

HDI oligomers, isocyanurate

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CAS Number: 28182-81-2

IUPAC name: HDI Oligomers, isocyanurate

IUCLID Endpoint Summary Information

The information compiled in this document consists mainly of the IUCLID endpoint summaries regarding environmental and health hazards and the rationale for DNEL and PNEC derivation. This information is included in the REACH registration dossier for HDI Oligomers, isocyanurate but is currently not disseminated on the ECHA website. However, this information is deemed necessary to comprehend the conclusions as derived in the REACH registration dossier for HDI Oligomers, isocyanurate.

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1. PHYSICAL AND CHEMICAL PROPERTIES

Molecular formula: $(C_8H_{12}N_2O_2)_n$

Appearance/physical state/colour: Clear, colourless, and viscous liquid

Melting / freezing range: -51.3 to -28.4 °C

Boiling point: Decomposition at approx. 250 °C. Calculated: 418 °C

Mass density: 1.17 g/cm³ at 20 °C and 1.09 g/cm³ at 23 °C

Vapour pressure: $2.46 \cdot 10^{-03}$ Pa at 20 °C, $2.55 \cdot 10^{-03}$ Pa at 25 °C

Water solubility: Hydrolytically unstable (half-life <12 hours)

Partition coefficient n-octanol/water (log value): Calculated for the ideal HDI Trimer: 9.81. Test cannot be performed, as the substance decomposes in water within a few hours.

Flash point: 228 °C

Stability in organic solvents: In protic solvents like alcohols, isocyanates react rapidly. Stability is expected with non-protic solvents like toluene, acetone, dioxane etc. The concentration of HDI Trimer in an acetonitrile solution without addition of water was stable within 26 hours.

Dynamic viscosity: 3851.69 +/- 17.458 mPa*s

2. ENVIRONMENTAL FATE PROPERTIES

2.1. Hydrolysis

The following information is taken into account for any hazard / risk / persistency assessment:

In a screening test at 50°C the HDI Trimer was found to hydrolyse by 84 – 89% within less than 1 hour at pH values of 4, 7, and 9 (Bayer Industry Services, 2007). Approximate mean half lives of 3 hours at 25°C were estimated at any pH and environmental relevant temperatures. A hydrolysis product based on the hydrolysis of the 3 Isocyanate groups to the corresponding amine functions has been proposed (BIS, 2007).

Based on the determination of the Isocyanate function, the half-time of HDI Trimer in the acetonitrile/water solution is approx. 7.7 hour at room temperature (23 °C) (Bayer AG, 1999). Hydrolysis products have not been elucidated. However similar substances containing several isocyanate groups like HDI, MDI are known to react rapidly with water forming insoluble oligomeric and polymeric ureas. The below mentioned corresponding triamine is only a theoretical worst-case assumption in order to have a basis for assessment but which in reality reflects only insignificant traces.

2.2. Phototransformation in air

The following information is taken into account for any hazard / risk / persistency assessment:

The atmospheric oxidation rate constant of the main component HDI Trimer (Isocyanurat, n=3) of Desmodur N 3300 and Desmodur N 3600 is $37.5 \cdot 10^{-12} \text{cm}^3/(\text{molecule} \cdot \text{s})$ and its atmospheric half-life is 10.3 hrs (Currenta, 2009a).

The atmospheric oxidation rate constant of the corresponding triamine of the main component HDI Trimer (Isocyanurat, n=3) of Desmodur N 3300 and Desmodur N 3600 is $129.1 \cdot 10^{-12} \text{cm}^3/(\text{molecule} \cdot \text{s})$ and its atmospheric half-life is 3.0 hrs (Currenta, 2009b).

2.3. Biodegradation

2.3.1. Biodegradation in water

Discussion (screening testing)

Beside valid tests, there is a study according to a modified MITI-I where the substance was determined to be not readily biodegradable (Bayer AG, 1988). This study is not regarded as reliable: within 28 days only 48 % degradation of the reference substance (aniline) was observed.

The following information is taken into account for any hazard / risk / persistency assessment:

Within 28 days, a degradation of 1 % was determined for HDI Trimer (Desmodur N 3600) in a 'Closed Bottle Test' (Bayer AG, 2001). HDI Trimer is regarded as "not readily biodegradable".

In a 'Modified Manometric Respirometry Test' with adapted inoculum no degradation of HDI Trimer (Desmodur N 3600) could be obtained within 28 days (BayerAG, 2001).

In a biodegradation test with adapted industrial bacteria it was shown that the substance is not degradable. This result is used for assessing the behaviour of the substance in STPs.

Value used for CSA: Biodegradation in water: under test conditions no biodegradation observed

Discussion (simulation testing)

The following information is taken into account for any hazard / risk / persistency assessment:

The test is scientifically unjustified. In test for ready biodegradation as well as in a test with adapted inoculum no signs for biodegradation were observed. Therefore, it is not expected that biodegradation will occur in a simulation test.

2.3.2. Biodegradation in soil

The following information is taken into account for any hazard / risk / persistency assessment:

Because of the relatively rapid reaction of HDI Trimer with hydroxyl radicals in the atmosphere (Currenta, 2009), and the rapid hydrolysis in water (Bayer AG, 1999/BIS, 2007) significant concentrations of HDI Trimer would be expected not to occur in soil with the exception of environmental spills for example. Hydrolysis of HDI Trimer is expected to occur much more rapidly than biodegradation, Therefore, the reaction with water is expected to be the only significant fate process of HDI Trimer in moist soil. Only small amounts of unreacted HDI Trimer may persist in soil, if encapsulated in water-insoluble polyurea crusts formed during hydrolysis. Therefore no data are required.

2.3.3. Summary and discussion of degradation

Abiotic degradation

HDI Trimer hydrolyses rapidly. At environmental relevant temperatures The half life of HDI Trimer in an acetonitrile/water solution is 3-7.7 hours..

In the atmosphere the main component HDI Trimer (Cyanurat, n=3) will be degraded due to indirect photodegradation in about 10 hours. Based on the low adsorption potential in UV-B range, no significant direct photodegradation is expected.

Biotic degradation

According to the available biodegradation results HDI Trimer is not readily biodegradable.

Degradation rates

Degradation rate in water:	Not readily biodegradable, hydrolysis: half live <1h
Degradation rate in sediment:	Not readily biodegradable
Degradation rate in soil:	Not readily biodegradable
Degradation rate in air:	Indirect photolysis: $37.5 * 10^{-12} \text{ cm}^3 / (\text{molecule} * \text{s})$

2.4. Bioaccumulation

The following information is taken into account for any hazard / risk / bioaccumulation assessment:

The direct and indirect exposure of the aquatic compartment is unlikely because Desmodur N 3300 hydrolysis completely in water within 3-7.7 hours. Therefore the BCF-values were calculated. Bioconcentration factors (BCF) of 3.16 and 367.7 for the main component HDI Trimer (Isocyanurat, n=3) of Desmodur N 3300 and Desmodur N 3600 and its corresponding triamine were obtained (Currenta, 2009a).

