Annex XV report

PROPOSAL FOR IDENTIFICATION OF SUBSTANCES OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance Names: Bumetrizole (UV-326)
2-(2*H*-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol (UV-329)

EC Numbers: 223-445-4 (UV-326); 221-573-5 (UV-329)

CAS Numbers: 3896-11-5 (UV-326); 3147-75-9 (UV-329)

Submitted by: Germany

Date: August 2023

This document has been prepared according to template: TEM-0049.04

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ABBREVIATIONS

AR:	applied radioactivity
B:	bioaccumulative (pertaining to REACH Annex XIII)
BAF:	bioaccumulation factor
BCF:	bioconcentration factor
BCF_K:	kinetic bioconcentration factor
BCF_{KL}:	lipid-normalised kinetic bioconcentration factor
BCF_{KgL}:	lipid-normalised growth corrected kinetic bioconcentration factor
BCF_{ss}:	steady-state bioconcentration factor
BCF_{ssL}:	lipid-normalised steady-state bioconcentration factor
BMF:	biomagnification factor
BMF_{Kg}:	growth-corrected kinetic biomagnification factor
BOD:	biochemical oxygen demand
bw:	body weight
CAS RN:	CAS registry number
C_f:	test substance concentration in fish
C_w:	test substance concentration in water
CLH:	Harmonised classification and labelling
CLP:	Classification, labelling, and packaging of substances
DF:	detection frequency
DMEL:	Derived minimum effect level
DNEL:	Derived no-effect level
DT50:	half-life
DegT50	degradation half-life
dw:	dry weight
EC:	effect concentration
es-BANK:	Environmental Specimen Bank of Ehime University
GC-HRMS:	gas chromatography/ high resolution mass spectrometry
GC/MS:	gas chromatography/ mass spectrometry
GC-MS/MS:	gas chromatography tandem mass spectrometry
GLP:	good laboratory practice
H. Azteca:	*Hyalella Azteca*
HPLC:	high performance liquid chromatography
HYBIT:	*Hyalella Azteca* Bioconcentration Test
IB:	Iles des Boucherville

IUCN: International Union for Conservation of Nature
IV: Iles Vert
k_1: uptake rate constant
k_2: depuration rate constant
k_{2g}: growthcorrected depuration rate constant
K: Kaveri River, India
K_{OA}: octanol-air partition coefficient
K_{OW}: octanol-water partition coefficient
LSL: Lake St. Louis, Montreal
LC50: Lethal concentration to 50% of test animals
LC-HRMS: liquid chromatography/ high resolution mass spectrometry
LC-MS/MS: liquid chromatography tandem mass spectrometry
LOD: limit of detection
LOEC: lowest observed effect concentration
LOQ: limit of quantification
lw: lipid weight
M1: 3-[3-(2*H*-1,2,3-benzotriazol-2-yl)-5-*tert*-butyl-4-hydroxyphenyl]propanoic acid (EC 630-348-4)
MDL: method detection limit
MSC: Member State Committee
MQL: method quantification limit
NA: not analysed
ND: not detected
NER: non-extractable residues
NOAEC: No observed adverse effect concentration
NO(A)EL: no observed (adverse) effect level
NOEC: no observed effect concentration
OEL: occupational exposure limit
P: Persistence (pertaining to REACH Annex XIII) or persistent
PBT: persistent, bioaccumulative, and toxic
PLE: pressurised liquid extraction
(Q)SAR: (quantitative) structure-activity relationship
R2: coefficient of determination
RAC: Committee for Risk Assessment
RMSE: Root Mean Square Error
SAR: structure-activity relationship
SEV: Substance Evaluation
SFO: Single First Order
SVHC: Substance of very high concern
STOT RE: Specific Target Organ Toxicity – Repeated exposure
T: Toxic (pertaining to REACH Annex XIII)
TG: Test guideline
TGR: Transgenic rodent
TMF: Trophic magnification factor
TOC: total organic carbon
TWA: time weighted average
UPLC-MS/MS: ultra-high performance liquid chromatography tandem mass spectrometry
UM-PPS: University of Minnesota Biocatalysis/Biodegradation Prediction System
UV-320: 2-benzotriazol-2-yl-4,6-di-*tert*-butylphenol (EC 223-346-6)
UV-326: Bumetrizole, 2-*tert*-butyl-6-(5-chloro-2*H*-benzotriazol-2-yl)-4-methylphenol (EC 223-445-4)
UV-327: 2,4-di-*tert*-butyl-6-(5-chlorobenzotriazol-2-yl)phenol (EC 223-383-8)
UV-328: 2-(2*H*-benzotriazol-2-yl)-4,6-ditertpentylphenol (EC 247-384-8)
UV-329: 2-(2*H*-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol (EC 221-573-5)
UV-350: 2-(2*H*-benzotriazol-2-yl)-4-(*tert*-butyl)-6-(sec-butyl)phenol (EC 253-037-1)
UV-384: A mixture of branched and linear C7-C9 alkyl 3-[3-(2*H*-benzotriazol-2-yl)-5-(1,1-dimethylethyl)-4-hydroxyphenyl]propionates (EC 407-000-3)

UV-P:	2-(2*H*-benzotriazol-2-yl)-p-cresol (EC 219-470-5)
V:	Vellar River, India
vB:	very bioaccumulative (pertaining to REACH Annex XIII)
vP:	very persistent (pertaining to REACH Annex XIII)
vPvB:	very persistent and very bioaccumulative (pertaining to Annex XIII REACH)
WoE:	weight-of-evidence
ww	wet weight

PROPOSAL FOR IDENTIFICATION OF SUBSTANCES OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance names:

Bumetrizole (UV-326) and

2-(2*H*-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol (UV-329)

EC numbers: 223-445-4 (UV-326); 221-573-5 (UV-329)

CAS numbers: 3896-11-5 (UV-326); 3147-75-9 (UV-329)

- It is proposed to identify the substances as very persistent and very bioaccumulative (vPvB) according to Article 57 (e) of Regulation (EC) No 1907/2006 (REACH).

Summary of how the substances meet the criteria set out in Article 57 of the REACH Regulation

A weight of evidence determination according to the provisions of Annex XIII of REACH has been used to identify UV-326 and UV-329 as vPvB substances. All available relevant information (such as the results of standard tests, monitoring and modelling, information from the application of the read-across and (Q)SAR results) was considered together in a weight-of-evidence approach.

Persistence

The screening criterion for persistence (P) is fulfilled for both UV-326 and UV-329. The results from the available screening studies (reliable with or without restrictions) showed that these substances are not readily biodegradable. This is confirmed by the available (Q)SAR results with BIOWIN and CATALOGIC which indicate that UV-326 and UV-329 screen as potentially P or vP. The outcomes of the screening tests and the (Q)SARs predictions have been assigned a low weight in the weight-of-evidence approach (WoE) for the P assessment.

Hydrolysis of UV-326 and UV-329 is not expected due to the absence of functional groups susceptible to hydrolysis. As a conclusion, abiotic degradation of UV-326 and UV-329 is not considered to be a significant degradation pathway in the environment.

In a water-sediment simulation study for UV-326 and UV-329 at 20 °C (reliable with restrictions), no degradation was observed after 100 days. At an environmentally relevant temperature of 12 °C this corresponded to a half-life significantly larger than 212 days for UV-326 and UV-329 thus indicating their very persistent properties in sediment (DegT50>180 days). The outcome of this higher tier study is given a high weight in the WoE approach as it provides information directly comparable with the P and vP criteria set out in Annex XIII, points 1.1.1 (d) and 1.2.1 (b) of the REACH Regulation.

Faster dissipation of UV-326 and UV-329 in an aquifer test (reliable with restrictions) may be related to the different sediment type tested. This study has been assigned a low weight in the WoE approach considering its deviating test conditions and the difficulty to derive an appropriate DT50. Simulation test results (reliable with restrictions) for a structurally related substance 3-[3-(2*H*-benzotriazol-2-yl)-5-*tert*-butyl-4-hydroxyphenyl]propionicacid (M1) *H*-support both very high persistence in sediment (DegT50 in sediment >180 days) for UV-326 and the impact of

different sediment types on dissipation. This study on a structurally related substance is assigned a medium weight in the WoE approach.

UV-P (a structurally related substance to UV-329), UV-326 and further phenolic benzotriazoles have been detected in sediment cores that date back years and even decades (starting from the 1960s), both in samples downstream from a former point source and in samples from urban estuaries. This information provides indirect evidence that UV-326 and potentially UV-329 (as a structurally related substance to UV-P) can persist in sediments for several decades. Monitoring data in sediment cores are used as supporting information in the WoE approach for UV-326 and UV-329. They are in line with the outcome of the water-sediment simulation study, the screening studies and the QSAR predictions as they point towards the persistence of UV-326 and potentially UV-329 (based on results of the structural analogue UV-P) in sediments.

UV-326 and UV-329 are persistent (and potentially very persistent) in two soil dissipation studies (reliable with restrictions) (at least DegT50>120 days).

As an overall conclusion, based on the above information used in a weight-of-evidence-approach, it is concluded that UV-326 and UV-329 meet the 'persistence' criterion (P) and the 'very persistent' criterion (vP) in accordance with Annex XIII, points 1.1.1 and 1.2.1, of the REACH Regulation on the basis of their persistent and very persistent (P/vP) properties in sediment (DegT50 > 180 days). Furthermore, UV-326 and UV-329 meet the 'persistence' criterion (P) and potentially the 'very persistent' criterion (vP) in accordance with Annex XIII, points 1.1.1 and 1.2.1, of the REACH Regulation on the basis of their persistent and potentially their very persistent (P/vP) properties in soil (at least DegT50 > 120 days).

Bioaccumulation

Both UV-326 and UV-329 screen as potentially B/vB due to the available log K_{ow} values above the screening trigger value of 4.5.

An OECD TG 305 study (aqueous exposure; reliable with restrictions) with rainbow trout (*Oncorhynchus mykiss*) performed on UV-326 indicates a high bioaccumulation potential with a lipid-normalised growth corrected kinetic bioconcentration factor (BCF_{kgL}) value in the range of 7093—14225 L/kg (whole fish BCF back calculated from edible and non-edible portions and based on total radioactive residues of the test substance). This study is given a high weight and its results are used to conclude that UV-326 has B/vB properties (BCF>5000 L/kg) in accordance with REACH Annex XIII. Monitoring data tend to confirm this prediction as UV-326 has been found in human breast milk and in biota including in top predators such as the polar bears which are listed as vulnerable to extinction, according to the International Union for Conservation of Nature (IUCN) Red List. Based on the weight of evidence of the data available, it is concluded that UV-326 meets the 'bioaccumulation' criterion (B) and the 'very bioaccumulative' criterion (vB) in accordance with Annex XIII, points 1.1.2 and 1.2.2, of the REACH Regulation.

The conclusion for UV-329 is based on a weight-of-evidence assessment using different pieces of information. The outcome of the *Hyalella azteca* bioconcentration test (HYBIT; reliable with restrictions) for UV-329 is given a high weight in the WoE approach with 3 %-lipid-normalised steady-state bioconcentration factor (BCF_{ssL}) and 3%-lipid-normalised kinetic bioconcentration factor (BCF_{kL}) values in the range of 11063—11876 L/Kg. This study provides information directly comparable with the B (BCF>2000) and vB criteria (BCF>5000) set out in Annex XIII. Re-calculated fish BCF_{kgL} >2000 and >5000 derived from an OECD TG 305 study (aqueous exposure; reliable with restrictions) with rainbow trout (*Oncorhynchus mykiss*) are all supporting the vB conclusion for UV-329. Monitoring data tend to confirm this prediction as UV-329 has been found in human breast milk and in biota including in top predators such as the polar bears which are listed as vulnerable to extinction, according to the IUCN Red List. Based on the weight of evidence of the data available, it is concluded that UV-329 meets the 'bioaccumulation' criterion (B) and the 'very bioaccumulative' criterion (vB) in accordance with Annex XIII, points 1.1.2 and 1.2.2, of the REACH Regulation.

Conclusion

In conclusion, UV-326 and UV-329 are proposed to be identified as vPvB substances according to Art. 57(e) of REACH by comparing all relevant and available information listed in Annex XIII of REACH with the criteria set out in the same Annex, in a weight-of-evidence determination.

Registration dossiers submitted for the substances: Yes

PART I

Justification

1 Identity of the substances and physical and chemical properties

1.1 Name and other identifiers of the substances

Table 1: Substance identity for UV-326

(Bumetrizole)

EC number:	223-445-4
EC name:	Bumetrizole
CAS number (in the EC inventory):	3896-11-5
CAS number:	3896-11-5
IUPAC name:	2-tert-butyl-6-(5-chloro-2H-benzotriazol-2-yl)-4-methylphenol
Index number in Annex VI of the CLP Regulation	-
Molecular formula:	$C_{17}H_{18}ClN_3O$
Molecular weight:	315.8 g/mol
Synonyms:	2-(2'-Hydroxy-3'-t-butyl-5'-methylphenyl)-5-chlorobenzotriazole 2-(2-Hydroxy-3-*tert*-butyl-5-methylphenyl)-5-chloro-2*H*-benzotriazole 2-(3'-*tert*-butyl-2'-hydroxy-5'-methylphenyl)-5-chlorobenzotriazole 2-(5-Chloro-2-benzotriazolyl)-6-*tert*-butyl-p-cresol 2-(5-Chloro-2*H*-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-methylphenol 2-*tert*-butyl-6-(5-chloro-2*H*-1,2,3-benzotriazol-2-yl)-4-methylphenol 2-*tert*-Butyl-6-(5-chloro-2*H*-benzotriazol-2-yl)-p-cresol 2-*tert*-Butyl-6-(5-chloro-2*H*-benzotriazol-2-yl)-4-methylphenol 2-*tert*-butyl-6-(5-chlorobenzotriazol-2-yl)-4-methylphenol Phenol, 2-(5-chloro-2*H*-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-methyl- UV-326

Structural formula:

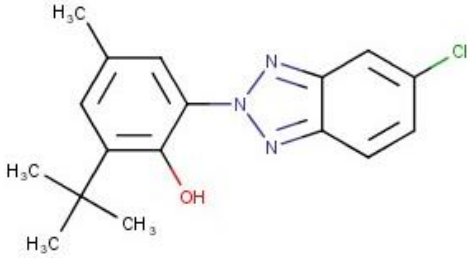
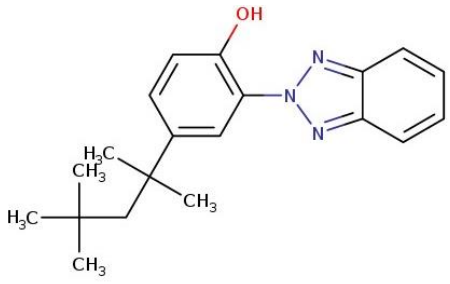


Table 2: Substance identity for UV-329

(2-(2*H*-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol)

EC number:	221-573-5
EC name:	2-(2*H*-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol
CAS number (in the EC inventory):	3147-75-9
CAS number:	3147-75-9
IUPAC name:	2-(2*H*-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol
Index number in Annex VI of the CLP Regulation	-
Molecular formula:	$C_{20}H_{25}N_3O$
Molecular weight range:	323.4 g/mol
Synonyms:	2-(2*H*-*H*-1,2,3-benzotriazol-2-yl)-4-(2,4,4-trimethylpentan-2-yl)phenol *H*-2-(2*H*-Benzotriazol-2-yl)-4-(2,4,4-trimethylpentan-2-yl)phenol 2-(2*H*-Benzotriazol-2-yl)-4-*tert*-octylphenol 2-[2'-Hydroxy-5'-(1,1,3,3-tetramethylbutyl)phenyl]benzotriazole 2-(2-Hydroxy-5-t-octylphenyl)-2*H*-benzotriazole 2-(2-Hydroxy-5-t-octylphenyl)benzotriazole 2-(2-Hydroxy-5-*tert*-octylphenyl)-2*H*-benzotriazole 2-(2-Hydroxy-5-*tert*-octylphenyl)benzotriazole 2-(2'-Hydroxy-5'-*tert*-octylphenyl)benzotriazole 2-(5-t-Octyl-2-hydroxyphenyl)benzotriazole 2-(5'-*tert*-Octyl-2'-hydroxyphenyl)benzotriazole 2-Benzotriazolyl-4-*tert*-octylphenol UV-329 UV 5411

