	Lonza

Section No / in Doc.III B	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
			[redacted] GLP; Unpublished		
B4.1(3)	[redacted]	2003	Validation method of analysis [redacted] No GLP, Unpublished	Y	Lonza
B5.10(1)	[redacted]	2000	[redacted] Test Certificate [redacted] Unpublished	Y	Lonza
B5.10 (2)	[redacted]	2004	[redacted]Test Certificate [redacted] Unpublished	Y	Lonza
B5.10(3)	[redacted]	2003	[redacted] Test Certificate [redacted] Unpublished	Y	Lonza
B6.1.1	[redacted]	2004	[redacted] Acute Oral Toxicity in the Rat - Acute Toxic Class Method. [redacted] GLP; Unpublished	Y	Lonza
B6.1.2	[redacted]	2004	[redacted] Acute Dermal Toxicity (Limit Test) in the Rat. Safepharm [redacted] GLP; Unpublished	Y	Lonza
B6.2(1)	[redacted]	2004a	Acute Dermal Irritation in the Rabbit. [redacted] GLP; Unpublished	Y	Lonza

Section No / in Doc.III B	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
B6.2(2)	[redacted]	2004b	Acute Eye Irritation in the Rabbit. [redacted] GLP; Unpublished	Y	Lonza
B7.1(2)	[redacted]	2007	Leaching Test – Superficial Application (Dipping): Estimation of emission from preservative-treated wood to the environment: laboratory method for wood held in storage after treatment and for wood commodities that are not covered, and are not in contact with ground. [redacted] GLP; Unpublished	Y	Lonza
B7.1(3)	[redacted]	2001	Determination of the Leachability of [redacted] from treated wood. [redacted]	Y	Lonza
B7.1(4)	[redacted]	2001	Determination of the Leachability of [redacted] from treated wood. [redacted]	Y	Lonza
B7.4.1.1(1)	[redacted]	2004	[redacted] Acute Toxicity to Fish. [redacted]. [redacted]	Y	Lonza

Section No / in Doc.III B	Author(s)	Year	Title. Source (where different from company) Company, Report No GLP (where relevant)/(Un)Published	Data Protection Claimed (Yes/No)	Owner
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B7.4.1.3(1)	[redacted]	2004	Protocol [redacted] Growth Inhibition test on algae. [redacted]	Y	Lonza

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