Even the corresponding triamine of HDI Trimer (Isocyanurat, n=3) with a bioconcentration factor of 367.7 does not have high bioaccumulation potential (Currenta, 2009b).

Only minor amounts (ca. 4%) of the hydrolysed substance are soluble in water indicating that bioaccumulation is not expected.

2.5. Adsorption / desorption

The following information is taken into account for any environmental exposure assessment:

The main component HDI Trimer (Isocyanurat, n=3) of Desmodur N 3300 and Desmodur N 3600 is characterized by a Koc of $5.7 * 10^{07}$ being calculated with PCKOCWIN v. 1.66 (Currenta, 2009a). According to the method of Gerstl (1999) the Koc of $2.1 * 10^{07}$ accounts for the main component (Currenta, 2009a).

The corresponding triamine of the main component (Isocyanurat, n=3) of Desmodur N 3300 and Desmodur N 3600 is characterized by a Koc of $6.1 * 10^{05}$ being calculated with PCKOCWIN v. 1.66 (Currenta, 2009b). According to the method of Gerstl (1999) the Koc of $2.7 * 10^{04}$ accounts for the corresponding triamine (Currenta, 2009b).

2.6. Volatilisation

With a vapour pressure of about 0.001 Pa volatilisation of the substance is unlikely.

2.7. Distribution modelling

HDI Trimer hydrolyses rapidly in the presence of water yielding a complex mixture of oligomeric and polymeric urea derivatives which are non-soluble in water. Due to the rapid hydrolysis of HDI Trimer, a transport of the substance between environmental compartments is unlikely. Consequently, a calculation of the distribution between the environmental compartments according to the Mackay fugacity model level 1 or 3 is not suitable.

2.8. Secondary poisoning

The key step for the risk estimation of accumulation through the food chain is to consider whether there are indications for bioaccumulation potential. As discussed in chapter 4.3, HDI Trimer and its degradation products have only a low bioaccumulation potential. For this reason there is no risk for secondary poisoning. It is not required to carry out a risk characterisation for secondary poisoning.

3. ENVIRONMENTAL HAZARD ASSESSMENT

3.1. Aquatic compartment (including sediment)

3.1.1. Toxicity test results

The inherent property of HDI Trimer is to hydrolyse rapidly in an aquatic environment.

In the following the toxicity of the hydrolysis product(s) are reported for tests which have been conducted with specially laid down test conditions and which are thus reproducible tests:

For fish (*Danio rerio*) the acute toxicity expressed in terms of lethal loadings (LL0, 96 h) of HDI Trimer was ≥ 100 mg/l. The studies were conducted according to Directive 92/69/EEC, C1 (Bayer AG, 2000/Bayer AG, 2001).

HDI Trimer was tested with respect to the acute toxicity towards invertebrates (*Daphnia magna*) according to Directive 92/69/EEC, C2. After 48 hours effective concentration values expressed in terms of effective loadings (EL0, 48 h) of ≥ 100 mg/l and 25 mg/l, respectively were obtained. The 48 h-EL100 for HDI Trimer was > 100 mg/l (Bayer AG, 2001).

The effect of HDI Trimer towards the growth inhibition of algae (*Desmodesmus subspicatus*) was assessed performing a study according to the German standard method "DIN 38 412, Part 9 (1989) "Zellvermehrungshemmtest: *Scenedesmus subspicatus* CHODAT (Grünalge)", which is in most part equivalent to the OECD TG. In 72 hours the nominal concentration which reduces the growth rate by 10 % was 370 mg/L and the one which reduces by 50 % was > 1000 mg/L (Bayer AG, 1989).

In another test the toxicity of HDI Trimer to algae (*Desmodesmus subspicatus* CHODAT) was assessed performing a study according to the Directive 92/69/EEC, C.3: "Algal inhibition test", which is in most parts equivalent to the OECD TG 201. No inhibition of the algal population as reduction in growth rate was observed after 72 h at a test concentration of 100 mg/l (Bayer AG, 2001).

Based on the presented results above HDI Trimer has to be scored as not toxic towards aquatic organisms.

3.1.2. Short-term toxicity to fish

Discussion

Two acute toxicity studies were performed on HDI Trimer in accordance with the EU Method C.1 and under GLP. Considering the variable composition of the test substance, a Water Accommodated Fraction procedure was used (100 mg of the test substance was added to 1L of water). Fish (species: *Danio rerio*) were exposed to the WAF under static conditions (Bayer AG 2000a, Bayer AG 2001c). The endpoint is lethal loading rate. In both studies, the 96 -h LL0 was found to be higher than 100 mg/L (nominal concentration).

Disregarded study: For fish (*Danio rerio*) a LC 50 of 8.9 mg/l (geom. mean.) after 96 h was obtained. The study was conducted according to the German standard method "UBA- Verfahrensvorschlag: Letale Wirkung beim Zebraäbrbling (*Brachydanio rerio*), May 1984" (Bayer AG, 1988). This study is not regarded as being reliable. Even if the validity criteria are fulfilled according to the validity criteria of 1988 the study design does not meet the criteria of today standard methods. The stirring period of 60 seconds was regarded as too short for a complete hydrolysis of HDI Trimer.

The following information is taken into account for acute fish toxicity for the derivation of PNEC:

The toxicity to fish (*Danio rerio*) was assessed according to Directive 92/69/EEC, C.1. The effective concentration expressed in terms of lethal loadings (LL0, 96 h) is estimated to be ≥ 100 mg/l. The result relates to nominal concentration (Bayer AG, 2000/Bayer AG, 2001).

3.1.3. Long-term toxicity to fish

Data waiving

Reason: other justification

Justification: According to column 2 of Reach Annex VII-X, a long-term ecotox study should be proposed by the registrant if the chemical safety assessment indicates the need to further investigate the effects on those organisms.

For the risk characterisation of the aquatic compartment, a PNEC has been derived on the basis of three acute aquatic toxicity data. According to the CSA, the risk characterisation yields a PEC/PNEC ratio smaller than 1. Further test are not necessary as the risk is sufficiently described based on the already available data.