Structural formula:



1.2 Composition of the substances

Name: Bumetrizole (UV-326)

Substance type: mono-constituent

Table 3: Constituents other than impurities/additives (for UV-326)

Constituents	Typical concentration	Concentration range	Remarks
2-(2'-hydroxy-3'-tert-butyl-5'-methylphenyl)-5-chloro benzotriazole (EC: 223-445-4)	≤100 %		

Name: (2-(2*H*-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol (UV-329))

Substance type: mono-constituent

Table 4: Constituents other than impurities/additives (for UV-329)

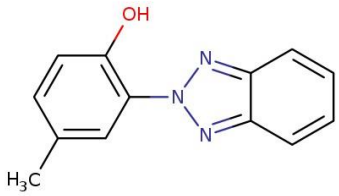
Constituents	Typical concentration	Concentration range	Remarks
2-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol (EC: 221-573-5)	≤100 %		

1.3 Identity and composition of structurally related substances UV-P and M1 (read-across approach)

Table 5: Structurally related substance identity of UV-P

EC number:	219-470-5
EC name:	2-(2*H*-benzotriazol-2-yl)-*p*-cresol
SMILES:	CC1=CC(=C(C=C1)O)N2N=C3C=CC=CC3=N2
CAS number (in the EC inventory):	2440-22-4
CAS number:	2440-22-4
IUPAC name:	2-(2*H*-1,2,3-benzotriazol-2-yl)-4-methylphenol
Index number in Annex VI of the CLP Regulation	-
Molecular formula:	$C_{13}H_{11}N_3O$
Molecular weight range:	225.246 g/mol
Synonyms:	*2-(2H-benzotriazol-2-yl)-4-methylphenol* *2-(2H-benzotriazol-2-yl)-p-cresol* *2-(2'-hydroxy-5'-methylphenyl)-benzotriazole* *2-benzotriazol-2-yl-4-methylphenol* *UV-P*

Structural formula:



Substance type: mono-constituent

Table 6: Constituents of structurally related substance UV-P

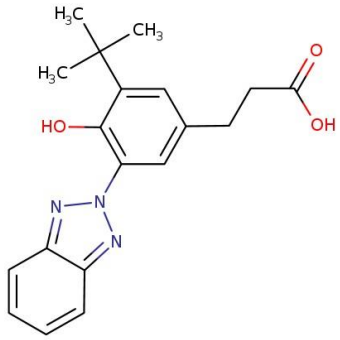
Constituents	Typical concentration	Concentration range	Remarks
2-(2H-benzotriazol-2-yl)-p-cresol (EC: 219-470-5)	≤100 %		

Table 7: Structurally related substance identity of M1

List [1]number:	630-348-4
List name:	3-[3-(2*H*-benzotriazol-2-yl)-5-*tert*-butyl-4-hydroxyphenyl]propanoic acid
SMILES:	CC(C)(C)c1cc(CCC(O)=O)cc(n2nc3ccccc3n2)c1O
CAS number (in the EC inventory):	84268-36-0
CAS number:	84268-36-0
IUPAC name:	3-[3-(2*H*-benzotriazol-2-yl)-4-hydroxy-5-(2-methyl-2-propanyl)phenyl]propanoic acid
Index number in Annex VI of the CLP Regulation	-
Molecular formula:	$C_{19}H_{21}N_3O_3$
Molecular weight range:	339.39 g/mol
Synonyms:	*3-(2H-benzotriazol-2-yl)-5-(1,1-dimethylethyl)-4-hydroxybenzenepropanoic acid* *3-[3-(2H-1,2,3-benzotriazol-2-yl)-5-tert-butyl-4-hydroxyphenyl]propanoic acid* *3-[3-(2H-Benzotriazol-2-yl)-5-tert-butyl-4-hydroxyphenyl]propionic acid* *M1*

Structural formula:

[1] Explanation on the role of List numbers is provided in the ECHA website at: https://echa.europa.eu/information-on-chemicals/registered-substances/information



Substance type: mono-constituent

Table 8: Constituents of structurally related substance M1

Constituents	Typical concentration	Concentration range	Remarks
3-[3-(2H-1,2,3-benzotriazol-2-yl)-5-tert-butyl-4-hydroxyphenyl]propanoic acid (EC: 630-348-4)	≤100 %		

1.4 Physicochemical properties

Table 9: Overview of physicochemical properties of UV-326

(2-(2'-hydroxy-3'-*tert*-butyl-5'-methylphenyl)-5-chloro benzotriazole)[2]

Property	Description of key information	Value [Unit]	Reference/source of information
Physical state at 20°C and 101.3 kPa	*visual inspection*	*solid* *slightly yellow powder*	*ECHA dissemination page*
Melting/freezing point	*Differential Scanning Calorimetry (DSC) method*	*139.7 °C* *(137 – 141 °C by Capillary method)*	*ECHA dissemination page*
Boiling point	*TGA - dynamic screening method*	*>225 °C (decomposition; w/o boiling)*	*ECHA dissemination page*
Vapour pressure	*The calculation was based on Modified Grain Method using recommended MPBPVP (v1.43) module of software EPI Suite v.4.00*	*0.00000075 Pa (at 20 °C)*	*ECHA dissemination page*
Density	*Internal analytical method*	*1320 kg/m³ (at 20 °C)*	*ECHA dissemination page*
Water solubility	*OECD Guideline 105 (Water Solubility)* *Column elution method (HPLC)*	*4 µg/L (at 20 °C; pH 6.3)*	*ECHA dissemination page*
Partition coefficient n-octanol/water (log value)	*OECD Guideline 117 (Partition Coefficient (n-octanol / water), HPLC Method)*	*5.4 – 6.4 (at 23 °C)* *≥6.5 (at 23 °C, pH 6.4)*	*ECHA dissemination page*
	Estimated using COSMOtherm	*6.7*	*COSMOconf[3]* *COSMOtherm[4]*
	Experimental	*7.38*	*Do et al. (2022)*

[2] https://echa.europa.eu/de/substance-information/-/substanceinfo/100.021.315
Access date ECHA dissemination page for all information on 08.03.2023
[3] COSMOconf conformer generation performed using the BP-TZVP-COSMO+GAS template; BIOVIA COSMOconf, Release 2021; Dassault Systèmes. http://www.3ds.com
[4] COSMOtherm property estimation performed using the BP_TZVP_21-parameterisation; BIOVIA COSMOtherm, Release 2021; Dassault Systèmes. http://www.3ds.com;

Dissociation constant	*The calculation was using the recommended software program SPARC v4.5*	*pKa = 10 (at 25 °C)*	*ECHA dissemination page*
	Calculated with Chemicalize	*Strongest acidic pKa = 10.18 (at 25°C)*	*Chemicalize*[5]
	ACD Percepta prediction	*pKa = 10.2 (at pH 9, no temperature available)*	*ACD/Labs*[6]
For UV-326 ionisation can only occur at the hydroxyl group, as this is the only functional group that could act as proton acceptor/donor. However, this group is stabilized by the aromatic system as well as via hydrogen bonds by the nitrogen atoms. Thus, dissociation is very unlikely to occur at environmentally relevant pH values of 4 – 9. ACD Percepta predicts a pKa of 10.2 and that at pH 9 6 % of UV-326 is present in ionised form (hydroxy group negatively charged). At lower pH values the share of the ionised form is further reduced leading to an even higher share of the non-ionised form. In the relevant pH range (4 – 9) the non-ionised form is dominant.			

Table 10: Overview of physicochemical properties of UV-329 (2-(2H-*H*-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol)[7]

Property	Description of key information	Value [Unit]	Reference/source of information
Physical state at 20°C and 101.3 kPa	*Visual inspection*	*Solid* *White powder*	*ECHA dissemination page*
Melting/freezing point	*Differential Scanning Calorimetry (DSC) method*	*104.3 °C*	*ECHA dissemination page*
Boiling point	*TGA measurement*	*>225 °C (decomposition)*	*ECHA dissemination page*
Vapour pressure	*The measurement was based on heats of evaporation by DSC.*	*0.0000041 Pa (at 20 °C)*	*ECHA dissemination page*
Density	*Internal analytical method*	*1180 kg/m³ (at 20 °C)*	*ECHA dissemination page*

[5] 27.10. 2022, https://chemicalize.com/ developed by ChemAxon (http://www.chemaxon.com)
[6] ACD Percepta. ACD/Labs release 2019.2.1 (2019), Advanced Chemistry Development, Inc.

[7] Access date ECHA dissemination page for all information on 08.03.2023
https://echa.europa.eu/de/substance-information/-/substanceinfo/100.019.612

Water solubility	*OECD Guideline 105 (Water Solubility)* *Column elution method (HPLC)*	*2 µg/L (at 20 °C, pH 6.2 – 7.1)*	*ECHA dissemination page*
Partition coefficient n-octanol/water (log value)	*OECD Guideline 117 (Partition Coefficient (n-octanol / water), HPLC Method)*	*6.8 – 7.4 (at 23 °C)* *≥6.5 (at 23 °C; pH 6.4)*	*ECHA dissemination page*
	Estimated using COSMOtherm	*6.4*	*COSMOconf*[8] *COSMOtherm*[9]
	Experimental	*6.91*	*Do et al. (2022)*
Dissociation constant	*The calculation was using the recommended software program SPARC v4.5*	*pKa = 8.9 (at 25 °C)*	*ECHA dissemination page*
	Calculated with Chemicalize	*Strongest acidic pKa = 9.4* *(at 25°C)*	*Chemicalize*[10]
	ACD Percepta prediction	*pKa = 10.2 (at pH 9, no temperature available)*	*ACD/Labs*[11]
Using ACD Percepta for the prediction of the dissociation constant resulted in a pKa of 10.3. At pH 9 in total 5 % of UV-329 is ionised (hydroxy group negatively charged). Although a higher pKa compared to 8,9 (ECHA dissemination page) is predicted by ACD Percepta, the computation is regarded as conclusive based on the chemical structure and the same stabilizing effect of the hydroxyl group as in the case of bumetrizole: For UV-329 ionisation can only occur at the hydroxyl group, which is the only functional group that could act as proton acceptor/donor. However, this group is stabilized by the aromatic system as well as via hydrogen bonds by the nitrogen atoms. Thus, dissociation is very unlikely to occur at environmentally relevant pH values of 4 – 9 and therefore in this pH range (4 – 9) the non-ionised form is dominant.			

Table 11: Overview of physicochemical properties of structurally related substance UV-P

Property	Description of key information	Value [Unit]	Reference/source of information
Physical state at 20°C and 101.3 kPa	*Visual inspection*	*Solid* *Slightly yellow powder*	*ECHA dissemination page*
Melting/freezing point	*DSC according to the ASTM E537*	*130 °C*	*ECHA dissemination page*

[8] COSMOconf conformer generation performed using the BP-TZVP-COSMO+GAS template; BIOVIA COSMOconf, Release 2021; Dassault Systèmes. http://www.3ds.com
[9] COSMOtherm property estimation performed using the BP_TZVP_21-parameterisation; BIOVIA COSMOtherm, Release 2021; Dassault Systèmes. http://www.3ds.com;
[10] 27.10. 2022, https://chemicalize.com/ developed by ChemAxon (http://www.chemaxon.com)
[11] ACD Percepta. ACD/Labs release 2019.2.1 (2019), Advanced Chemistry Development, Inc.

Boiling point	*DSC according to the ASTM E537*	*>398 °C (decomposition)*	*ECHA dissemination page*
Vapour pressure	*The measurement was based on heats of evaporation by DSC.*	*1.47 10^{-4} Pa (at 20 °C)*	*ECHA dissemination page*
Density	*OECD Guideline 109*	*1385 kg/m³ (at 20 °C)*	*ECHA dissemination page*
Water solubility	*OECD Guideline 105 (flask method)*	*173 µg/L (at 20 °C, pH 6.5)*	*ECHA dissemination page*
Partition coefficient n-octanol/water (log value)	*OECD Guideline 107 (shake flask method)*	*4.20 (at 25 °C, pH 6.3)*	*ECHA dissemination page*
	Estimated using COSMOtherm	*3.95*	*COSMOconf[12] COSMOtherm[13]*
Dissociation constant	*The calculation was using ACD/Labs software V8.14 (©1994 – 2010 ACD/Labs) cited in SciFinder Database*	*pKa = 8.15 (at 25 °C)*	*ECHA dissemination page*
	Calculated with Chemicalize	*Strongest acidic pKa = 9.53 (at 25°C)*	*Chemicalize[14]*
For UV-P ionisation can only occur at the hydroxyl group, as with is the only functional group that could act as proton acceptor/donor. However, this group is stabilized by the aromatic system as well as via hydrogen bonds by the nitrogen atoms. Thus, dissociation is very unlikely to occur at environmentally relevant pH values of 4 – 9. Although the pKa was computed to be 8.15, the dominant form in the pH range of 4 – 9 is the non-ionised molecule.			

Table 12: Overview of physicochemical properties of structurally related substance M1

Property	Description of key information	Value [Unit]	Reference/source of information
Physical state at 20°C and 101.3 kPa	*Visual inspection*	*Solid* *Light yellow powder*	*ECHA dissemination page*
Melting/freezing point	*DSC according to OECD Guideline 102*	*195 °C*	*ECHA dissemination page*
Boiling point	*DSC according to OECD Guideline 103*	*no boiling observed up to 400 °C*	*ECHA dissemination page*

[12] COSMOconf conformer generation performed using the BP-TZVP-COSMO+GAS template; BIOVIA COSMOconf, Release 2021; Dassault Systèmes. http://www.3ds.com
[13] COSMOtherm property estimation performed using the BP_TZVP_21-parameterisation; BIOVIA COSMOtherm, Release 2021; Dassault Systèmes. http://www.3ds.com;
[14] 27.10. 2022, https://chemicalize.com/ developed by ChemAxon (http://www.chemaxon.com)

Vapour pressure	*No method given*	*2.933 10^{-10} Pa (at 25 °C)*	*ECHA dissemination page*
Density	*OECD Guideline 109 (pycnometer)*	*785 kg/m³ (at 20 °C)*	*ECHA dissemination page*
Water solubility	*OECD Guideline 105 (flask method)*	*<0.001 g/L (at 20 °C, pH 7.1)*	*ECHA dissemination page*
Partition coefficient n-octanol/water (log value)	*OECD Guideline 107 (shake flask method)*	*≥ 2.75 (at 25 °C, pH 6.9)*	*ECHA dissemination page*
	Estimated using COSMOtherm via pKa from M1-Anion	*3.32 (no temperature available)*	*COSMOconf*[15] *COSMOtherm*[16]
Dissociation constant	*Calculated with Chemicalize*	*Strongest acidic pKa = 4.25 (at 25°C)*	*Chemicalize*[17]
The substance M1 comprises two functional groups that could act as proton acceptor/donor. The hydroxyl group is stabilized via the aromatic system and protected via hydrogen bonds by the nitrogen atoms. Thus, dissociation is very unlikely to occur. The carboxyl group instead will dissociate in the environmental relevant pH range of 4 – 9. Due to the pKa of 4.25 and the chemical structure it is expected that the substance will be mainly present in its ionised form at pH 4 – 9.			

[15] COSMOconf COSMOtherm C_30_1601.ctd Dassault Systèmes. http://www.3ds.com;
[16] COSMOtherm COSMOtherm C_30_1601.ctd Dassault Systèmes. http://www.3ds.com;
[17] 19.08. 2023, https://chemicalize.com/ developed by ChemAxon (http://www.chemaxon.com)

2 Harmonised classification and labelling

2-(2'-hydroxy -3' -*tert*-butyl-5'-methylphenyl)-5-chloro benzotriazole (UV-326 (EC: 223-445-4; CAS 3896-11-5) has no harmonised classification in part 3 of Annex VI to the CLP Regulation.