3.1.4. Short-term toxicity to aquatic invertebrates

Discussion

The 48-hr acute toxicity of HDI Trimer to Daphnids (*Daphnia magna*) was studied under static conditions. The experiment was carried out in accordance with the EU Method C.2. The medium composition was compliant with the Guideline requirement. Considering the variable composition of the substance, a Water Accommodated Fraction (=WAF) procedure was used (ratio: 100 mg of the test item was added to 1 L of water). The results are expressed in terms of effective loadings (EL). Immobilization was observed daily. Mobility was recorded daily in, control and treated groups. No immobiles were observed after 24h in any groups. After 48 hours, 4 of 20 daphnids were immobile (20%) in the 50 mg/l group and 7 daphnids in the 100 mg/l group (35%). In the test report, no EL50 was given, but an EL100 > 100mg/l. The EL50 was later (2010) extrapolated and calculated using TOXRAT (EL50=127 mg/l). (Bayer AG, 2001d).

Disregarded study: For *Daphnia magna* STRAUS an EC 0 of ≥ 100 mg/l was obtained after 24 hours. The study was conducted according to the German standard method „UBA- Verfahrensvorschlag: Bestimmung der Schwimmfähigkeit beim Wasserfloh (*Daphnia magna*), EC0/EC50/EC100, 24 Std. statisches System“. The result relates to the nominal concentration. This study is not regarded as being reliable. Even if the validity criteria are fulfilled according to the validity criteria of 1989 the study design does not meet the criteria of today standard methods. According to international standard methods an exposure time of 48 hours follows the state-of-the-art of science (Bayer AG, 1989).

The following information is taken into account for short-term toxicity to aquatic invertebrates for the derivation of PNEC:

The acute toxicity to *Daphnia magna* STRAUS expressed in terms of effective loadings (EL0, 48 h) lead to an EL0 of ≥ 100 mg/l and 25 mg/l for HDI Trimer, respectively. After 48 h the EL50 for HDI Trimer was 127 mg/l. The studies were conducted according to Directive 92/69/EEC, C2 (Bayer AG, 2001). The results relate to the nominal concentration.

3.1.5. Long-term toxicity to aquatic invertebrates

Data waiving

Reason: other justification

Justification: According to column 2 of Reach Annex VII-X, a long-term ecotox study should be proposed by the registrant if the chemical safety assessment indicates the need to further investigate the effects on those organisms.

For the risk characterisation of the aquatic compartment, a PNEC has been derived on the basis of three acute aquatic toxicity data. According to the CSA, the risk characterisation yields a PEC/PNEC ratio smaller than 1. Further test are not necessary as the risk is sufficiently described based on the already available data.

3.1.6. Algae and aquatic plants

Discussion

Effects on algae / cyanobacteria

The following information is taken into account for effects on algae / cyanobacteria for the derivation of PNEC:

The toxicity of HDI Trimer to algae (*Desmodesmus subspicatus*) was assessed performing a study according to the German standard: DIN 38 412, Part 9 (1989) "Zellvermehrungshemmtest: *Scenedesmus subspicatus* CHODAT (Grünalge)", which is in most parts equivalent to the OECD TG 201 (Bayer AG, 1989). The 72h-EC10 was 370 mg/l. The EC50 was > 1000 mg/L.

In a supporting study the toxicity of HDI Trimer to algae (*Desmodesmus subspicatus* CHODAT) was assessed performing a study according to the Directive 92/69/EEC, C.3: Algal inhibition test, which is in most parts equivalent to the OECD TG 201 (Bayer AG, 2001). No inhibition of the algal population as reduction in growth rate was observed after 72 h at a test concentration of 100 mg/l. The results are expressed in terms of nominal concentrations.

3.1.7. Sediment organisms

Data waiving

Reason: study scientifically unjustified

Justification: According to section 1 of Reach Annex XI, performing of a test is scientifically unjustified. Reach guidance document R7b states that a log Pow should be used as a trigger value for assessing sediment toxicity. For the substance, a log Kow of 6.11 was calculated. However, the substance hydrolyses rapidly to either oligomeric or polymeric ureas. The ureas are insoluble in water and therefore not bioavailable.

For the risk characterisation of the sediment compartment, a PNEC sediment has been derived on the basis of the equilibrium partition theory from aquatic toxicity data. As the risk characterisation yields a PEC/PNEC ratio smaller than 1, a test towards sediment dwelling organisms is not necessary as the risk towards the sediment compartment is sufficiently described based on the already available data.

3.1.8. Predicted No Effect Concentration (PNEC)

3.1.8.1. PNEC water

	Value	Assessment factor	Remarks/Justification
PNEC aqua - freshwater (mg/L)	0.127	1000	Short-term toxicity results are available from three species representing three trophic levels (fish, daphnia and algae). An assessment factor of 1000 is applied using the lowest available effect concentration (EL50 mg/l: 127 mg/l) for daphnia.
PNEC aqua - marine water (mg/L)	0.0127	10000	For the marine compartment no tests are available. For PNEC derivation, short-term toxicity results from three species representing three trophic levels (fish, Daphnia and algae) for the freshwater compartment are taken into account. An assessment factor of 10000 is applied using the lowest available effect concentration, which was obtained for daphnia.
PNEC aqua - intermittent releases (mg/L)	1.27	100	Short-term toxicity results are available from three species representing three trophic levels (fish, daphnia and algae). The default assessment factor of 100 is applied using the lowest available effect concentration, which was obtained for daphnia.

3.1.8.2. PNEC sediment

	Value	Assessment factor	Remarks/Justification
PNEC sediment (mg/kg d.w.)	266700		<p>extrapolation method</p> <p>The PNEC sediment was derived on the basis of aquatic toxicity data applying the Equilibrium Partitioning Theory (EPT) as no data is available covering sediment organisms.</p> <p>To derive the PNEC_{sediment} on the basis of EPT, the Koc, the Henry's Law Constant as well as the PNEC_{aqua} are crucial. Following values have been used for the main component of HDI Trimer (Isocyanurat, n=3):</p> <p>Koc= $2.1 \cdot 10^{07}$ (calc. acc. to EPIWIN)</p> <p>HLC= $1.31 \cdot 10^{-12}$ Pa*m³/mole (calc. acc. to EPIWIN)</p> <p>PNEC_{aqua}= 0.127 mg/L</p> <p>Due to dissociating properties, the adsorption/desorption behaviour, expressed as Koc, is characterized by a range rather than a single value. Describing processes in the sediment, lower values are linked to a lower sorption potential, what in turn</p>

			<p>means higher concentrations in the pore water. As effects towards sediment organisms are assumed to be caused by the fraction dissolved in the pore water, lower Koc values are synonymous with a higher exposure of sediment organisms and were thus used to calculate the PNEC_{sediment}.</p> <p>The PNEC sediment concerning the wet weight is 57978 mg/kg Conversion factor for sediment concentrations (wwt to dwt): 4.6</p>
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3.2. Terrestrial compartment

3.2.1. Toxicity to soil macro-organisms

Data waiving

Information requirement: Toxicity to soil macro-organisms except arthropods

Reason: exposure considerations

Justification: According to column 2 of Reach Annex VII-X, these studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely. A test towards soil macroorganisms is not proposed by the registrant as the chemical safety assessment indicates the need to further investigate the effects on terrestrial organisms.