The following hazard classes are contained in self-classifications notified to the CLP inventory[18]:

- Aquatic Chronic 4 (H413)
- Aquatic Chronic 3 (H412)
- Skin Irrit. 2 (H315)
- Eye Irrit. 2 (H319)
- STOT SE 3 (H335)
- Acute Tox. 4 (H312))
- Aquatic Acute 1 (H400)
- Aquatic Chronic 2 (H411)

2-(2*H*-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol (UV-329 (EC: 221-573-5; CAS 3147-75-9) has no harmonised classification in part 3 of Annex VI to the CLP Regulation.

The following hazard classes are contained in self-classifications notified to the CLP inventory[19]:

- Aquatic Chronic 4 (H413)
- Aquatic Chronic 3 (H412)
- Aquatic Chronic 1 (H410)
- Skin Irrit. 2 (H315)
- Eye Irrit. 2 (H319)
- STOT SE 3 (H335)
- Acute Tox. 4 (H312)
- Skin Sens. 1 (H412)

[18] https://echa.europa.eu/de/information-on-chemicals/cl-inventory-database/-/discli/details/44804
[19] https://echa.europa.eu/de/information-on-chemicals/cl-inventory-database/-/discli/details/68877

3 Environmental fate properties

Considerations on chemical structure and properties and justification for read-across

UV-326 and UV-329 are part of a group of phenolic benzotriazoles which are also called UV-benzotriazoles. These substances share the 2-(2-hydroxyphenyl)-2*H*-benzotriazole moiety as a common structural feature. The intramolecular hydrogen bond between the hydroxy group and the nitrogen of the benzotriazole ring is essential for their function as UV absorbers (see Figure 1).

Information on some structurally related phenolic benzotriazoles is used in this dossier for a read-across or as supporting evidence. Thus, a brief general description of the group is given along with a more detailed discussion of the substances relevant for the assessment. A data matrix is given in the appendix to support the read-across.

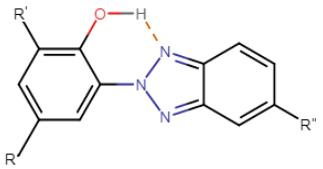


Figure 1: Structures of phenolic benzotriazoles

(R = alkyl, alkylphenyl; R‘ = H, alkyl, alkylphenyl; R‘‘ = H, Cl).

Due to the structural similarity of the substances, similar properties are expected which vary depending on the different substituents. In combination with the substituents described in Figure 1, the 2-(2-hydroxyphenyl)-2*H*-benzotriazole moiety common to all substances is associated with high stability and lipophilicity. Accordingly, water solubility is rather low and adsorption potential is expected to be high. This is confirmed by the available data (see Annex I and ECHA 2014a, 2014b, 2015a, 2015b). The substances are not volatile and volatilisation is not expected to impact degradation (see Annex I and ECHA 2014a, 2014b, 2015a, 2015b, ECHA 2022).

Generally, the alkyl substituents are considered to increase lipophilicity and to reduce water solubility – the larger the substituents, the more lipophilic the molecule. Furthermore, substituents in ortho position to the hydroxy group provide a steric stabilisation to the intramolecular hydrogen bond. Finally, the absence of substituents at the phenyl moiety might theoretically enable enzymatic attacks at the respective molecular sites.

The very high persistence and very high bioaccumulation of the structurally related substances UV-320, UV-328, UV-327 and UV-350 has previously been confirmed by their identification as SVHC substances due to their vPvB properties.

UV-326 bears a high similarity to these substances, especially to UV-327: there are alkyl substituents in ortho and para position to the hydroxy group. Both UV-326 and UV-327 have a chlorine substituent in the benzotriazole moiety. Hence, UV-326 is expected to have comparable physico-chemical and degradation properties to UV-327. This expectation is supported by the available data, i.e. QSAR predictions, ready biodegradation tests, a water sediment study, findings in sediment cores and a soil dissipation study (see Annex I and ECHA 2015a). While a read-across from UV-327 to UV-326 could be justified based on structural similarity, the data set for both substances is too similar to gain significant information.

The main structural difference of UV-329 to the confirmed vPvB benzotriazoles is the lack of a substituent in ortho-position to the hydroxyl group. UV-P is another phenolic benzotriazole that shares this structural feature with UV-329. However, while the substituent in para position to

the hydroxy group is a *tert*-octyl group for UV-329, it is a methyl group for UV-P. Thus, UV-P is less lipophilic than UV-329 and has a higher water solubility. It is expected to be adsorptive, but to a lesser extent than UV-329. The vapour pressure of UV-P is borderline with respect to soil field studies (ECHA 2022); however, available data of a soil dissipation study do not support volatilisation of UV-P. In summary, bioavailability is expected to be slightly higher for UV-P than for UV-329.

According to their structural similarity, UV-329 and UV-P should have a comparable degradation behaviour. These expectations are supported by the available data, i.e. CATALOGIC predictions, ready biodegradation tests and the soil dissipation study (see Annex I).[20] If the missing substituent had an impact on persistence, this impact would be expected to be similar for UV-329 and UV-P.

Another structurally related substance is M1 (EC 630-348-4), a metabolite of UV-384 (EC 407-000-3). Information on M1 has been used for read-across in the persistence assessments of UV-320, UV-328, UV-327, and UV-350 in order to conclude on their vP properties and is provided in this dossier for read-across as well.

M1 differs from UV-326 regarding the substituent in para position to the hydroxy group, which is a carboxyethyl group for M1 and a methyl group for UV-326, respectively. Furthermore, UV-326 has a chlorine substituent in the benzotriazole moiety and M1 has not. These differences – carboxyethyl group vs. alkyl group, chlorine substituent vs. no chlorine substituent are comparable to the differences between M1 and UV-327. M1 differs from UV-329 regarding the substituent in para position to the hydroxy group, which is a carboxyethyl group for M1 and a *tert*-octyl group for UV-329, respectively. Furthermore, in ortho position to the hydroxy group, UV-329 is not substituted whereas M1 contains a *tert*-butyl group.

The carboxyethyl group is a characteristic structural feature that differentiates M1 from the group of phenolic benzotriazoles described in figure 1. As described above in section 1.4 , the carboxyethyl group has an impact on dissociation. M1 is expected to be present in the dissociated form under environmentally relevant pH values. Therefore, M1 is expected to have a higher water solubility and a lower octanol water partition coefficient than UV-326 and UV-329. However, as adsorption of M1 might be enhanced by ionic interactions, it is expected to have a high adsorption potential as well. These expectations are supported by the available physico-chemical data (see Annex I). Thus, the bioavailability of M1 is expected to be similar as compared to UV-326 and UV-329. The carbonic acid group might also enhance degradability of the respective side chain (Gao et al. 2010, EAWAG 2023).

In summary, M1 is structurally more similar to UV-326 than to UV-329. Based on mechanistic considerations and biodegradation estimations[21] it is expected that M1's susceptibility to degradation is similar to or higher than that of UV-326 (DegT50(M1) ≤ DegT50(UV-326)).

The impact of impurities is not considered relevant for a read-across from M1 to UV-326 and from UV-P to UV-329: The data used for read-across either refer to detection of the substance in the environment (UV-P) or to detection of the substance as a major metabolite in a simulation test (M1).

As outlined above, the available data support the proposed similarity of UV-326 and M1 and the proposed similarity of UV-329 and UV-P in degradation properties (see Annex I).

[20] BIOWIN models even indicate a better degradability of UV-P. However, the other data are considered more reliable and more relevant.

[21] All BIOWIN models predict a better biodegradability for M1 than for UV-326.
The CATALOGIC model 301C v12.17 predicts UV-326 and M1 to be not readily biodegradable. The extrapolated primary half-life values predicted with this model are 9 months 26 days for UV-326 and 1 year 3 months 26 days for M1.
As discussed further below, CATALOGIC 301C v12.17 is preferred because its training set contains the most phenolic benzotriazoles. The automatic applicability domain check shows that this model is also the best for M1 while it is still denoted "out of domain"due to 5% unknown fragments.

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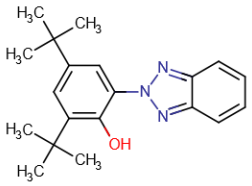
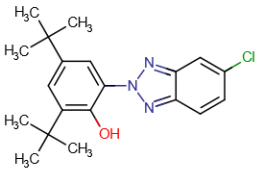
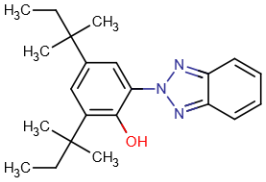


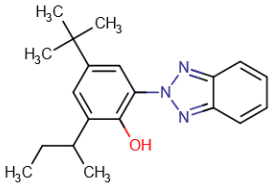
UV-320



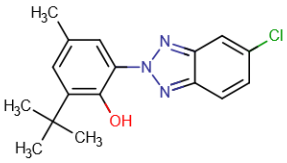
UV-327



UV-328

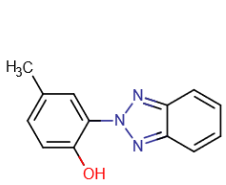


UV-350

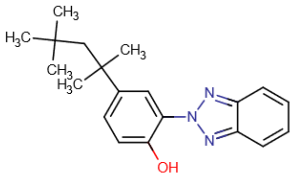


UV-326

Figure 2: Structures of UV-326 and the known SVHC substances UV-320, UV-328, UV-327 and UV-350 identified as vP.

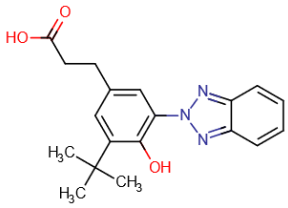


UV-P



UV-329

Figure 3: Structures of UV-329 and UV-P.



M1

Figure 4: Structure of M1.

3.1 Degradation

A weight-of-evidence approach is applied for the assessment of persistence. The "Weight of Evidence/Uncertainty Analysis Template[22]" is applied to structure the data.

[22] https://echa.europa.eu/documents/10162/17169198/template_for_weight_of_evidence_en.docx/eb183c2e-c360-cbce-7a58-ad2d1270e5bd

3.1.1 Problem Formulation

A weight of evidence determination according to the provisions of Annex XIII of REACH is used to assess if the substances meet the criteria for P/vP.

3.1.2 Documentation of search strategy & documentation/reporting of evidence

Information/evidence used in the approach includes:

- Experimental studies from ECHA dissemination site
- (Q)SAR results
- Published Literature
- Research Project
- Information on structurally related substances

3.1.3 Collection and documentation of all information

In addition to the information from the registration dossiers, further studies were used for persistence assessment. These are documented in the Reference List.

The assessment includes field studies in sediment and soil. Various further field studies are available: UV-326 and UV-329 have been detected in freshwater and marine sediments (for example Wick *et al.*, 2016a and 2016b[23]; Kameda *et al.*, 2011; Nakata *et al.*, 2009; Apel *et al.*, 2018) and, to a lesser extent, in surface water (for example Tashiro and Kameda, 2013; Khare *et al.*, 2023).

According to the PBT guidance, monitoring data may be indicative of persistence, but the impact of factors other than persistence need to be taken into account (ECHA, 2017). In many cases, it is not clear to which extent the detection of a substance is due to slow degradation, and to which extent due to exposure. Actually, both factors are expected to have an impact for UV-326 and UV-329.

The available data from sediment cores (cf. section 3.1.4.2.4) and soil dissipation studies (cf. section 3.1.4.3.1) contain information on contamination after a certain time span. Thus, their informative value for persistence assessment is greater than that of the other studies. The other available studies are not considered further in the assessment because they contain a high degree of uncertainty and they are not considered to have a significant impact on the conclusion.

[23] Wick et al. 2016a and 2016b contain both monitoring data and water sediment studies. While this section refers to the monitoring data, the water sediment studies are discussed below.

3.1.4 Assessment of quality of individual evidence

3.1.4.1 Abiotic Degradation

Table 13: Data on abiotic degradation for UV-326 and UV-329

Type of Evidence / Source Name - Reference	Relevance	Reliability	Adequacy
HYDROWIN[24]	The program reports that the substances do not belong to the substance classes for which hydrolysis is predicted. This result indicates the absence of "classical" hydrolysable groups, but does not prove that the substance is hydrolytically stable.	Phenolic benzotriazoles are outside the application domain; the program reports that they do not belong to the substance classes for which hydrolysis is predicted. Klimisch score 3	Adequacy to be considered within integration of evidence
CATALOGIC Abiotic[25]	Screening information on aerobic abiotic degradation under OECD TG 301 C testing conditions. This model was calibrated on experimental data on parent chemicals and their transformation products. The model predicts abiotic degradation under the conditions of a ready biodegradability test, including hydrolysis as a major abiotic transformation pathway.[26]	CATALOGIC includes an automatic check of application domain.[27] The domain check accounts for molecular fragments and is stricter as compared to HYDROWIN. UV-326 and UV-329 are in the parameter range of the models. However, all substances are out of the applicability domain due to > 50% unknown structural fragments. Klimisch score 3	Adequacy to be considered within integration of evidence
Literature on hydrolysis of organic compounds	General publications on hydrolysis reactions of organic compounds without clear reference to phenolic benzotriazoles or benzotriazoles.	The publications indicate the absence of "classical" hydrolysable groups, but do not prove that the substance is hydrolytically stable. Klimisch score 2	Adequacy to be considered within integration of evidence

No experimental data on hydrolysis are available. The registration dossier for UV-329 cites literature that is not specific for UV-329, but deals with the hydrolysis of organic compounds in general. The HYDROWIN and CATALOGIC results are outside the applicability domain and thus considered as not reliable (Klimisch score 3).

The structures of UV-326 and UV-329 do not contain functional groups that are susceptible to hydrolysis, a finding that is supported by HYDROWIN results and by the general literature cited in the UV-329 registration dossier. The CATALOGIC Abiotic 301 C model predicts no abiotic transformation for UV-329 and UV-326 under the testing conditions of OECD TG 301 C. Thus, it is assumed that the substances are hydrolytically stable.

No data on photolysis or oxidation are available in the registration dossiers for UV-326 and UV-329.

[24] 2010 U.S. Environmental Protection Agency. HYDROWIN v2.00 in EPISUITE v4.11. Result for all structures: The chemical structure does not contain typical functional groups that are susceptible to hydrolysis.
[25] OASIS CATALOGIC v.5.15.2.14. http://oasis-lmc.org/products/software/catalogic.aspx (November 2022); CATALOGIC Abiotic 301C v.01.08
[26] http://oasis-lmc.org/products/models/environmental-fate-and-ecotoxicity.aspx (November 2022)
[27] Default setting tolerates a certain percentage of unknown fragments; adjusted setting: No unknown fragments accepted.

3.1.4.2 Biodegradation in aqueous media or aqueous environment

3.1.4.2.1 Estimated data

Table 14: Estimated data on biodegradation for UV-326 and UV-329

Type of Evidence / Source Name - Reference	Relevance	Reliability	Adequacy
BIOWIN[28]	Screening information on biodegradation. BIOWIN models 1,2,5,6 were calibrated based on screening tests for ready biodegradability, i.e., these models predict respective test results. BIOWIN 3 and 4 are based on results of an expert survey and predict the semi-quantitative timeframe for Ultimate and Primary Biodegradation, respectively. As these models were not calibrated to experimental data, but to an expert survey, BIOWIN 3 and 4 can be regarded to predict the result of a respective expert judgement. [29]	The BIOWIN user guide recommends to assess the applicability domain using the Molecular Weight range and the fragment count, i.e., to check whether the occurrence of a given fragment in the predicted compound exceeds the maximum occurrence of that fragment per molecule in the training set. UV-326 and UV-329 are in the Molecular Weight range of the model's training sets. For UV-326 and UV-329, the molecular fragments used for calculation do not exceed the maximum number of such fragments per molecule observed in the training set. A search for structurally related structures in the available information on the training set was carried out: The training set for BIOWIN 1 and 2 does not contain benzotriazoles. BIOWIN 3 and 4 were trained on the structurally related substance 2-(2*H*-Benzotriazol-2-yl)-phenol[30] which enhances their applicability to the target substance. The predicted BIOWIN 3 and 4 values for this substance are in good agreement with the survey average. The training set (old) for BIOWIN 5 and 6 does not contain benzotriazoles, but 1*H*-Benzotriazole is in the validation set[31] and is correctly predicted as not readily biodegradable.	Adequacy to be considered within integration of evidence
CATALOGIC[32]	Screening information on biodegradation. The applied CATALOGIC biodegradation models were calibrated on data from OECD 301 test results and on information on biodegradation pathways. These models predict biodegradation under the conditions of a ready biodegradability	CATALOGIC includes automatic check of application domain.[34] The domain check accounts for molecular fragments and is stricter as compared to BIOWIN. UV-326 and UV-329 are in the parameter range of the models. The structural domain check is stricter than that recommended for BIOWIN. Only the result of the CATALOGIC 301C v12.17 model for UV-326 is considered in domain. All other predictions for UV-329 and UV-326 are considered out of domain. It is noted that applying such a domain check to	Adequacy to be considered within integration of evidence

[28] 2010 U.S. Environmental Protection Agency. BIOWIN v4.10 in EPISUITE v4.11
[29] 2010 U.S. Environmental Protection Agency. BIOWIN v4.11 in EPISUITE v4.11. User Guide.
[30] Substance no. 88, 2-(2H-Benzotriazol-2-yl)-phenol
[31] Substance no. 95147, 1H-Benzotriazole
[32] OASIS CATALOGIC v.5.15.2.14. http://oasis-lmc.org/products/software/catalogic.aspx (November 2022); CATABOL 301B v.02.07; CATABOL 301C v.02.08; CATALOGIC 301C v.12.17; CATALOGIC Kinetic 301B v.02.11; CATALOGIC Kinetic 301F v.15.18
[34] Default setting tolerates a certain percentage of unknown fragments; adjusted setting: No unknown fragments accepted.

	test.[33]	models like BIOWIN would result in all or almost all predictions being out of domain as well.	