For the risk characterisation of the terrestrial compartment, a PNEC soil has been derived on the basis of the equilibrium partition theory from aquatic toxicity data. As the risk characterisation yields a PEC/PNEC ratio smaller than 1, a test towards soil macroorganisms is not necessary as the risk towards the terrestrial compartment is sufficiently described based on the already available data.

Information requirement: Toxicity to terrestrial arthropods

Reason: exposure considerations

Justification: According to section 3 of Reach Annex XI, these studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely. A test towards terrestrial arthropods is not proposed by the registrant as the chemical safety assessment indicates the need to further investigate the effects on terrestrial organisms.

For the risk characterisation of the terrestrial compartment, a PNEC soil has been derived on the basis of the equilibrium partition theory from aquatic toxicity data. As the risk characterisation yields a PEC/PNEC ratio smaller than 1, a test towards terrestrial arthropods is not necessary as the risk towards the terrestrial compartment is sufficiently described based on the already available data.

3.2.2. Toxicity to terrestrial plants

Data waiving

Reason: exposure considerations

Justification: According to section 3 of Reach Annex XI, these studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely. A test towards terrestrial plants is not proposed by the registrant as the chemical safety assessment indicates the need to further investigate the effects on terrestrial organisms.

For the risk characterisation of the terrestrial compartment, a PNEC soil has been derived on the basis of the equilibrium partition theory from aquatic toxicity data. As the risk characterisation yields a PEC/PNEC ratio smaller than 1, a test towards terrestrial plants is not necessary as the risk towards the terrestrial compartment is sufficiently described based on the already available data.

3.2.3. Toxicity to soil micro-organisms

Data waiving

Reason: exposure considerations

Justification: According to section 3 of Reach Annex XI, these studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely. A test towards soil microorganisms is not proposed by the registrant as the chemical safety assessment indicates the need to further investigate the effects on terrestrial organisms.

For the risk characterisation of the terrestrial compartment, a PNEC soil has been derived on the basis of the equilibrium partition theory from aquatic toxicity data. As the risk characterisation yields a PEC/PNEC ratio smaller than 1, a test towards soil microorganisms is not necessary as the risk towards the terrestrial compartment is sufficiently described based on the already available data.

3.2.4. Toxicity to other terrestrial organisms

No data.

3.2.5. Predicted No Effect Concentration (PNEC soil)

	Value	Assessment factor	Remarks/Justification
PNEC soil (mg/kg.d.w.)	53182		<p>The PNEC sediment was derived on the basis of aquatic toxicity data applying the Equilibrium Partitioning Theory (EPT) as no data is available covering soil organisms.</p> <p>To derive the PNECsoil on the basis of EPT, the Koc, the Henry's Law Constant as well as the PNECaqua are crucial. Following values have been used for the main component of HDI Trimer (Isocyanurat, n=3):</p> <p>Koc= $2.1 \cdot 10^{07}$ (calc. acc. to EPIWIN)</p> <p>HLC= $1.31 \cdot 10^{-12}$ Pa*m³/mole (calc. acc. to EPIWIN)</p> <p>PNECaqua= 0.127 mg/L</p> <p>Due to dissociating properties, the adsorption/desorption behaviour, expressed as Koc, is characterized by a range rather than a single value. Describing processes in the soil, lower values are linked to a lower sorption potential, what in turn means higher concentrations in the pore water. As effects towards sediment organisms are assumed to be caused by the fraction dissolved in the pore water, lower Koc values are synonymous with a higher exposure of sediment organisms and were thus used to calculate the PNECsoil.</p> <p>The PNEC soil concerning the wet weight is 47064 mg/kg Conversion factor for soil concentrations (wwt to dwt): 1.13</p>

3.3. Atmospheric compartment

Direct data on biotic and abiotic effects of 6PPD in the atmospheric compartment are not available. On one hand, it is nearly impossible to obtain reliable data for risk assessment on the biotic effects of chemical substance in air, due to lack of well developed methods. On the other hand, no indications suggest that 6PPD causes abiotic hazard in air compartment.

3.4. Microbiological activity in sewage treatment systems

3.4.1. Toxicity to aquatic micro-organisms

Discussion

The following information is taken into account for effects on aquatic micro-organisms for the derivation of PNEC:

For HDI Trimer a test with activated sludge with a duration time of 3 hours was performed using a method comparable to OECD 209. A 3h-EC50 value of 3828 mg/ was obtained (Bayer 1989).

3.4.2. PNEC for sewage treatment plant

	Value	Assessment factor	Remarks/Justification
PNEC STP (mg/L)	38.28	100	There is only one reliable toxicity test result to microorganisms available. In a respiration inhibition test conducted with activated sludge a 3 h-EC50 of 3828 mg/l obtained. This result is used for PNEC STP derivation. An assessment factor of 100 applied.

3.5. Non compartment specific effects relevant for the food chain (secondary poisoning)

3.5.1. Toxicity to birds

Data waiving

Information requirement: Toxicity to birds

Reason: study scientifically unjustified

Justification: According to section 1 of Reach Annex XI, there is no need for testing taking into account the mammalian dataset that is available for the substance.

3.5.2. PNECoral (secondary poisoning)

	Value	Assessment factor	Remarks/Justification
PNEC oral (mg/kg food)			As the main component of HDI Trimer (Isocyanurat, n=3) has only a moderate bioaccumulation potential, no risk characterisation for secondary poisoning is carried out.

3.6. Conclusion on the environmental classification and labelling

Classification and labelling according to aquatic toxicity data

Justification for classification or non classification

Three acute tests have been performed with fish, daphnia and algae. No effects have been observed up to the concentrations of 100 mg/l. Therefore, a classification related to risk phrases R50, 51, 52 can be ruled out.

Classification and labelling according to degradation and bioconcentration

Justification for classification or non classification

HDI Trimer is not readily biodegradable and has a logPow of 6.11 (calculated). However, the substance hydrolysis rapidly with a half life of 3-7.7 hours. The hydrolysis products are mainly insoluble oligomeric and

polymeric ureas. Theoretically the corresponding Triamine can be regarded which however is not formed in significant concentrations. The latter has a logPow of 5.5 (calculated). Therefore, a classification related to risk phrase R53 is not required.