3.1.4.2.1.1 BIOWIN

The BIOWIN software, as described in Table 14, yields the following results:

Table 15: BIOWIN results

Name	BIOWIN1 (Linear Model)	BIOWIN2 (Non-Linear Model)	BIOWIN3 ultimate	BIOWIN4 primary	BIOWIN5 (Linear MITI Model)	BIOWIN6 (Non-Linear MITI Model)	R11 screening
UV-329	0.3415	0.016	2.1165	3.1139	0.0704	0.0081	fulfilled
UV-326	0.4013	0.0235	2.0641	3.0445	0.0650	0.0086	fulfilled

For the BIOWIN models 1, 2, 5 and 6 a result greater than or equal to 0.5 indicates that the substance is predicted to be readily biodegradable. A result below 0.5 indicates that the substance is not readily biodegradable. While none of these models were trained on benzotriazoles[35], the validation set of BIOWIN 5 and 6 at least contained the structurally related 1*H*-Benzotriazole, which was predicted correctly as not readily biodegradable. The updated training and validation sets contain UV-320 (training set) and UV-P, UV-326 and 1H-Benzotriazole (all validation set). Therefore, BIOWIN 5 and 6 are considered more reliable than BIOWIN 1 and 2.

UV-326 and UV-329 are predicted to be not readily biodegradable by BIOWIN 1, 2, 5 and 6.

BIOWIN models 3 and 4 indicate the timeframe for ultimate and primary biodegradation, respectively. BIOWIN 3 and 4 were trained on the structurally related substance 2-(2*H*-Benzotriazol-2-yl)-phenol which enhances their applicability to the target substance. Predicted biodegradation timeframes for UV-326 and UV-329 are "Months" (ultimate) and "Weeks" (primary).

According to REACH Chapter R.11 (ECHA, 2017[36]), a substance is considered as potentially P or vP if the estimated probability value for Biowin 2 or 6 is below 0.5, and the estimated probability value for Biowin 3 is below 2.25 (to 2.75).

Based on the screening criteria from the guidance, UV-326 and UV-329 are considered to be potentially P or vP.

[33] http://oasis-lmc.org/products/models/environmental-fate-and-ecotoxicity.aspx (November 2022)

[35] Additional training set data from 2017 update to BIOWIN 5 and 6 were not available. If these contained benzotriazoles, they might improve the applicability of the model. In summary, this would not change the finding that BIOWIN 5 and 6 are assumed to be more reliable for these substances than BIOWIN 1 and 2.

[36] ECHA 2017. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.11: PBT/vPvB assessment. Version 3.0. https://echa.europa.eu/documents/10162/13632/information_requirements_r11_en.pdf/a8cce23f-a65a-46d2-ac68-92fee1f9e54f (accessed November 2022)

3.1.4.2.1.2 CATALOGIC

The CATALOGIC software includes an automatic applicability domain check. The following results were obtained:

Table 16: Results of CATALOGIC applicability domain check

Name	CATALOGIC 301C v12.17	CATABOL 301C v02.08	CATABOL 301B v02.07	CATALOGIC Kinetic 301B v02.11	CATALOGIC Kinetic 301F v15.18
UV-329	Out of Domain (5.26% unknown fragments)	Out of Domain (47.37% unknown fragments)	Out of Domain (63.16% unknown fragments)	Out of Domain (63.16% unknown fragments, out of mechanistic domain)	Out of Domain (57.89% unknown fragments)
UV-326	In domain, belongs to training set	Out of Domain (5.88% unknown fragments)	Out of Domain (64.71% unknown fragments)	Out of Domain (76.47% unknown fragments, out of mechanistic domain)	Out of Domain (64.71% unknown fragments)

If the default settings of the structural domain for the model are changed to allow for unknown fragments with inert additions (meaning fragments that are not expected to have an impact), then also UV-329 would be 100 % within structural domain. The training set of CATALOGIC 301 C v12.17 contains UV-326 and the structurally related phenolic benzotriazoles UV-P, UV-327, UV-328, UV-350 and UV-320. The training set of CATABOL 301 C v02.08 contains UV-327. In summary, CATALOGIC 301 C v12.17 is considered the preferred model for both substances, as its training set contains structurally related compounds and the substances are either in the applicability domain or show the smallest deviation from the applicability domain.

The CATALOGIC 301 C v12.17 model yields the following results for ultimate biodegradation in 28 days under OECD 301 conditions:

Table 17: CATALOGIC results for ultimate biodegradation in 28 days

Name	CATALOGIC 301C v12.17
UV-329	1%
UV-326	0%

The substances are predicted not readily biodegradable. CATALOGIC 301 C v12.17 predicts 1% of biodegradation for UV-329 and 0% for UV-326.

The model additionally predicts ultimate and primary half-life values that are estimated based on extrapolated data from OECD 301 tests:

Table 18: CATALOGIC results for extrapolated ultimate and primary half-life values (expressed as days (d), months (m) and years (y))

Name	CATALOGIC 301C v12.17	
	Primary Half-life	Ultimate Half-life
UV-329	2m 28d	6y 9m 11d
UV-326	9m 26d	more than 10 y

Degradation kinetics observed in OECD 301 tests cannot be extrapolated to relevant conditions of REACH Annex XIII. Therefore, the respective results should be treated with caution. However, they may give an indication of the expected degradation kinetics under prolonged / extrapolated OECD 301 testing conditions.

CATALOGIC 301 C v12.17 predicts primary half-life values in the range of months and ultimate half-life values in the range of years for UV-329 and UV-326 thus indicating the substances screen as potentially P/vP.

3.1.4.2.2 Screening tests

Table 19: Screening tests on ready biodegradability

Type of Evidence / Source Name - Reference	Relevance	Reliability	Adequacy
Biodegradation Screening test OECD TG 301B (Testing Laboratory 1989) UV-329	Yes, according to test guideline protocol covering parameters required for assessment.	Klimisch score 2	Adequate study for biodegradation in water
Biodegradation Screening test OECD TG 301B (Testing Laboratory 2007) UV-326	Yes, according to test guideline protocol covering parameters required for assessment.	Klimisch score 2	Adequate study for biodegradation in water
Biodegradation Screening test OECD TG 301C (Testing Laboratory 1996) UV-326	Yes, according to test guideline protocol covering parameters required for assessment.	Klimisch score 1	Adequate study for biodegradation in water
Biodegradation Screening test OECD TG 301B (Testing Laboratory 1988) UV-326	Yes, according to test guideline protocol covering parameters required for assessment.	Klimisch score 2	Adequate study for biodegradation in water

Relevant and reliable screening tests on ready biodegradability are available for UV-329 and UV-326. The highest degradation observed in the OECD 301 screening tests was ≤20% in one OECD 301B study on UV-326. No biodegradation was observed in the other OECD 301 tests.

One screening test on ready biodegradability is available for **UV-329**:

- The OECD 301 B study from the registration dossier is considered as key study by the registrant. For the applied testing concentrations of 10.2 mg/L and 21.5 mg/L, 0 and 1% CO_2 evolution were observed after 28 days, respectively.

Three screening tests on ready biodegradability are available for **UV-326**:

- The registration dossier contains an OECD 301 B study from 2007 that is considered as key study by the registrant. For the applied testing concentration of 16 mg/L, the observed CO_2 evolution after 28 days was ≥10% and ≤20%.
- The OECD 301 C study from the registration dossier is also considered as key study by the registrant. The applied test concentration was 100 mg/L and the test duration 28 days. The degree of degradation was determined by BOD measurement and test material analysis, both yielding 0% of degradation.

- Another OECD 301 B study is available in the registration dossier. This study was conducted in 1988 and is considered as supporting study by the registrant. For the applied testing concentrations of 10 mg/L and 20 mg/L, 10% and 2% CO_2 evolution were observed after 28 days, respectively.

3.1.4.2.3 Simulation tests

Table 20: Water sediment simulation tests

Type of Evidence / Source Name - Reference	Relevance	Reliability	Adequacy
Water-sediment simulation study (non-GLP study) (Wick et al 2016a, Wick et al 2016b) UV-329, UV-326	Yes, according to test guideline protocol covering parameters required for assessment.	Klimisch score 2	Adequate study for biodegradation in water sediment systems
Aquifer simulation study (Liu et al. 2013) UV-329, UV-326	Relevant with restriction: Study design specifically targeted on aquifer systems, but study contains information on dissipation in a system of water and aquifer sediment. Methodology described, covering most parameters required for assessment	Klimisch score 2	Adequate study for biodegradation in aquifer systems
OECD TG 308 Simulation study on UV-384 (EC 407-000-3) and its metabolite M1 (ECHA 2014a)	Yes, according to test guideline protocol covering parameters required for assessment.	Klimisch score 2	Adequate study for biodegradation of a structurally related substance (M1) in water sediment systems.

3.1.4.2.3.1 Study on UV-benzotriazoles in a river water-sediment system (Wick et al. 2016a, Wick et al 2016b)

Wick *et al.* (2016a, 2016b) investigated the biodegradation of UV-329, UV-326 and other phenolic benzotriazoles[37] in an aerobic water-sediment study. This non-GLP study shows some variations to the OECD TG 308:

- Only one sediment was used with a relatively high TOC of 4.22% (fine texture, as required);
- the sediment was freshly collected at a site where previous contamination with organic chemicals may be expected[38], resulting in possible pre-adaptation of micro-organisms;
- volatiles were not collected.

Besides that, test conditions were in accordance with OECD TG 308: equilibration time 4 weeks; test temperature 20 °C; a pH range of 7.8 to 8.4 and O_2 concentrations of 8.8 to 9.1 mg/L. No information on redox potential is available. The test was conducted in 250 mL amber glass bottles that were filled with sediment and surface water at a ratio of 1:4 (w/w). 2 µg radioactively non-labelled test substance was dissolved in 100 µL methanol and spiked into the water phase. The initial test concentration for each individual benzotriazole was 10 µg/L in the supernatant, which was applied as a mixture.
Triplicate sampling was conducted at 0 (30 min), 2, 4, 8, 16, 25, 50 and 100 days after spiking; test duration was 100 days. Extraction of the freeze-dried sediment samples was done by pressurised liquid extraction (PLE) followed by silica clean-up. Analysis of the test substances was accomplished by LC-MS/MS measurements. An external standard calibration with 14 calibration points ranging from 0 to 100 µg/L and a linear fitting were used for quantification.

A parallel test with the reference substance Lenacil showed degradation of up to 50% on day 100 in the total system, thus demonstrating the microbial viability of the test system. Results for this test are presented in Figure 5.

For all analysed phenolic-benzotriazoles, a gap in the mass balance was observed at the beginning of the incubation period (until day 16), before the sorption equilibrium between water and sediment was reached (see Figure 5). This is probably due to an underdetermination of the dissolved concentrations due to a strong sorption of the substances on the vessel walls. In the subsequent period between day 16 and day 100, however, the recoveries were mostly within the range of the OECD Guideline 308 target (70-110%). From day 16 onwards, recoveries were relatively constant and the standard deviations were mostly below 20%.

The results confirmed the high sorption affinity of the phenolic-benzotriazoles. After 16 days, no substance could be detected in the water phase. Taking into account the quantification limits for the water phase[39], it was found that >99.5% of the amount of UV-326 and UV-329 were sorbed on the sediment. Due to the intensive extraction method, which was specifically designed to recover as much of the non-radioactive test substance as possible, there were practically no "non-extractable residues" (NER). No significant decrease in total concentration was observed for any of the phenolic benzotriazoles investigated during the 100 d incubation period. Therefore, no degradation kinetics could be modelled – applying kinetic models to these data would result

[37] This study also includes results for UV-327 and UV-350 that are discussed in the respective SVHC dossiers for these substances (ECHA 2015a, ECHA 2015b).
No clear information is available on whether the different phenolic benzotriazoles were tested together in common test vessels or whether separate test vessels were set up for every substance. However, the impact of co-exposure to other phenolic benzotriazoles is expected to be negligible because:

- similar susceptibility to degradation is expected (see discussion on structure and properties above in section 3)
- no degradation was observed, i.e. enhanced biodegradation by co-metabolism was not significant under testing conditions
- no toxicity to microorganisms is expected based on the available data for the tested substances.

[38] River Rhine, Germany (Koblenz, harbor, river km 591.4)
[39] Limit of quantification in water (LOQ_{water}):
LOQ_{water} = 0.04 µg/L for UV-326, UV-329, UV-328 and UV-327 and UV-350
LOQ_{water} = 0.01 µg/L for UV-928 and UV-234

in half-life values that are extrapolated way beyond the magnitude of test duration.
Consequently, the phenolic benzotriazoles were persistent in the experiment and the half-life was significantly higher than the observation period of 100 d. At an environmentally relevant temperature of 12 °C this corresponded to a half-life significantly larger than 212 days for UV-326 and UV-329.

The impact of the deviations from OECD TG 308 is not considered detrimental in this test because:

- the chosen sediment was appropriate for the test and as no biodegradation was observed, it can be considered as worst case;
- the possible pre-adaptation of micro-organisms did not lead to the observation of biodegradation;
- volatiles were not collected but recovery was sufficient and neither degradation nor volatilisation were observed.

This study is considered as reliable with restrictions.

In conclusion, the examined phenolic-benzotriazoles rapidly and nearly completely adsorb to sediment in a water/sediment system and hardly degrade over a period of 100 days (DegT50, sed. >>100 d).

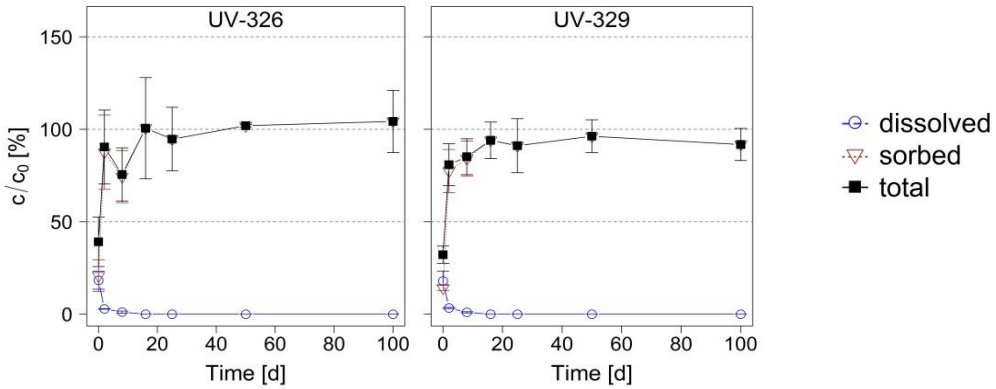


Figure 5: Average relative concentrations [% of initial concentration c0] of UV-benzotriazoles in sediment-water systems
incubated for 100 d at 20 ± 1 °C in a climate cabinet (n=3). The error bars represent the standard deviation (taken from Wick et al., 2016a, supporting data).

3.1.4.2.3.2 Study on UV-329 and UV-326 in aquifers

Dissipation of a mixture of different UV-filters in an aquifer system was studied by Liu et al., 2013. Among the test substances there are UV filters that are significantly more susceptible to biodegradation than phenolic benzotriazoles, e.g. benzophenone-3.[40] The authors assume that interaction effects on degradation are negligible; however, co-metabolism could potentially have occurred. The study was conducted using in different treatments, one of which was aerobic. The other treatments referred to specific anaerobic conditions that are considered not relevant for persistence assessment. The aerobic treatment is reported as it is considered the relevant part of the study. The study appears to be well-conducted, but it simulates the fate of UV filters in aquifers rather than in ponds, rivers or in the sea. Hence, there are some characteristic differences to OECD TG 308:

- Only one sediment was tested (low TOC of 0.4%[41], coarse texture)
- Material for sediment was taken from the aquifer 5 m below the ground surface
- Groundwater sampled from a well nearby with a very low level of dissolved oxygen (0.4 mg/L)

[40] According to the registration dossier, this substance is readily biodegradable but failing the 10 day window. It shows rapid dissipation in the aquifer test with a half-life of 5.3 days.
[41] This value is slightly below the range recommended in the OECD 308 TG.

- Smaller test systems & deviating water sediment ratio (5 g aquifer + 5 mL water)[42]
- The test system was not checked for transformation products.

As no information on equilibration time is available, it is uncertain whether and how equilibration was conducted. The aerobic treatment was conducted in a laminar flow chamber by opening the caps three times a day; however, no information on the level of dissolved oxygen during the test is available.

The incubation temperature was 20 °C and the initial concentration of each compound was given as 1 mg/L. A stock solution was prepared from the radioactively non-labelled test substances and methanol; this solution was used to apply the tests substances in the reaction tubes. The description indicates that the substances were spiked to the sediment with an applied concentration of 1 µg/g per substance in the aquifer sediment. Triplicate sampling was conducted for each treatment at days 0, 7, 14, 21, 28, 35, 49, 63, and 77; test duration was 77 days. Extraction of the freeze-dried sediment samples was done by pressurised liquid extraction (PLE). Analysis of the test substances was accomplished by GC-MS/MS measurements. Based on sterile groundwater and aquifer material systems; recoveries of 94% and 111% were determined for UV-326 and UV-329, respectively.

Fast dissipation of the UV-326 and UV-329 from the water to the sediment in the sterile and non-sterile sample at the beginning of the test was observed. In the sterile controls, the parent concentration in the test system remained constant during the test.

In the non-sterile treatments, a rapid growth of biomass was observed during the first 28 days, which might have been caused by the fast degradation of UV filters like benzophenone-3. During this initial phase of microbial growth, fast dissipation of UV-326 and UV-329 was observed, followed by a phase with significantly slower dissipation. The authors used first-order kinetics to calculate dissipation half-lives of 52 d and 34 d for UV-326 and UV-329, respectively. A re-modelling conducted using the reported data (Cake 3.3, see Annex II) shows that the data were affected by some process that the models cannot adequately compensate for as there is an unsatisfactory visual fit. The residuals confirm that a conclusion based on the data reported by this source should be made with caution as they are quite regularly distributed in every model. Due to these uncertainties, no modelled DT50 is preferred. Model results other than SFO reflect the slow dissipation observed after the initial phase of fast dissipation.[43] At an environmentally relevant temperature of 12 °C, this corresponded to half-life values that are larger, with temperature corrected slow phase DT50 values > 180 days.

Sterile controls were autoclaved at 120 °C for 20 minutes on three consecutive days followed by treatment with sodium azide. The authors report that all tested UV-filters did not dissipate under sterile conditions.

As the substances were not radio-labelled, no information on the formation of non-extractable residues (NER) or transformation products is available. Based on the constant test concentrations in the sterile controls, no significant amounts of NER were formed in this treatment. As UV-326 and UV-329 do not dissipate in the sterile controls, their dissipation in the nonsterile tests appears to be associated with the presence of microorganisms.

The impact of the several deviations from the OECD TG 308 guideline on the study results is unclear. The following conditions may have contributed to the observed dissipation:

[4242] OECD TG 308 outcome can be affected both by test vessel and system geometry and the associated water-sediment interface size (ECHA 2017). There is no specification of the vessel size or geometry in the test guideline, but the system geometry should be consistent with the range indicated in the OECD TG 308.

[43] Calculation results:

	SFO DT50	DFOP		HS		FOMC	
	DT50	DT50_fast	DT50_slow	DT50_fast	DT50_slow	DT50	DT90
UV-326	52.4	19.5	>10,000	38.8	182	47.3	614
UV-329	34.5	25.8	>10,000	24.2	95.2	33.1	133

- In contrast to the study of Wick et al. (2016a, 2016b), this study has a sediment/aquifer with a low organic carbon content. The study on UV-384 described below shows rather fast dissipation of the structurally related metabolite M1 in the sediment with low organic carbon content, but DT50 >180 d for the sediment with high organic carbon content. Thus, the type of sediment may impact the observed dissipation.
- Co-metabolism might have occurred due to the presence of further substances, some of which are more readily biodegradable than phenolic benzotriazoles.
- The formation of non-extractable residues (NER) could have occurred in the sediment phase in the presence of microorganisms. The positive impact of microorganisms on NER formation is also reported in other studies (Botterweck *et al.*, 2014). The biomass growth promoted by other test substances might have contributed to this. No such effect was observed in the study of Wick et al. (2016a, 2016b). However, both studies show some characteristic differences.
- The location from which aquifer and water were sampled possibly resulted in the use of a pre-adapted microbial population. Both were drawn in the vicinity of the waste water treatment plant of Bolivar, a district of Adelaide, Australia that feeds its water into reservoirs for irrigation use. Exposition of the withdrawal site with phenolic benzotriazoles may have occurred beforehand as a complete withholding of particles in a wastewater treatment plant seems unrealistic.
- Several deviations from the OECD TG 308 guideline may have an impact on the study results, although there is no straightforward interpretation to explain the observed results. However, as mentioned above, results of the re-modelling were not satisfactory and the derived DT50 values should be treated with caution.

This study is considered as reliable with restrictions. Derivation of DT50 values is challenging. Testing conditions were designed to simulate aquifers and the test system does not correspond to common water sediment studies.

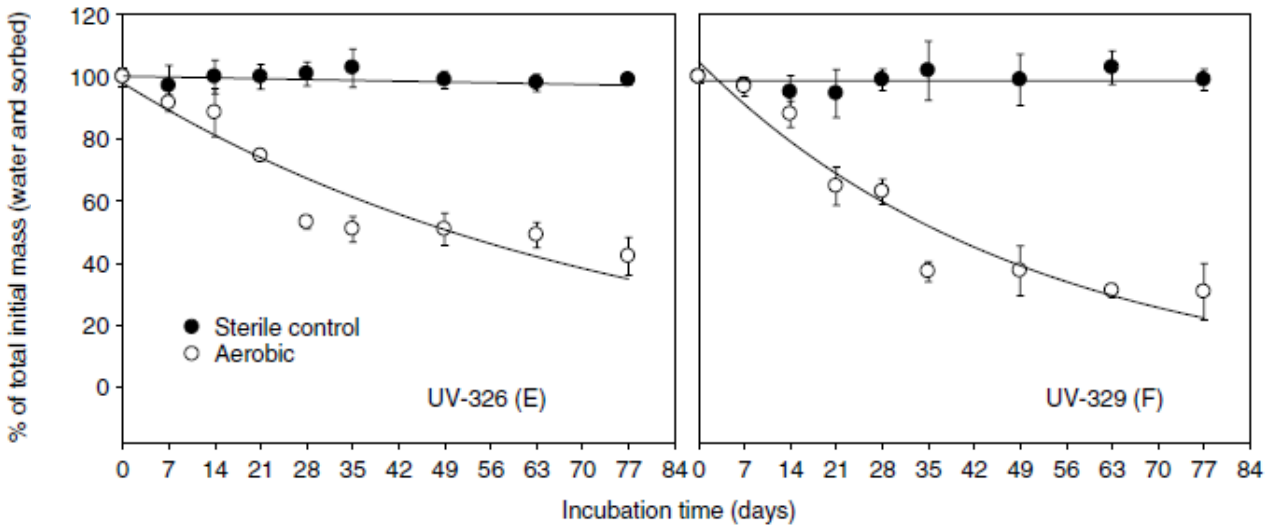


Figure 6: Dissipation of UV-326 and UV-329 (initial concentration of µg/g) in aerobic aquifer microcosms media. Error bars indicate standard deviations of the residual concentrations (n = 3) (Liu et al., 2013).

3.1.4.2.3.3 Study on UV-384 and its metabolite M1 in river and pond sediment systems

A detailed discussion of this study is given in the SVHC support documents for UV-328, UV-320, UV-327 and UV-350 (ECHA 2014a, ECHA 2014b, ECHA 2015a, ECHA 2015b). Therefore, only a short summary is provided here:

From the simulation studies on radiolabelled UV-384 (EC 407-000-3), the first metabolite of the substance (M1) is its carboxylic acid. M1 is structurally very similar to UV-326 and, to a lesser extent, also structurally similar to UV-329 (see beginning of section 3 on structurally related substances).

Two simulation tests for the substance EC 407-000-3 and its main metabolite M1 were evaluated. These tests were conducted according to OECD TG 308 at a test temperature of 20 °C. One test was done under aerobic conditions for a river system and a pond system, the other test was conducted under anaerobic conditions for a pond system. It was not possible to derive degradation half-lives for comparison with the trigger values as given in Annex XIII of REACH, but dissipation half-lives were derived. The absolute values for the pond system have to be interpreted with care as only part of the degradation curves of M1 were monitored.

Depending on the test system the observed dissipation half-lives DT50 for M1 varied:

- The aerobic river system had a low organic carbon content (0.95%); the DT50 values for M1 in the water and the sediment phase were 3 days and 32 days, respectively.
- The aerobic pond system had a high organic carbon content (5.04 %); the DT50 values for M1 in the water and the sediment phase were 4 days and 248 days, respectively.
- The anaerobic pond system had a high organic carbon content[44]; the DT50 values for M1 in the water and the sediment phase were 12 days and 238 days, respectively.

In summary, M1 has a DT50 > than 180 days both in the aerobic and in the anaerobic pond sediment, but a DT50 < 120 days in the aerobic river sediment.[45]

M1 is structurally more similar to UV-326 than to UV-329. Based on biodegradation estimations it is expected that M1's susceptibility to degradation is similar or higher than that of UV-326 (DegT50(M1) ≤ DegT50(UV-326)). As a consequence and based on structural similarities, it can be concluded that UV-326 is expected to have comparable degradation behaviour as M1 and thus it is expected to fulfil the vP criteria of REACH Annex XIII (DegT50 >180 days).

3.1.4.2.4 Field data with information from sediment cores

Table 21: Field data with information from sediment cores and related studies

Type of Evidence / Source Name - Reference	Relevance	Reliability	Adequacy
Field study with dated sediment cores from Pearl River (Peng *et al.*, 2017)	Yes, covering parameters required for assessment.	Klimisch score 2	UV-326: Adequate study for time profiles of sediment contamination, indicative of persistence in sediments. UV-329: Adequate study for time profiles of sediment contamination.
Field study with dated sediment cores from Salem Sound & Narragansett Bay (Cantwell *et al.*, 2015)	Yes, covering parameters required for assessment.	Klimisch score 2	UV-326: Adequate study for time profiles of sediment contamination, indicative of persistence in sediments. UV-329: Adequate study for time profiles of sediment contamination with a structurally related substance, indicative of persistence in sediments.
Field Study with sediment cores from Pawtuxet River (all) & Narragansett Bay (UV-P, UV-327, UV-328) (Reddy *et al.*, 2000)	Yes, covering parameters required for assessment.	Klimisch score 2	UV-326: Adequate study for time profiles of sediment contamination, indicative of persistence in sediments UV-329: Adequate study for time profiles of sediment contamination with a structurally related substance, indicative of persistence in sediments.

[44]The organic carbon content is not explicitly given, but the sediment is sampled from the same site as the aerobic pond, i.e. TOC is expected to be equal or at least similar.
[45] Correction to an environmentally relevant temperature of 12°C would lead to higher half-life values, but not to a difference regarding fulfilment of the P and vP criterion for freshwater sediment.

Field Study with sediment cores from Pawtuxet River (Lopez-Avila and Hites, 1980)	Supporting, covering some parameters required for assessment.	Klimisch score 2	Study for profiles of sediment contamination, adequacy limited because study is on structurally related substances and not on the target. Study supports findings of Cantwell *et al.*, 2015; Reddy *et al.*, 2000; White *et al.*, 2008.
Field Study with sediment cores from Narragansett Bay (Hartmann *et al*., 2005)	Supporting, covering some parameters required for assessment.	Klimisch score 2	Study for profiles of sediment contamination, adequacy limited because study is on structurally related substances and not on the target. Study supports findings of Cantwell *et al.*, 2015; Reddy *et al.*, 2000; White *et al.*, 2008.
Field Study with sediment cores from Providence River & Narragansett Bay (Pruell and Quinn, 1985)	Supporting, covering some parameters required for assessment.	Klimisch score 2	Study for profiles of sediment contamination, adequacy limited because study is on structurally related substances and not on the target. Study supports findings of Cantwell *et al.*, 2015; Reddy *et al.*, 2000; White *et al.*, 2008.
Field Study including sediment samples from Pawtuxet River (White *et al.*, 2008)	Supporting, covering some parameters required for assessment.	Klimisch score 2	UV-326: Adequate study for sediment contamination, supporting indication of persistence in sediments. UV-329: Adequate study for sediment contamination with a structurally related substance, supporting indication of persistence in sediments.
Field study including sediment cores from Providence River & Narragansett Bay but without profiles (Latimer and Quinn, 1996)	Supporting, covering some parameters required for assessment.	Klimisch score 2	UV-326 & UV-329: Adequacy limited because study is on structurally related substances and not on the target. Measured data for phenolic benzotriazoles are used as markers but not given in the study; study includes data on production history of phenolic benzotriazoles in Cranston, Rhode Island. Study supports findings of Cantwell *et al.*, 2015; Reddy *et al.*, 2000; White *et al.*, 2008.
Field Study (Jungclaus *et al.*, 1978)	Supporting, covering some parameters required for assessment.	Klimisch score 2	UV-326 & UV-329: Study for contamination of water and sediment by industrial wastewater, adequacy limited because study is on structurally related substances and not on the target. Study supports findings of Cantwell et al., 2015; Reddy et al., 2000; White et al., 2008.

Sediment cores and detections related to sediment cores include information on whether pollutants emitted in the past are still detectable after a certain time span. The original exposure is often unknown. Detection of a substance in sediment layers dating back years or decades ago can be considered indicative of high persistence. In these cases, the concentration profiles can be considered to reflect past exposure. The lack of detection of a substance does not necessarily mean that it is not persistent.

Data are available for UV-326, UV-P, UV-327, UV-328, and UV-320. UV-P is structurally very similar to UV-329. The phenolic benzotriazoles UV-327, UV-328, and UV-320 are structurally very similar to UV-326 (see beginning of section 3 on structurally related substances).

Observed concentrations are particularly high near point sources like the former chemical production plant at Cranston in Rhode Island. While the lower concentrations influenced by diffuse entries are of higher environmental relevance, the contaminated sites in Rhode Island are well-examined by a variety of studies and the high concentrations allow to study the fate of the substances more comprehensively.

3.1.4.2.4.1 Sediment cores from Pearl River

The Pearl River Estuary in China is influenced by diffuse sources. Peng *et al.* (2017) sampled sediment cores and analysed them for several pollutants, including the phenolic benzotriazoles UV-329, UV-326, UV-P, UV-327 and UV-328. Available data on sedimentation rate were used to estimate the year of deposition.[46] The sediment layers of detection of UV-326 date back several decades (covering the period 1965 to 2004), indicating very high persistence in sediment. Data on UV-329, UV-P and UV-327 were not reported in the publication. According to a personal communication with the study author, UV-329 was mostly not detected or close to the method quantification limit (MQL), whereas UV-P fluctuated at 0.41-1.45 ng/g dw in the first sediment core C1 and at 0.19-1.77 ng/g dw in the second sediment core C2, without obvious trends (Peng 2023). As a comparison, the structurally related vP substances UV-327 and UV-328 were also detected. While UV-328 was reported in the publication as one of the more abundant UV absorbers, detected levels of UV-327 were about 0.74-1.84 ng/g dw along C1 and trace level in some layers of C2 (Peng 2023).