4. HUMAN HEALTH HAZARD ASSESSMENT

4.1. Toxicokinetics (absorption, metabolism, distribution and elimination)

The following remarks on the toxicokinetics of HDI Trimer are based on physicochemical properties of the compound and on toxicological data. Experimental toxicokinetic studies were not performed.

HDI Trimer is a colourless, clear and viscous organic liquid (Currenta GmbH & Co. OHG, 2010; melting range: between -51.3 and 28.4°C, Laus GmbH, 2010) with a low vapour pressure ($2.46 \cdot 10^{-3}$ Pa at 20°C and $2.55 \cdot 10^{-3}$ Pa at 25°C, Laus GmbH, 2010) and a high viscosity (dynamic viscosity 3851.69 mPa*s, Laus GmbH, 2010).

In water the substance is hydrolytically unstable (half-life <12 hours, cf. chapter "Water solubility"). Therefore experimental data such as pH, pKa, log Pow can not be obtained for HDI Trimer.

Due to the low vapour pressure and the high viscosity inhalation exposure via vapour is not to be expected. Wherever aerosolization occurs exposure is possible. There are no indications of systemic toxicity and systemic availability after inhalative exposure of the aerosol (Pauluhn, 1984, 1985, 1987). No organ lesions other than at the respiratory tract could be found, and the clinical signs could all be related to respiratory distress and were seen as a consequence of the irritant properties of the substance (Pauluhn, 1984, 1985, 1987). These effects most probably are related to the chemical nature of the isocyanate-groups of HDI Trimer.

Limited human experience give some evidence of systemic availability after aerosol exposure to HDI Trimer. An 8 hour-exposure (no air concentration monitored) was correlated to the hexamethylene diamine (HDA) level in urine, determined after an acid hydrolyzation work-up of the urine (Yu et. al., 2005). HDA, the degradation product of HDI Trimer, has never been detected in blood, tissue, urine or faeces after HDI Trimer exposure without an acid hydrolysis procedure.

Dermal absorption of HDI Trimer is assumed to be very low, due to its physico-chemical properties (lack of water solubility/ reaction with water, reaction with nucleophiles e. g. OH, NH, SH-groups). Furthermore no signs of systemic toxicity were observed in an acute dermal toxicity study (Pooles, 2004). HDI Trimer has shown skin sensitizing properties (OECD TG 429: Pooles, 2004; OECD TG 406: Stropp, 1997), thus indicating that a dermal uptake, even though small, can occur.

An oral absorption could in spite of the physico-chemical properties, e. g. presumably labile in gastric acid, not be excluded at all. In fact, no systemic signs could be observed at all after oral exposure with 2000 mg/kg (Pooles, 2004).

The excretion of absorbed HDI Trimer or its degradation products should be at least partly via urine (Yu et. al., 2005).

HDI Trimer is a skin sensitizer (OECD TG 429: Pooles, 2004; OECD TG 406: Stropp, 1997). Deducing from that the substance has the property to react with nucleophilic groups of proteins or peptides and form hapten-protein complexes or conjugate-antigens.

Based on the results of several in vitro genotoxicity tests (OECD TG 471: Thompson, 2004; OECD TG 476: Schulz, Mellert, Landsiedel, 2006/2007; OECD TG 473: Schulz, Landsiedel, 2007; all performed with and without metabolic activation) it is concluded that DNA-reactive metabolites of HDI Trimer will not be generated in mammals in the course of hepatic biotransformation.

4.2. Acute toxicity

Acute toxicity: oral

An acute oral toxicity study (Acute Toxic Class Method; OECD TG 423) revealed no mortalities, no signs of systemic toxicity and no effects on body weight gain up to the limit dose of 2000 mg/kg bw. At necropsy no abnormalities were noted. The LD50 of the test material was estimated from the flow chart of the OECD TG

423, Annex 2d, to be > 2500 mg/kg bw.

Acute toxicity: dermal

An acute dermal toxicity study according to OECD TG 402 also revealed no mortalities, no signs of systemic toxicity and no effects on body weight gains up to the limit dose of 2000 mg/kg bw. No signs of dermal irritation were seen and no abnormalities were noted at necropsy. Another acute dermal toxicity study according to EPA Health Effects Test Guideline (40 CFR 798) on rabbits revealed also no mortality, but effects on body weight gain for one male and abnormalities at necropsy for one male (dark red lungs) and two females (one with light tan kidneys and one with pale tan lungs). Local skin reactions including scabs, desquamation and alopecia were reported, but could be attributed to the physico-chemical properties of the substance, which constitutes a clear, hard sample residue at the end of contact period, causing complete adherence of the gauze sheeting to the skin and preventing its easy removal. The resulting LD50 for both studies were > 2000 mg/kg bw.

Acute toxicity: inhalation

The acute aerosol inhalation toxicity study (OECD TG 403) for HDI Trimer revealed an LC50 (4h, head/nose only) of 390 mg/m³ (approximate value) for female rats and 543 mg/m³ for male rats, a second study with HDI Trimer containing 10% solvent has comparable LC50-values (OECD TG 403, LC50 (4h, head/nose only): female rats 472 mg/m³, male rats 573 mg/m³). Exposure to concentrations of 150 mg/m³ and higher were followed by concentration-dependent signs suggestive of irritation to the respiratory tract, e. g. dyspnoea, bloody snouts, and nonspecific signs, e. g. limp, ataxia. The mortality is regarded as a causal effect of the rapid developed lung edema. A pulmonary irritant potency study on female rats, which analyzed concentration- and time-dependent within bronchoalveolar lavage fluid (BALF) biomarkers indicative for injury of the bronchoalveolar region, following a 6-hours nose-only exposure, revealed a NO(A) EL of 3 mg/m³ air.

Justification for classification or non classification

Acute toxicity: oral and dermal

No classification required for acute oral and dermal toxicity according to Regulation (EC) No 1272/2008, Annex I.

Acute toxicity: inhalation

Despite the 4 hour LC50 of 390 mg/m³ (approximate value) for female rats and 543 mg/m³ for male rats the substance is not classified according to Regulation (EC) No 1272/2008, Annex I for acute inhalation toxicity Cat. 2 due to the following reasons:

The Guidance on the Application of Regulation (EC) No 1272/2008 acknowledges (e.g. chapter 3.1.2.3.2) that special consideration is required if a substance is tested in a form (i.e. specific particle size distribution) that is different from the forms in which the substance is placed on the market and in which it can reasonably be expected to be used. According to Pauluhn (Experimental and Toxicologic Pathology 60, 2008, 111-124) there is an option for a modified Classification and Labelling (C&L), called "split-entry concept". While the current test principles for acute inhalation uses a predetermined particle size in the breathing zone of exposed animals in order to allow a robust relative ranking of the acute lethal toxic potency of different substances, split entry takes into account for an assessment of potential human hazards the actual percentage of the critical percentage of particles present in the product as commercialized and used (→ thoracic fraction). For HDI Trimer the prerequisites for employing split-entry are given, e.g. the substance is a liquid with a very low volatility causing local toxicity (irritation) in the lower respiratory tract, but no systemic toxicity after acute inhalation exposure to rats (Pauluhn, 2001 and 1984). The irritating potential of the substance on the portal-of-entry is confirmed by other acute and repeated studies on animals, where only minor indications for systemic toxicity could be observed at all (e.g. positive skin sensitisation potential) that are not regarded to be of relevance for the assessment of acute toxicity. Currently available data on particle size during worst-case end-use of HDI Trimer indicate a thoracic percentage below the requested threshold justifying a modified C&L for acute inhalation toxicity for the substance. On this basis the classification for the substance is for acute inhalation toxicity Cat. 4, H332: Harmful if inhaled. Further studies regarding the particle size distribution are presently ongoing.