As historic exposure data are missing, the non-detection / low detection of UV-329 cannot be interpreted unambiguously. While all phenolic benzotriazoles are used as UV filters, their respective history of production and use in China is expected to differ. Available data from ready biodegradation tests and structural considerations do not indicate a significantly different biodegradation behaviour for UV-P and UV-329. Thus, it is assumed that exposure to UV-329 was lower than exposure to the other phenolic benzotriazoles, resulting in concentrations below or close to the analytical limits.

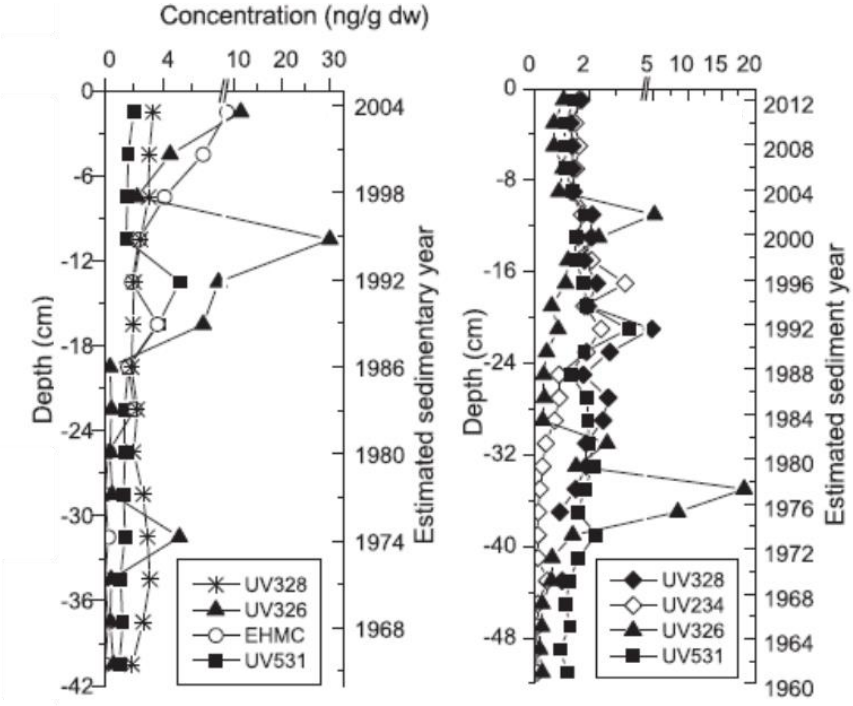


Figure 7: Vertical profiles of UV absorbents in the sediment cores C1 (left) and C2 (right) from the Pearl River Estuary (adapted from Peng *et al.*, 2017).

[46] The available sedimentation rate is based on radiometric dating, see https://doi.org/10.1016/j.scitotenv.2007.05.043 .

3.1.4.2.4.2 Sediment cores from Salem Sound

Cantwell *et al.* (2015) studied benzotriazole contamination in Salem Sound, Massachusetts, USA. Salem Sound is an urban estuary not influenced by nearby benzotriazole production sites; sediment cores were sampled in May 2010 near the South Essex Sewage District outfall pipe. Radiometric dating was used to develop an age model. One sediment core was analysed for several phenolic benzotriazoles, among them UV-326 and UV-P. Results are depicted in Figure 8. The sediment layers from 11 cm depth to the surface of the core are considered undisturbed, while deeper sediment layers are considered affected by physical disruption.[47] The sediment layers of detection of UV-326, UV-P and other phenolic benzotriazoles date back several decades, indicating very high persistence in sediment.

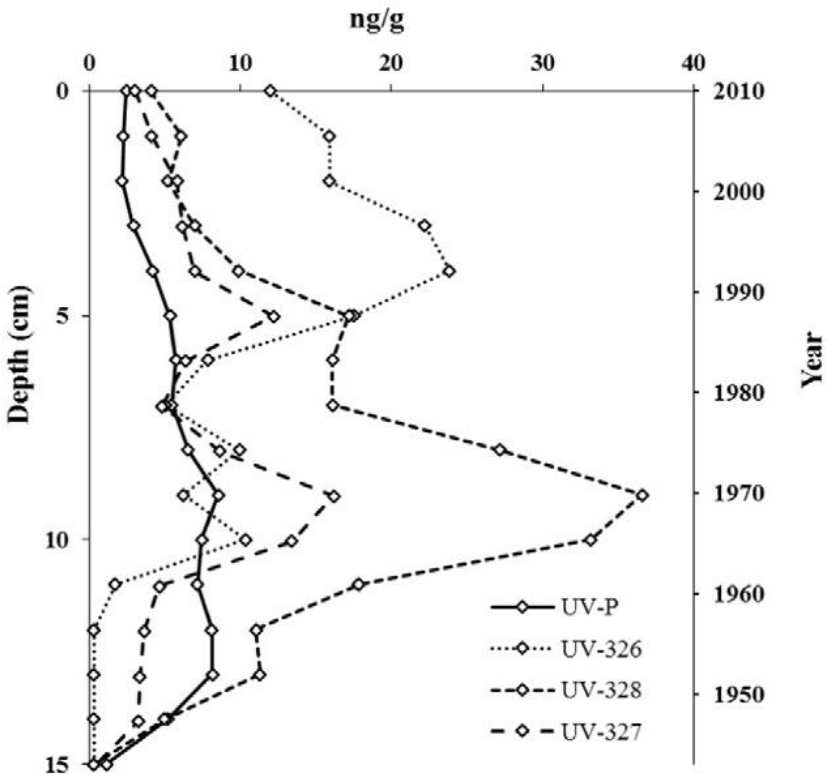


Figure 8: UV-Benzotriazoles in Salem Sound sediments (from Cantwell *et al.*, 2015).

3.1.4.2.4.3 Sediment cores and associated data from Pawtuxet River, Providence River and Narragansett Bay [48]

Until its closure in 1985 (Latimer and Quinn, 1996), a former chemical plant in Cranston, Rhode Island, USA discharged its industrial wastewaters in the Pawtuxet River. These wastewaters contained various chemicals produced at the plant, among them several phenolic benzotriazoles (Jungclaus *et al.*, 1978; Lopez-Avila and Hites, 1980). Consequently, contamination of Pawtuxet river sediments with phenolic benzotriazoles has been shown in several studies (Jungclaus *et al.*, 1978; Lopez-Avila and Hites, 1980; Reddy *et al.*, 2000; White *et al.*, 2008). Furthermore, these contaminated sediments from the Pawtuxet river are resuspended and transported, resulting in contamination of sediments downstream in the Providence River and the Narragansett Bay as well (Lopez-Avila and Hites, 1980; Pruell and Quinn, 1985; Latimer and Quinn, 1996, Reddy *et al.*, 2000; Hartmann *et al.*, 2005; Cantwell *et al.*, 2015).

[47] The presence of phenolic benzotriazoles in deeper sediment layers would correspond to decades prior to their production and thus, these findings indicate a past physical disruption of the sediment. However, based on radiometric data, there appears to be no significant post-sedimentation disturbance from 11 cm to the surface of the core.
[48] Except for the most recent study from Cantwell, these monitoring data have been discussed in the SVHC dossiers for UV-328, UV-320, UV-327 and UV-350 (ECHA 2014a, ECHA 2014b, ECHA 2015a, ECHA 2015b).

Based on this set of studies, environmental contamination of this area with phenolic benzotriazoles is quite well-documented. Hence, studies on sediment cores from this area can use a comprehensive data set to support the interpretation of the analytical results. Based on the available data, UV-P, UV-327 and UV-328 appear to be the most abundant (Reddy *et al.*, 2000); UV-326 was detected in some studies as well (Reddy *et al.*, 2000; White *et al.*, 2008; Cantwell *et al.*, 2015; potentially[49] also in Lopez-Avila and Hites, 1980).

UV-P, UV-327 and UV-328 were used as markers along with other characteristic contaminants; known data on start and stop of production were used to estimate the age of sediment core sections (Lopez-Avila and Hites, 1980; Pruell and Quinn, 1985; Latimer and Quinn, 1996; Hartmann *et al.*, 2005). While the dating of these sediment cores is partially based on the substances themselves, the agreement with other markers indicates that they are present in sediment layers deposited years / decades before sampling.

White and co-workers (2008) analysed sediments from Pawtuxet River that were sampled in 2003, i.e., about 18 years after closure of the chemical plant. No phenolic benzotriazoles were detected in the sample upstream the chemical plant, while several phenolic benzotriazoles were detected in the samples downstream, including UV-326 and UV-P.

Two studies on sediment cores from this area are of particular interest:

Sediment core from Narragansett Bay with radiometric dating

Cantwell et al. (2015) studied benzotriazole contamination in a sediment core from Narragansett Bay that was sampled in October 2007. Radiometric dating was used to develop an age model. The sediment core was analysed for several phenolic benzotriazoles, including UV-326[50] and UV-P (see Figure 9). The results were compared with available data on production history: Sediment layers of detection of UV-326, UV-P and other phenolic benzotriazoles date back to 1961 when first patents for some of these compounds were documented. Phenolic benzotriazoles are also detected in sediment layers that correspond to the years after the production stop in 1985. The authors explain this by the transport of resuspended sediments from Pawtuxet River to the Bay. The concentration peak of UV-326 at ca. 1991 cannot be explained based on the available data and no comparable behaviour is observed for the other phenolic benzotriazoles examined in this study.

As expected, measured concentrations at Narragansett Bay were significantly higher as concentrations at the core from Salem Sound examined in the same paper and described above.

[49] Detected substance is given as 2-(hydroxy-tert-butyl methylphenyl)-5-chloro-2*H*-benzotriazole, a name which is not specific about the position of the hydroxy group, the t-butyl group and the methyl group. However, it is assumed that it is UV-326 as this is the only isomer known to be manufactured.
[50] UV-P, UV-327, UV-328 and UV-320.

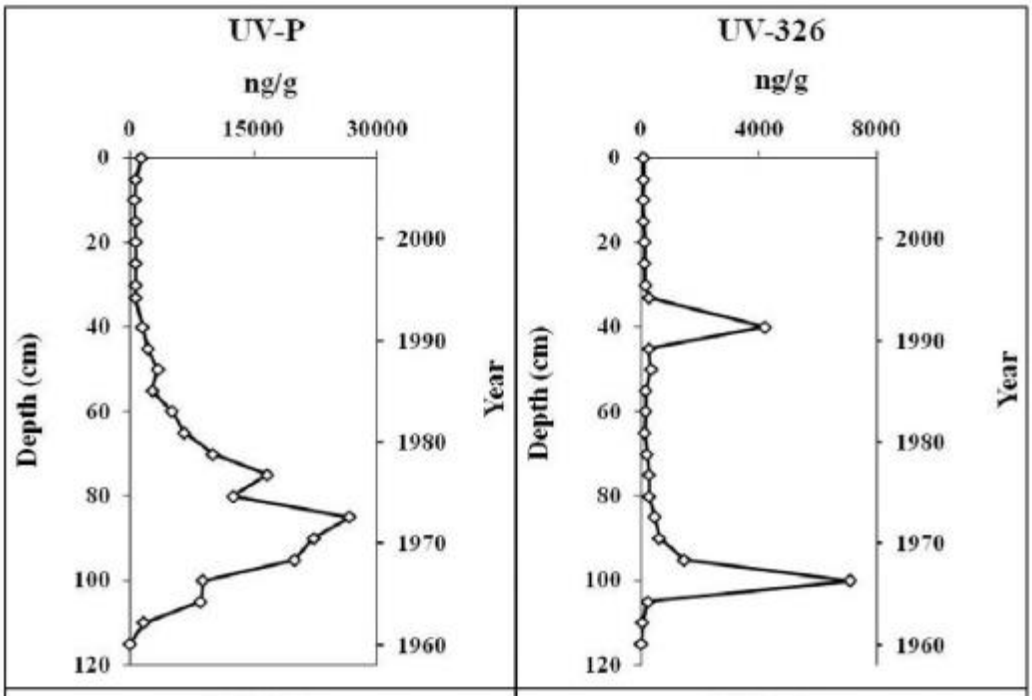


Figure 9: UV-326 and UV-P in Narragansett Bay(from Cantwell et al. (2015)).

Sediment cores from Narragansett Bay and Pawtuxet River

Reddy *et al.* (2000) analysed two sediment cores for UV-326, UV-P and other phenolic benzotriazoles. Free and bound benzotriazoles were analysed and the ratio between free and bound benzotriazoles was discussed. One of the cores had been sampled from Pawtuxet River and the other from Narragansett Bay. The core sections were not assigned to specific dates, but sedimentation rates of the sample locations were known and the authors estimate that the deepest core sections approximately date back to the start of phenolic benzotriazoles production, which they specify as about 1961-1970.

In the Narragansett Bay core, the most abundant phenolic benzotriazoles UV-P, UV-327 and UV-328 were significantly more concentrated than UV-326 and other phenolic benzotriazoles; only their results are presented in the study. UV-P was detected in all sections of the sediment core. The authors give a sedimentation rate of 0.3 cm/yr for the sampling location; the respective core was sampled in 1997. The deepest section of the core with a depth from 13 to 10 cm would thus correspond to the years from 1954 to 1964.

The sampling site at Pawtuxet River is closer to the chemical plant and the authors give a sedimentation rate of 2-3 cm/yr. The core was sampled in 1989. The deepest section with a depth of 52 cm to 50 cm would thus correspond to the years 1963-1964 (2 cm/yr) or to the year 1972 (3 cm/yr), respectively. UV-P was detected in all sections of the core. UV-326 was detected in sections up to a depth of about 20 cm, which would correspond to the years 1979 (2 cm/yr) or 1982 (3 cm/yr), respectively.

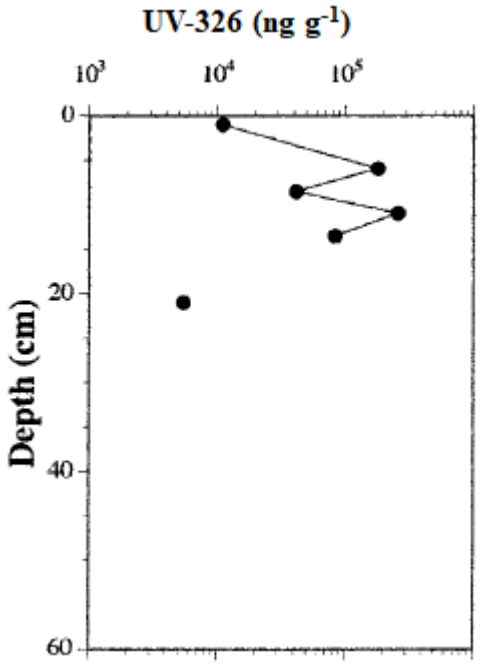


Figure 10: free UV-326 in the Pawtuxet River core (adapted from Reddy *et al.,* 2000).

Sediment core studies described above provide indirect evidence that UV-326 and potentially UV-329 (as a structurally related substance to UV-P) can persist in sediments for several decades.

3.1.4.3 Biodegradation in soil

3.1.4.3.1 Soil dissipation studies

Table 22: Soil dissipation studies

Type of Evidence / Source Name - Reference	Relevance	Reliability	Adequacy
Soil dissipation study (Lai *et al.*, 2014a)	Yes, covering parameters required for assessment.	Klimisch score 2	Adequate study for dissipation in soil, indicative of persistence in soil
Soil dissipation study (Lai *et al.*, 2014b)	Yes, covering parameters required for assessment.	Klimisch score 2	Adequate study for dissipation in soil, indicative of persistence in soil

Lai and co-workers (Lai *et al.*, 2014a; 2014b) examined the dissipation behaviour of several phenolic benzotriazoles (UV-326, UV-329, UV-327, UV-328, and UV-P) in order to assess whether the application of biosolids as fertilisers in agricultural land might be a relevant pathway for environmental contamination.[51]

In the first study (Lai *et al.*, 2014a), dewatered sludge from a WWTP in Beijing was applied onto agricultural land in Shandong, China. The sludge was not further amended with reference substances or benzotriazoles meaning that all benzotriazoles were incorporated in it. In the first

[51] The first study (Lai *et al.*, 2014) has been discussed in the SVHC dossiers for UV-328, UV-320, UV-327 and UV-350 (ECHA 2014a, ECHA 2014b, ECHA 2015a, ECHA 2015b).

experiment (Treatment T1) this was done only once in May 2007 while in the second experiment (Treatment T2) application was repeated every year in October from 2007 until 2010. Each treatment consisted of application of the same dewatered sludge on four replicates. In addition, there was a control site where no treatments were conducted. In order to incorporate the sludge, the trial fields were ploughed to a depth of 20 cm. On the fields wheat and maize were cultivated.

Starting from October 2010 until October 2011, soil samples were taken monthly at a depth between 0 and 20 cm. Each sampling of the four replicates consisted of five subsamples that were mixed. Due to experimental problems this practice was stopped in winter and resumed in March 2011. The soil samples were extracted with methanol/dichloromethane (50:50, v/v) at 120 °C for 5 minutes in two cycles. Concentrations of the benzotriazoles were detected via GC-MS. The recovery in soil was 81.7% for UV-326 and 117% for UV-329. For UV-326 the limit of detection in soil was 0.2 ng/g and the limit of quantification in soil 0.67 ng/g. For UV-329 the respective limits were slightly higher (limit of detection 0.25 ng/g and limit of quantification 0.84 ng/g).

At the beginning of the measurements (October 2010 to March 2011), considerable variability (i.e., a rise) of the concentrations was reported by Lai *et al*., 2014a. The authors attribute this to problems with obtaining a homogenous sample during the frost period or the degradation processes in samples during storage until extraction. No information is given if these were the reasons for the occurring variability and how this problem was finally solved. Beginning with March 2011 the problem was eliminated. In all the control samples only trace concentrations at the limit of quantification of UV-327 were detected, but other phenolic benzotriazoles were not found.

Due to the problem described above the authors performed a dynamic curve-fitting only between March 2011 and October 2011. They report the following times for field dissipation:

Table 23: Overview of reported DT50-values (dissipation in the field) by Lai *et al.* (2014a)

Substance	**UV-326**		**UV-329**	
Treatment	**T1**	**T2**	**T1**	**T2**
DT50 [d]	104	141	129	98
Error [d]	10	17	28	16

As the authors employed SFO-kinetics there should be essentially no difference in DT50-values between T1 and T2 as this kinetic model is independent of concentration. As can be seen in Table 23 in some cases T1 is larger and in some T2, but when additionally taking into account the reported errors there is an overlap of the band of T1- and T2-values for all substances with the exception of UV-326.

- For UV-326, DT50 values of 104 days and 141 days were determined for treatment 1 and treatment 2, respectively.
- For UV-329, DT50 values of 129 days and 98 days were determined for treatment 1 and treatment 2, respectively.

A detailed discussion of this study is given in the SVHC support documents for UV-328, UV-320, UV-327 and UV-350 (ECHA 2014a, ECHA 2014b, ECHA 2015a, ECHA 2015b). .

A very similar study from the same authors on the same type of test soil at the same location is available (Lai *et al.*, 2014b). This study includes treatment groups with repeated biosolid applications every year (OT1, OT2, OT3, OT4), groups with biosolid applications only during the first year (NT2, NT3, NT4) and control sites. Field studies started in October 2006, with sampling conducted from October 2010 to October 2011.

The soil samples were extracted with methanol/dichloromethane (50:50, v/v) at 120 °C for 5 minutes in two cycles. Concentrations of the benzotriazoles were detected via GC-MS. The recovery in soil was 81.7% for UV-326 and 117% for UV-329. For UV-326 the limit of detection in soil was 0.1 ng/g and the limit of quantification in soil 0.32 ng/g. For UV-329 limit of detection was 0.09 ng/g and the limit of quantification was 0.30 ng/g.
The phenolic benzotriazoles were detected in all samples from sites with biosolid application, but not in the control groups. Concentrations of the target compounds increased from October 2010 to March 2011 – an effect observed in the other study (Lai *et al.*, 2014a) as well. Hence, in analogy to the approach from the related study, the authors performed dynamic curve fitting for the period of March 2011 to October 2011.

Table 24: Overview of reported DT50-values (dissipation in the field) by Lai *et al.* (2014b)

Treatment	Biosolid application [t ha^{-1}]	Substance	
		UV-326	UV-329
OT1	5 every year	90	91
OT2	10 every year	96	93
OT3	20 every year	128	97
OT4	40 every year	122	94
NT2	10 once	81	79
NT3	20 once	120	106
NT4	40 once	135	155

The observed dissipation shows variation with respect to the different treatments:

- For UV-326, modelled DT50 values in the different treatments ranged from 81 days to 135 days.
- For UV-329, modelled DT50 values in the different treatments ranged from 79 days to 155 days.

The results of these two soil dissipation studies have to be regarded as best cases for the disappearance in the environment as:

- they only reflect the warmer period of the year. Longer DT50s are expected during colder period of the year;[52]
- three (Lai et al 2014a) to four (Lai et al 2014b) years passed between (first) application and measurements, therefore potentially allowing microorganisms to adapt;
- only dissipation was monitored;
- NER were not considered at all.

The field studies of Lai *et al.* (2014a, 2014b) have some practical shortcomings: The concentrations of the different benzotriazoles in the sludge are missing and no initial concentration values for the different field trials after the first[53] applications of the biosolids are given. In addition, the limits of detection and quantification are quite high, at least compared to the concentrations found in some applications. To assess the method, it would also have been helpful to determine the level of NERs. Furthermore, the concentration values during the sampling time varied: for unknown reasons there was a rise in concentration levels during the

[52] The average annual temperature of the site is 12.9°C but no information on seasonal variation is given. It can be assumed that the average temperature during the modelled timeframe was larger than 12°C and that a longer DT50 could be expected for the whole year.
[53] In case of repeated application, concentration values for the subsequent applications before October 2010 are missing as well.

winter months. This was solved by not considering them in the kinetic simulation, which in turn lowers the number of data points for fitting. Finally, it would have been helpful to employ a substance with known DT50 value as a point of reference. A shortcoming for the use in this dossier is that the study gives information on primary disappearance only, since none of the metabolites were determined.

Based on the above two field studies, it is concluded that UV-326 and UV-329 are persistent (and potentially very persistent) in soil (at least D1 T50 in soil >120 days).

3.1.5 Integration and Weighing of evidence (WoE analysis) and Application of Levels of Confidence

3.1.5.1 Abiotic Degradation

Based on general chemistry knowledge, UV-326 and UV-329 are not expected to be susceptible to hydrolysis. The registration dossier for UV-329 contains references to general texts about the hydrolysis of organic compounds that support this expectation. HYDROWIN does not find hydrolysable groups and CATALOGIC predicts no abiotic transformation under OECD 301 C testing conditions. Thus, all available lines of evidence support the assumption that the substances do not hydrolyse under environmental conditions.

Table 25: Integration and weighing of evidence for abiotic degradation

Type of Evidence	Consistency & Specificity	Likelihood/ Biological Plausibility	Temporality	Confidence / Strength of Evidence	Remaining Uncertainty
HYDROWIN	Prediction of hydrolysis, result consistent with general knowledge about hydrolysis of organic compounds	Plausible	Not relevant	low strength of evidence	Medium
CATALOGIC Abiotic	Prediction of abiotic transformation under OECD 301 C testing conditions; result consistent with general knowledge about hydrolysis of organic compounds	Plausible	Not relevant	low strength of evidence	Medium
References to Literature	General knowledge about hydrolysis of organic compounds	Plausible	Not relevant	High/Medium strength of evidence	Low
Conclusion from overall confidence	No hydrolysis under environmental conditions (High/Medium Confidence)				

The (Q)SAR predictions are not all valid as some of the predictions are not within the applicability domain. Thus, their overall weight is low. Based on general principles of chemistry, the chemical structure does not contain functional groups that are susceptible to hydrolysis. This finding is given the highest weight. The registrants of UV-329 included some general references on the hydrolysis of organic compounds which support this finding. In summary, it is concluded that the substances are expected to show no hydrolysis under environmental conditions with high confidence.

3.1.5.2 Biodegradation in aqueous media or aqueous environment

The (Q)SAR results can be considered as screening information and as prediction of ready biodegradability. Based on both EPISUITE and CATALOGIC results, the substances are not expected to be readily biodegradable.

While all CATALOGIC models predicted ultimate half-life values in the range of months or years, some predicted primary half-life values are in the range of days. However, the preferred model CATALOGIC 301 C v12.17 predicts primary half-life values in the range of months.

UV-326 and UV-329 were found to be not readily biodegradable in the available screening tests.

For both substances, no biodegradation after 100 days was observed in a water sediment study conducted at 20 °C, i.e., the respective DegT50 is >>100 days. The reference temperature for simulation tests is 12 °C[54], and degradation at 12 °C is expected to proceed even more slowly[55]. Application of the Arrhenius equation to extrapolate from 20 °C to 12 °C would result in a factor of about 2.12; i.e., the corresponding DegT50 at 12 °C would be >>212 days.

In an aquifer study (Liu 2013) conducted at 20 °C, observed dissipation was larger than expected based on the other data. Application of first order kinetics yielded dissipation half-lives of 52 d and 34 d for UV-326 and UV-329, respectively. Other kinetic models indicate lower dissipation in the slow phase. The corresponding DT50 values at 12°C would be higher.

M1 is a structurally related substance to UV-326 and UV-329 and a metabolite of UV-384. Water sediment simulation studies on UV-384 showed that M1 is very persistent.

UV-P is a structurally related substance to UV-329. UV-P, UV-326 and further phenolic benzotriazoles have been detected in sediment sections that date back years or even decades, both in samples downstream from a former point source and in samples from urban estuaries. 18 years after closure of a chemical plant, UV-326 and UV-P were still detected in sediments sampled downstream the site, but not in sediment samples from upstream the site.

With exception of the aquifer study, all available lines of evidence support the assumption that the UV-326 and UV-329 are very persistent in sediment.

[54] ECHA 2017a. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.11: PBT/vPvB assessment. Version 3.0, p. 59.
https://echa.europa.eu/documents/10162/13632/information_requirements_r11_en.pdf/a8cce23f-a65a-46d2-ac68-92fee1f9e54f (accessed February 2022)
ECHA 2017b. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.7b: Endpoint specific guidance. Version 4.0, p. 219, 221-222.
https://echa.europa.eu/documents/10162/13632/information_requirements_r7b_en.pdf/1a551efc-bd6a-4d1f-b719-16e0d3a01919 (accessed February 2022)
EC (European Commission). 2003. Technical Guidance Document in support of Commission Directive 93/67/EEC on risk assessment for new notified substances and Commission Regulation (EC) No 1488/94 on risk assessment for existing substances and Commission Directive (EC) 98/8 on biocides. 2nd Edition, Luxembourg: European Commission.EC (European Commission) 2006, p. 49 and 53.

[55] Application of the Arrhenius equation to extrapolate from 20 °C to 12 °C would result in a factor of about 2.12. This would mean that DT50 >>212 days.

Table 26: Integration and weighing of evidence for biodegradation in water sediment systems.

Type of Evidence	Consistency & Specificity	Likelihood/ Biological Plausibility	Temporality	Confidence / Strength of Evidence	Remaining Uncertainty
BIOWIN	Consistent predictions indicating the substances are not readily biodegradable	Plausible	Not relevant	Low strength of evidence	High
CATALOGIC	Consistent predictions indicating the substances are not readily biodegradable	Plausible	Not relevant	low strength of evidence	High
Biodegradation Screening test OECD TG 301B 1989, UV-329	Consistent experimental study indicating UV-329 is not readily biodegradable	Plausible	Not relevant	low strength of evidence	High
Biodegradation Screening test OECD TG 301B 2007, UV-326	Consistent experimental study indicating UV-326 is not readily biodegradable	Plausible	Not relevant	low strength of evidence	High
Biodegradation Screening test OECD TG 301C 1996, UV-326	Consistent experimental study indicating UV-326 is not readily biodegradable	Plausible	Not relevant	low strength of evidence	High
Biodegradation Screening test OECD TG 301B 1988, UV-326	Consistent experimental study indicating UV-326 is not readily biodegradable	Plausible	Not relevant	low strength of evidence	High
Water sediment simulation study (Wick A *et al.*, 2016a, 2016b)	Consistent experimental study indicating the substances are very persistent in sediment	Plausible	Not relevant	High strength of evidence	Low
Aquifer simulation study (Liu Y-S *et al.*, 2013)	Experimental study indicating the substances dissipates in aquifer sediments, not consistent with other data	Limited plausibility: high stability of molecular structure and other experimental data on sediments show limited / no degradation	Not relevant	Low/Medium confidence; low strength of evidence	Medium / High
OECD 308 Simulation study on UV-384 (EC 407-000-3) and its metabolite M1	Consistent experimental study indicating a structural analogue is very persistent in sediment	Plausible	Not relevant	UV-326: Medium strength of evidence UV-329: Low strength of evidence	Medium / Low UV-326: Medium / Low UV-329: High
Field study with dated sediment cores from Pearl River (Peng *et al.*, 2017)	UV-326: Consistent monitoring study indicating UV-326 is very persistent in sediment UV-329: Consistent monitoring study	Plausible	Not relevant	UV-326: medium strength of evidence UV-329: low strength of evidence	UV-326: Medium / Low UV-329: High
Field study with dated	UV-326: Consistent	Plausible	Not relevant	UV-326:	UV-326:

sediment cores from Salem Sound & Narragansett Bay (Cantwell MG *et al.*, 2015)	monitoring study indicating UV-326 is very persistent in sediment UV-329: Consistent monitoring study indicating a structurally related substance (UV-P) is very persistent in sediment			medium strength of evidence UV-329: medium strength of evidence	Medium / Low UV-329: Medium
Field Study with sediment cores from Pawtuxet River (all) & Narragansett Bay (Reddy CM *et al.*, 2000)	UV-326: Consistent monitoring study indicating UV-326 is very persistent in sediment UV-329: Consistent monitoring study indicating a structurally related substance (UV-P) is very persistent in sediment	Plausible	Not relevant	UV-326: medium strength of evidence UV-329: medium strength of evidence	UV-326: Medium / Low UV-329: Medium
Field Study with sediment cores from Pawtuxet River (Lopez-Avila V and Hites, RA 1980)	UV-326: Consistent monitoring study supporting findings from Cantwell et al. and Reddy et al. UV-329: Consistent monitoring study indicating a structural analogue (UV-P) is very persistent in sediment	Plausible	Not relevant	low strength of evidence	Medium / High
Field Study with sediment cores from Narragansett Bay (Hartmann PC *et al.*, 2005)	UV-326: Consistent monitoring study supporting findings from Cantwell et al. and Reddy et al. UV-329: Consistent monitoring study indicating a structural analogue (UV-P) is very persistent in sediment	Plausible	Not relevant	low strength of evidence	Medium / High
Field Study with sediment cores from Providence River & Narragansett Bay (Pruell RJ and Quinn, JG 1985)	UV-326: Consistent monitoring study supporting findings from Cantwell et al. and Reddy et al. UV-329: Consistent monitoring study indicating a structural analogue (UV-P) is very persistent in sediment	Plausible	Not relevant	low strength of evidence	Medium / High
Field Study including sediment samples from Pawtuxet River (White *et al.*, 2008)	UV-326: Consistent monitoring study indicating UV-326 is very persistent in sediment UV-329: Consistent monitoring study indicating a structural analogue (UV-P) is very persistent in sediment	Plausible	Not relevant	low strength of evidence	Medium / High
Field study including sediment cores from Providence River &	UV-326: Consistent monitoring study supporting findings from Cantwell et al.	Plausible	Not relevant	low strength of evidence	Medium / High

Narragansett Bay but without profiles (Latimer JS and Quinn, JG 1996)	and Reddy et al. UV-329: Consistent monitoring study indicating a structural analogue (UV-P) is very persistent in sediment				
Field Study (Jungclaus GA *et al.*, 1978)	Consistent monitoring study supporting findings from Cantwell *et al.* (2015) and Reddy *et al.* (2000)	Plausible	Not relevant	low strength of evidence	Medium / High
Conclusion from overall confidence	UV-326 and UV-329 are very persistent in sediment (High Confidence)				

As the (Q)SAR models are trained on test results on ready biodegradability or - in the case of BIOWIN 3 and 4 - on expert judgement, they are considered as screening information with a low weight in the WoE approach for the P assessment of UV-326 and UV-329. Their results are consistent with the other data. Both UV-326 and UV-329 could be considered in the BIOWIN domain when following the recommendations of the User Guide, though the models are not trained on phenolic benzotriazoles. The CATALOGIC models include an automatic determination of applicability domain, which is much stricter. UV-329 is not in the domain of any of the CATALOGIC models, though the prefered model includes some structurally related phenolic benzotriazoles in the training set. UV-326 is in the applicability domain of this one preferred model as it was part of the training set.