4.3. Irritation

HDI Trimer was slightly irritating to the skin of rabbits (OECD TG 404) and very slightly irritating to the eye of rabbits (OECD TG 405).

HDI Trimer was proven to be respiratory irritating. In a pulmonary irritant potency study with nose only-aerosolized HDI Trimer, rats showed signs suggestive of respiratory tract irritation at concentrations of 60 mg/m³ and above (see chapter "Acute toxicity: inhalation", Pauluhn 2000/2001/2007). The NO(A) EL in this study, was determined to be 3 mg/m³, relating to biomarkers in bronchoalveolar lavage of rats (e. g. total protein), indicative for an injury of the bronchoalveolar region. Furthermore, respirable aerosolized HDI Trimer induced a slightly increased breathing rate and a slightly reduced tidal volume in mice (see chapter "Acute toxicity: inhalation", Pauluhn 1990), which is typical for lower respiratory tract irritants. The concentration inducing a 50% decrease in respiratory rate (RD50), could not be delineated from this specified sensory irritation study (according to ASTM E981-84) of the aerosolized test item, cause the changes in respiratory rate induced by pulmonary irritation interfere with that of sensory irritation, and therefore no reliable RD50-value could be obtained. The previously conducted sensory irritation studies of HDI Trimer are consequently of limited value for assessment purposes.

Justification for classification or non classification

No classification required for skin and eye irritation/corrosion according to Regulation (EC) No 1272/2008, Annex I.

For respiratory irritation a classification is required according to Regulation (EC) No 1272/2008, Annex I, as STOT SE 3 "May cause respiratory irritation" (H335).

4.4. Sensitisation

Skin sensitisation

HDI Trimer showed skin sensitisation potential in a Local Lymph Node Assay (OECD TG 429) performed on three groups, each of 4 animals, treated with the 10%, 20% and 50% test substance formulation. The determined stimulation indices were 22.16 (10%), 21.94 (25%) and 29.62 (50%). In a Guinea Pig Maximization Test (OECD TG 406, intradermal concentration during induction phase 5%) also a clear sensitization potential was observed with 19/20 animals showing skin reactions.

Respiratory sensitisation

HDI Trimer (residual content of monomeric HDI < 0.2%) revealed no respiratory sensitizing potential in two studies with guinea pigs. No specific immediate or delayed effects were observed in a study with respirable aerosolized HDI Trimer for induction (5 x 3 hours) and first challenge (both head/nose only exposure), as well as for second challenge with respirable aerosolized HDI Trimer-guinea pig-albumin-conjugate. Also no specific immediate or delayed effects were observed in a second study with respirable HDI Trimer aerosol-challenge (head/nose only exposure), following an induction with 3 consecutive intradermal injections. Diisocyanates in general are known respiratory sensitizers in humans. For HDI Trimer in particular no respective data are available in humans.

Justification for classification or non classification

Skin sensitisation

According to Regulation (EC) No 1272/2008, Annex I, classification is required as skin sensitising Cat.1; H317: May cause an allergic skin reaction.

Respiratory sensitisation

No classification is required for respiratory sensitisation according to Regulation (EC) No 1272/2008, Annex I. Reason: Animal data indicate no sensitisation potential and no respective data are available for humans.

4.5. Repeated dose toxicity

The repeated dose toxicity of HDI Trimer was investigated in a subchronic aerosol inhalation toxicity study according to OECD TG 413 (head/nose only). Repeated inhalation of respirable HDI Trimer in concentrations of 0.5, 3.3 and 26.4 mg/m³ was tolerated without mortality and virtually without symptoms. Specified examinations revealed a slightly reduced body weight gain (only observed for male rats), slight impairment of lung function parameter, significantly increased relative and absolute lung weights and, according to histology, inflammatory changes in the respiratory tract, all observed in the 26.4 mg/m³ group. Therefore the NO(A) EL, regarding to all of the named effects, was determined to be 3.3 mg/m³. The location of the damage was essentially limited to the lung periphery. All changes were nonspecific and are thus attributed to the primary irritant potential of HDI Trimer. There was no evidence of damage to any other organs except for the respiratory tract. This was confirmed in a 3 weeks aerosol inhalation study (OECD TG 412).

Justification for classification or non classification

No classification required according to Regulation (EC) No 1272/2008, Annex I. Reason: Classification as STOT repeated exposure is not justified, due to lack of cumulative toxicity.

4.6. Mutagenicity

HDI Trimer showed no mutagenic properties in two bacterial reverse mutation assays (OECD TG 471), in a mammalian cell gene mutation assay using chinese hamster ovary cells and mouse lymphoma cells (OECD TG 476), respectively, and in an in vitro chromosome aberration assay in V79 cells (OECD TG 473).

Justification for classification or non classification

No classification required according to Regulation (EC) No 1272/2008, Annex I.

4.7. Toxicity for reproduction

Effects on fertility

The toxicological database for inhaled HDI Trimer demonstrates consistently that toxicity is associated only with the portal of entry (respiratory tract), any other manifestations of toxicity are secondary to this. While no fertility studies are available for HDI Trimer, subchronic and subacute studies all show toxicity confined to the respiratory tract. Fertility studies with other aliphatic diisocyanates (H12MDI and HDI) show no effects on reproductive parameters, all effects are confined to the respiratory tract. Hence the databases for other aliphatic diisocyanates (IPDI, H12MDI and HDI) all show that primary toxicity for diisocyanates is to the respiratory tract, other effects, such as fetotoxicity in developmental studies, are secondary to this. This relationship applies to H12MDI and HDI when tested in fertility studies in the rat and is considered to apply equally to HDI Trimer, i. e., if any effects were to be seen in a fertility study, these would occur only as a secondary effect of the toxicity to the respiratory system of the exposed rats. Protection against respiratory tract toxicity will protect against any secondary effects.

Using the weight of evidence, it is concluded that reproductive toxicity is not an endpoint of concern for HDI Trimer and additional toxicity testing is not necessary.

Developmental toxicity

The toxicological database for inhaled HDI Trimer demonstrates consistently that toxicity is associated only with the portal of entry (respiratory tract), any other manifestations of toxicity are secondary to this. While no developmental study is available for HDI Trimer, subchronic and subacute (and acute) studies all show toxicity confined to the respiratory tract. Hence the databases for other aliphatic diisocyanates (IPDI, H12MDI, HDI) all show that primary toxicity for diisocyanates is to the respiratory tract, other effects, such as fetotoxicity in developmental studies, are secondary to this. This relationship applies to IPDI, H12MDI and HDI when tested in developmental toxicity studies in the rat and is considered to apply equally to HDI Trimer, i. e., if any effects were to be seen in a developmental study, these would occur only as a secondary effect of the toxicity to the respiratory system of the exposed rats. Protection against respiratory tract toxicity will protect against any secondary effects.

Using the weight of evidence, it is concluded that developmental toxicity is not an endpoint of concern for HDI Trimer and additional toxicity testing is not necessary.

Justification for classification or non classification

No classification required for toxicity to reproduction according to Regulation (EC) No 1272/2008, Annex I.

4.8. DNEL(s) / DMEL(s)

DN(M)ELs for workers

Exposure pattern	Route	Descriptor	DNEL / DMEL *)	Most sensitive endpoint
Acute - systemic effects	Dermal (mg/kg bw /day)			
Acute - systemic effects	Inhalation (mg/m ³)			
Acute - local effects	Dermal (mg/kg bw /day)	not quantifiable		sensitisation (skin)
Acute - local effects	Inhalation (mg/m ³)	DNEL	1	irritation (respiratory tract)
Long-term - systemic effects	Dermal (mg/kg bw /day)			
Long-term - systemic effects	Inhalation (mg/m ³)			
Long-term - local effects	Dermal (mg/kg bw /day)	not quantifiable		sensitisation (skin)
Long-term - local effects	Inhalation (mg/m ³)	DNEL	0.5	irritation (respiratory tract)

*) Unit as specified in column "Route"

Discussion

The most relevant route for assessing risk for HDI Trimer in humans is via inhalation. In rats effects from repeated aerosol exposure are limited to the respiratory tract caused by local irritation (Pauluhn, 1985 (OECD TG 412) and 1987 (OECD TG 413)). No indications of systemic toxicity were found in the named subacute and subchronic inhalation studies, respectively. It was shown, that if a non irritant threshold concentration is not exceeded, neither functional nor morphological indications of damage to the respiratory tract are observed.

For workers in industrial settings, which are exposed via inhalation, DNELs for local effects for acute and long-term inhalation exposure of HDI Trimer have to be derived. In addition, sensitisation after skin contact with HDI Trimer has to be assessed.

According to REACH (ECHA Guidance, chapter R.8-13) a national occupational exposure limit (OEL) could be used as a surrogate for a DNEL. The German Federal Ministry of Labour and Social Affairs (Bundesministerium für Arbeit und Soziales, BMAS) published the Technical Rule for Hazardous Substances (Technische Regel für Gefahrstoffe, TRGS) for regulating the workplace exposure of isocyanates (TRGS 430, BMAS, 2009). "This technical rule describes procedures for the assessment and surveillance of workplaces involved in the handling and use of polyurethanes and requires the assessment of isocyanates present either in the form of vapour, aerosol or both" (Pauluhn, J. Appl. Toxicol. 24, 2004, 231-247). In contrast to commonly employed workplace standards that focus solely on monomeric (di) isocyanates, the common unifying concept of TRGS 430 is to consider separate hazard assessment for monomeric and polymeric isocyanates, present as vapour and/or aerosol. The surrogate now used as DNEL for HDI Trimer is the exposure assessment value (Expositionsbeurteilungswert, EBW). The EBW is either derived from the acute pulmonary irritant threshold concentration using a benchmark extrapolation of the concentration dependence of protein in bronchoalveolar lavage fluid (BALF) of an 1 x 6 h inhalation study (TRGS 430 study) or, alternatively, if available, from the NOAEC (no observed adverse effect concentration) of a subchronic (13-week) inhalation study according to

OECD 413 (OECD, 1981) or OPPTS 870.3465 (1998). The approach suggested by TRGS 430 is inherently conservative, as a comparison of the irritant threshold concentration to the NOAEC from repeated inhalation studies show (Pauluhn, J. Appl. Toxicol. 24, 2004, 231-247).

If the irritant threshold concentration/NOAEC of the polymeric diisocyanate from either of the two studies is $\leq 10 * AGW$ (Arbeitsplatzgrenzwert, German national OEL) of the monomeric diisocyanate then $EBW = AGW$, if the threshold concentration is $> 10 * AGW$ then $EBW = 10 * AGW$, respectively.

This means: For the monomeric hexamethylen-1,6-diisocyanate (HDI) the AGW is 0.035 mg/m^3 . Since for HDI Trimer both the pulmonary irritant threshold concentration (3 mg/m^3 ; Pauluhn, Bayer AG, 2001) and the derived no observed adverse effect concentration of the subchronic study (3.3 mg/m^3 ; Pauluhn, Bayer AG, 1987) are $> 10 * AGW$ the $EBW = 10 * AGW$. According to TRGS 430 there is even an option to set the $EBW > 10 * AGW$. This was done for HDI Trimer due to the reason, that for HDI Trimer data for pulmonary irritation as well as data from a subchronic inhalation study are available and the data clearly show that the respiratory damage is linked to the inhaled irritating concentration, and does not exacerbate during repeated exposure (Pauluhn, Inhal. Toxicol., 13, 2001, 513-532 and 14, 2002, 287-301). Therefore the $EBW = DNEL_{\text{long-term}}$ local effects for inhalation is set to 0.5 mg/m^3 . This is in line with a published proposed TLV-TWA of 0.5 mg/m^3 (Pauluhn and Mohr, Inhal. Toxicol., 13, 2001, 513-532). The value is further in the same order of magnitude compared to a DNEL delineated according to ECHA guidance, chapter R.8.4.

AGWs are based on 8-hour time weighted average exposure. According to the German rule for OELs (TRGS 900, BMAS, 2006/2009) for short-term ceiling concentrations an exposure limit could be established by multiplication to an exceeding factor (Überschreitungsfaktor), which is set per default 1 (could be adjusted to max. 8). Pauluhn and Mohr proposed a maximum concentration limit of 1.0 mg/m^3 (exceeding factor 2) for HDI-derived polyisocyanates. This value could be used as surrogate DNEL acute local effects for inhalation for HDI Trimer.

This procedure is in accordance to ECHA Guidance, Chapter R.8., Appendix R. 8-8, Box 6.

According to the potency categorization approach HDI Trimer is classified as a moderate skin sensitizer, based on a guinea pig maximization test (5% intradermal concentration during induction; 95% incidence of sensitization).

The DNEL acute/long-term for inhalation for workers covers also reproductive toxicity, as the local effects at the respiratory tract are the most sensitive effects.

DN(M)ELs for the general population

Exposure pattern	Route	Descriptor	DNEL / DMEL *)	Most sensitive endpoint
Acute - systemic effects	Dermal (mg/kg bw /day)			
Acute - systemic effects	Inhalation (mg/m ³)			
Acute - systemic effects	Oral (mg/kg bw /day)			
Acute - local effects	Dermal (mg/kg bw /day)			
Acute - local effects	Inhalation (mg/m ³)			
Long-term - systemic effects	Dermal (mg/kg bw /day)			
Long-term - systemic effects	Inhalation (mg/m ³)			
Long-term - systemic effects	Oral (mg/kg bw /day)			
Long-term - local effects	Dermal (mg/kg bw /day)			

Long-term - local effects	Inhalation (mg/m ³)			
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*) Unit as specified in column "Route"

Discussion

The substance is not used in the public domain and exposure of consumers is thus not to be expected.

5. HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICO-CHEMICAL PROPERTIES

5.1. Explosivity

The following information is taken into account for any hazard / risk assessment:

Performing of a test is scientifically not necessary. According to United Nations (2003) (Annex 6, Table 6.1), the substance does not contain a chemical moiety suggesting a potential for explosivity.

5.2. Flammability

The following information is taken into account for any hazard / risk assessment:

- (a) No flammability in contact with water: The substance contains no metals or metalloids and therefore will not release flammable gases in contact with water.
- (b) Experience in production or handling; substance is known to be stable at room temperature.
- (c) Performing of a study according to EG A10 is technically not feasible, as the substance is a liquid.

Flash point

Reference:

Currenta, 2008

Guideline:

DIN EN 22719

The following information is taken into account for any hazard / risk assessment:

228 °C

Classification status: 67/548/EEC self classification (oligomerization product (isocyanurate type) of hexamethylene diisocyanate)

Reason for no classification: conclusive but not sufficient for classification

5.3. Oxidising potential

Data waiving: see CSR section 1.3 Physico-chemical properties.

The following information is taken into account for any hazard / risk assessment:

Performing of a test is scientifically not necessary. According to United Nations (2003) (Annex 6, Table 6.1), the substance does not contain a chemical moiety suggesting an oxidising potential.

Classification status: 67/548/EEC self classification (oligomerization product (isocyanurate type) of hexamethylene diisocyanate)

Reason for no classification: conclusive but not sufficient for classification

6. PBT AND vPvB ASSESSMENT

6.1. Assessment of PBT/vPvB Properties - Comparison with the Criteria of Annex XIII

The relevant PBT (persistent, bioaccumulative, toxic) criteria according to the REACH regulation and the corresponding properties of HDI Trimer (CAS No: 28182-81-2) are compiled in the following Table:

Criterion	PBT criteria	vPvB criteria	property	Criterion fulfilled?
P	Half-life in marine water > 60 d, or half-life in fresh- or estuarine water > 40 d, or half-life in marine sediment > 180 d, or half-life in fresh- or estuarine water sediment > 120 d, or half-life in soil > 120 d	Half-life in marine, fresh or estuarine water > 60 d, or Half-life in marine, fresh or estuarine sediment > 180 d, or half-life in soil > 180 d	Not readily biodegradable (Bayer 2001))	Preliminary yes
B	BCF > 2000	BCF > 5000	Not B not vB	no
T	Long-term NOEC for marine or freshwater organisms < 0.01 mg/l	Not applicable.	72h-EC ₁₀ = 110 mg/l for algae (Bayer 1989)	no
T	CMR	Not applicable.	Not classified as CMR	no
T	Other evidence of chronic toxicity, as identified by the classifications: T, R48, or Xn, R48 according to Directive 67/548/EEC	Not applicable	Not classified as T, R48, or Xn, R48 according to Directive 67/548/EEC	no

6.1.1. Persistence Assessment

HDI Trimer is not readily biodegradable with 1 % biodegradation in 28 days (Bayer AG, 2001), and hence it is classified as *preliminary* persistent according to screening criteria.

6.1.2. Bioaccumulation Assessment

Measured bioconcentration factors (BCF) for HDI Trimer are not available. HDI Trimer hydrolyses rapidly in the presence of water with a half life of 3-7.7 hours. Therefore a risk estimation regarding the bioaccumulation potential of HDI Trimer on the basis of a log Kow, determined by QSAR, is misleading. A calculated theoretical log Kow value of 9.81 reflects the unreacted molecule (n=3, generated from 3 molecules of HDI) without influence of water.

The substance is not persistent in water due to the rapid hydrolysis. Therefore it is not bio-available. Possible hydrolysis products are less lipophilic. For a theoretically possible model substance with the 3 free Isocyanate groups converted by hydrolysis to the corresponding triamine, a BCF of 368 was calculated based on the log Kow of 5.5. A calculated value should only be used for assessment in the absence of experimental data as a rough estimation. However, in this case the calculated BCF of 368 is far away from the criterion of BCF>2000 indicating that hydrolysis products of HDI Trimer have no significant bioaccumulation potential. Therefore the B and vB criterion is not fulfilled

6.1.3. Toxicity Assessment

There is one aquatic toxicity test for algae available which counts as a chronic test. A 72 h-EC₁₀ value of 110 mg/l is given for algae (Bayer AG, 1989). In the absence of a calculated NOEC the EC₁₀ value is considered as a NOEC, which is higher than 0.01 mg/l and hence support the conclusion that HDI Trimer is not toxic. Furthermore, the substance is not classified as carcinogenic, mutagenic or toxic for reproduction or R48. For these reasons, the substance does not meet the T-criterion.

6.1.4. Summary and overall Conclusions on PBT or vPvB Properties

A substance only is identified as a PBT substance if it fulfils all criteria described above. According to information summarized above, only the P criteria was preliminarily fulfilled and hence HDI Trimer is not a PBT substance.

A substance only is identified as a vPvB substance if it fulfils both vPvB criteria described above. The P criterion is preliminarily fulfilled, the B criterion is not fulfilled. Therefore, HDI Trimer is not a vPvB substance.

6.2. Emission Characterisation

It is concluded that HDI Trimer does not fulfil the PBT/vPvB criteria. An emission characterisation is therefore not required.

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