The available screening tests are considered valid and reliable. Their results are consistent with the other data. They are considered as screening information with a low weight in the WoE approach.

The water-sediment study for UV-326 and UV-329 shows slight deviations from OECD TG 308 but the impact of the deviations on the test is not considered detrimental. The results are consistent with the other data supporting the evidence that UV-326 and UV-329 are very persistent in sediment. The confidence level for this study is high and it is given the highest weight in the WoE evidence approach for the P assessment.

The aquifer study shows more dissipation than expected based on the other data. The study conditions represent aquifers rather than systems tested in common water sediment studies. Several deviations from the OECD TG 308 guideline may have an impact on the study results. Although there is no unambiguous interpretation to explain the observed results, results from the water-sediment simulation test on UV-384 and its degradation product M1 indicate that the applied sediment type may influence the observed dissipation. The confidence level for the aquifer study is low/medium and it is given a low weight in the WoE approach.

The water-sediment simulation studies on UV-384 indicate that the metabolite M1 is very persistent in sediment. This result is consistent with the other data. M1 is structurally more similar to UV-326 than to UV-329. Based on biodegradation estimations it is expected that M1's susceptibility to degradation is similar or higher than that of UV-326 (DegT50(M1) ≤ DegT50(UV-326)). As a consequence, and based on structural similarities, UV-326 is expected to have comparable degradation behaviour as M1 and thus it is expected to fulfil the vP criteria of REACH Annex XIII (DegT50 in sediment >180 days).
The confidence in the studies is high, but it is conducted for a structurally related substance. Thus, the overall confidence in this information is medium and it is given a medium weight for the assessment.

The confidence in the presence of UV-326 and UV-P in aged sediment sections that date back years or even decades is considered high. The ongoing contamination at a former point source is considered as supporting evidence to the P assessment of UV-326. Monitoring data are used as supporting information in the WoE approach for UV-326 and UV-329. They are in line with

the outcome of the water-sediment simulation study, the screening studies and the QSAR predictions as they point towards the persistence of UV-326 and potentially UV-329 (based on results of the structural analogue UV-P) in sediments. Non-detection and low detection of UV-329 and UV-P in the Pearl River sediment cores is not considered as contradicting information, as it probably reflects lower historic exposure of the site. Furthermore, both substances were detected at least in low concentrations in some sections of the core.

In summary, based on a weight-of-evidence approach it is concluded that UV-326 and UV-329 fulfil the P and vP criteria of REACH Annex XIII for the sediment compartment (DegT50 in sediment>180 days).

3.1.5.3 Biodegradation in soil

3.1.5.3.1 Soil dissipation studies

The two soil dissipation studies indicate that both substances are persistent and potentially very persistent in soil. This is consistent with the data on hydrolysis and biodegradation in water sediment systems.

Table 27: Integration and weighing of evidence for biodegradation in soil

Type of Evidence	Consistency & Specificity	Likelihood/ Biological Plausibility	Temporality	Confidence / Strength of Evidence	Remaining Uncertainty
Soil dissipation study (Lai *et al.*, 2014a)	Consistent field study indicating the substances are persistent in soil	Plausible	Not relevant	Medium/high strength of evidence	Medium/Low
Soil dissipation study (Lai *et al.*, 2014b)	Consistent field study indicating the substances are persistent in soil	Plausible	Not relevant	Medium/high strength of evidence	Medium/Low
Conclusion from overall confidence	Persistent and potentially very persistent in soil (Medium Confidence)				

The two studies are field studies and not equivalent to simulation tests. Their results describe dissipation. Confidence is medium/high and they are given a medium weight.

In summary, it is concluded that UV-326 and UV-329 fulfil the P criteria and potentially the vP criteria of REACH Annex XIII for the soil compartment (at least DegT50 in soil>120 days).

3.1.6 Uncertainty Analysis

No specific uncertainty analysis was considered necessary. The evidence was conclusive to decide on the vP properties of the substances. The evidence was of good quality and confidence levels were high.

No additional information is considered necessary.

3.1.7 Conclusions: Summary and discussion of degradation

The screening criterion for persistence (P) is fulfilled for the substances. The results from the available screening studies showed that these substances are not readily biodegradable. This is confirmed by the available (Q)SAR results.

Hydrolysis of the substances is not expected due to the absence of functional groups susceptible to hydrolysis.

In a water sediment simulation study at 20 °C, no degradation was observed after 100 days. At an environmentally relevant temperature of 12 °C this corresponded to a half-life significantly larger than 212 days.

Faster dissipation in an aquifer test may be related to the different sediment type tested. Simulation test results for a structurally related substance (M1) support both very high persistence in sediment for UV-326 and UV-329 and the impact of different sediment types on dissipation.

UV-P is a structurally related substance to UV-329. UV-P, UV-326 and further phenolic benzotriazoles have been detected in sediment sections that date back years and even decades, both in samples downstream from a former point source and in samples from urban estuaries.

The substances (UV-326 and UV-329) are persistent (and potentially very persistent) in two soil dissipation studies.

As an overall conclusion, based on the above information used in a weight-of-evidence-approach, it is concluded that UV-326 and UV-329 meet the 'persistence' criterion (P) and the 'very persistent' criterion (vP) in accordance with Annex XIII, points 1.1.1 and 1.2.1, of the REACH Regulation on the basis of their persistent and very persistent (P/vP) properties in sediment (DegT50 > 180 days). Furthermore, UV-326 and UV-329 meet the 'persistence' criterion (P) and potentially the 'very persistent' criterion (vP) in accordance with Annex XIII, points 1.1.1 and 1.2.1, of the REACH Regulation on the basis of their persistent and potentially their very persistent (P/vP) properties in soil (at least DegT50 > 120 days).

3.2 Environmental distribution

3.2.1 Adsorption/desorption

The registration dossiers for UV-326 and UV-329 contain (Q)SAR estimations of the adsorption potential. The KOCWIN program v2.00[56] was used to predict log K_{OC} values of 4.64 (MCI method) and 4.23 (log K_{OW} method) for UV-326, and log K_{OC} values of 5.11 (MCI method) and 4.93 (log K_{OW} method) for UV-329, respectively. According to the information from the dossier, both substances are in the applicability domain of the models.

3.2.2 Volatilisation

Except for the vapour pressure given in section 1.4, no data are available on volatilisation. For screening purposes, the data matrix in Annex I contains QSAR predictions for Henry's Law constant. However, these QSAR results are not documented according to Anne XI of REACH and are the results should be treated with caution.

Based on the available data, volatilisation is not expected to impact degradation studies.

[56] KOCWIN v2.00 in US EPA EPISuite v4.11.

3.2.3 Distribution modelling

No data are available on distribution modelling.

3.2.4 Summary and discussion of environmental distribution

Based on the available log K_{OC} values, both substances are expected to adsorb to soil and sediment.

3.3 Data indicating potential for long-range transport

Not assessed.

3.4 Bioaccumulation

A weight-of-evidence assessment is carried out for bioaccumulation assessment. The "Weight-of-Evidence/Uncertainty Analysis Template[57]" is applied to structure the weight-of-evidence.

3.4.1 Bioaccumulation in aquatic organisms (pelagic & sediment organisms)

3.4.1.1 Screening data

In addition to the available experimental data, the log K_{OW} of the substances was estimated using COSMOtherm. [58]

Table 28: Available log K_{OW} data of the substances

Name	Log K_{ow}	Method
UV-329	6.4	COSMOtherm
	≥ 6.5	OECD TG 117
	6.91	experimental, Do *et al.* (2022)
UV-326	6.7	COSMOtherm
	≥ 6.5	OECD TG 117
	7.38	experimental, Do *et al.* (2022)

COSMOtherm is an implementation of the COSMO-RS method. This approach has proven useful to predict a wide range of physico-chemical properties like liquid/liquid equilibria or solubilities (Klamt, 2011). The method is not a (Q)SAR but combines quantum chemical calculations and statistical thermodynamics. Consequently, there is no applicability domain in the classical sense. It is applicable to a much broader range of substances and the applied parameters are not specific of functional groups or molecule types (Eckert and Klamt, 2002).

For both substances the log K_{ow} values are above the screening trigger value of 4.5 for bioaccumulation. Consequently, they screen as potentially B/vB.

[57] https://echa.europa.eu/documents/10162/17169198/template_for_weight_of_evidence_en.docx/eb183c2e-c360-cbce-7a58-ad2d1270e5bd

[58] COSMOconf conformer generation performed using the BP-TZVP-COSMO+GAS template; COSMOtherm property estimation performed using the BP_TZVP_21-parameterisation;
BIOVIA COSMOtherm, Release 2021; Dassault Systèmes. http://www.3ds.com;
BIOVIA COSMOconf, Release 2021; Dassault Systèmes. http://www.3ds.com

3.4.1.2 Aquatic bioaccumulation data

3.4.1.2.1 Problem formulation

A weight of evidence determination according to the provisions of Annex XIII of REACH is used to identify if UV-329 and UV-326 meet the criteria for B/vB in aquatic organisms. For UV-326 a direct comparison with REACH Annex XIII criteria is possible due to the available standard information; for UV-329, a more detailed weight-of-evidence is required.

3.4.1.2.2 Collection and Documentation of all Information

Information/evidence used in the approach include:

- Experimental studies from endpoint study records from corresponding IUCLID Registration Dossiers and study reports
- Published Literature
- Research Project

Table 29: Collected information and documentation:

Source Name	Date of search	Type of information/ evidence	Link/Reference	Keywords Searched	Reason for inclusion / exclusion from WoE approach
OECD TG 305-I UV-329 Study having the highest weight	-	Experimental Study	ECHA Dissemination website and study report	-	N/A
OECD TG 305-I UV-326 Study having the highest weight	-	Experimental Study	ECHA Dissemination website and study report	-	N/A
Development of a bioaccumulation test using *Hyalella azteca* UV-329 Study having the highest weight	-	Experimental Study	Schlechtriem *et al.*, UBA TEXTE, no. 134/2022 https://www.umweltbundesamt.de/publikationen/development-of-a-bioaccumulation-test-using	-	N/A
"Bioaccumulation assessment of superhydrophobic substances." UV-329, Supporting Study	-	Estimated/Predicted	Goss and Ebert, UBA TEXTE, no. 40/ 2023 https://www.umweltbundesamt.de/publikationen/bioaccumulation-assessment-of-superhydrophobic	-	N/A
Published Literature: Several field studies UV-329: supporting evidence		Field Studies	See Table 33: UV-329 concentrations in aquatic biota samples from different field studies	-	N/A

3.4.1.2.3 Assessment of quality of individual evidence

Table 30: Assessment of quality of individual evidence

Type of Evidence / Source Name - Reference	Relevance	Reliability	Adequacy
OECD TG 305-I (aqueous exposure) UV-326 Study having the highest weight	Study appropriate for investigation of aquatic bioaccumulation	Klimisch score 2 Reliable without restrictions	Adequate on basis of reliability and relevance
OECD TG 305-I (aqueous exposure) UV-329 Study having the highest weight	Study appropriate for investigation of aquatic bioaccumulation	Klimisch score 2 Reliable with restrictions (restrictions: experimentally derived uptake rate k_1 and steady-state not reliable and disregarded)	Adequate on basis of reliability and relevance
Development of a bioaccumulation test using *Hyalella azteca* UV-329 Study having the highest weight	New study protocol (A draft OECD TG for the *Hyalella azteca* bioconcentration test is currently under preparation and is scheduled to be adopted in 2024), appropriate for investigation of aquatic bioaccumulation	Klimisch score 2 Reliable with restrictions (restrictions: new test system, uncertainties regarding k_1)	Adequate on basis of reliability and relevance
"Bioaccumulation assessment of superhydrophobic substances." UV-329 Supporting Study	Model development to predict k_1 and BCF for *Hyalella Azteca*, Study appropriate for investigation of aquatic bioaccumulation	Klimisch score 2 Reliable with restrictions (restriction: further validation with experimental data necessary)	Adequate on basis of reliability and relevance
Published Literature: Several field studies UV-329: supporting evidence	Field study appropriate as supporting information to investigate the bioaccumulation	Klimisch score 2 Reliable with restrictions (limitations of field studies are mentioned in the respective section	Adequate on basis of reliability and relevance

3.4.1.2.3.1 Robust Study Summaries of Key Studies

OECD TG 305 with UV-326 (aqueous exposure)[59]

Study design and test conditions:

The study investigated the bioconcentration potential of UV-326 in juvenile rainbow trout (*Oncorhynchus mykiss*) according to the guideline OECD 305-I (aqueous exposure). The fish were exposed to one solvent control group (0.02 mL/L acetone) and one concentration group of test substance at 0.2 µg/L in a flow-through-system for an uptake period of 44 days followed by a depuration period in clean water of 63 days. In the interest of animal welfare this study used only one concentration of test substance to determine bioconcentration as recommended in the 2012 revised OECD 305 test guideline for non-polar organic chemicals. Scientific publications (Creton et al. 2013, Burden et al. 2014) provide compelling evidence that BCF values do not differ when multiple concentrations are tested.

Over the entire test all water quality parameters were maintained within acceptable limits. The pH was stable during the whole test period and was in a range of 8.0 – 8.2. The concentrations

[59] ECHA Dissemination website and study report

of dissolved oxygen were maintained in a range between 8.3 – 10.3 mg/L in the test vessels and were not less than 60% of the maximum saturation at the test temperature of 13 ±1°C during the test. The concentration of total organic carbon in the test vessels did not exceed the concentration of organic carbon originating from the test substance and solvent by more than 10 mg/L (± 20%). The test substance concentrations remained within ±20% of the mean of determined concentrations during the 44-day uptake phase. Only on day 42 of the uptake period the measured concentration (123.4%) was slightly higher than 20% of the mean of determined concentration but had no considerable influence on the overall mean measured results. No toxic effects (i.e., mortality) or changes in behaviour or appearance were observed in the test treatment organisms in comparison to the control group. In summary, all validity criteria were achieved.

The theoretical concentration and homogeneity during test substance preparation can be confirmed by the measurement of radioactivity from 3 different regions of the test solution tank via centrifuged and uncentrifuged test water samples prior to the start of exposure. Since there was a difference in the results of the concentration measurement between in centrifuged and uncentrifuged samples, in addition to concentration measurements of uncentrifuged samples also concentrations of centrifuged samples were measured as worst-case scenario in the subsequent analyses. The results of centrifuged samples were below 500 dpm/10 mL and should therefore be taken with care, since they are not fully reliable as the scintillator needs a minimum activity of 500 dpm/10 mL for calculation of reliable results, comparable to a limit of quantification (LOQ).

During depuration the concentration in test water samples were measured on three occasions and in fish on 10 occasions. Test substance concentrations in fish were determined on 9 occasions during uptake by measuring the total radioactivity. Total radioactive residues in fish were measured separately in edible (e.g., fillet) and non-edible (e.g., remaining carcass) portions and the whole fish value was calculated from the weight normalised sum of the individually measured portions. Measuring the concentrations in separate portions add uncertainties to the whole body BCF value. The bioconcentration factor was based on analyses of total radioactive residues in water and fish tissue thus also includes residues of possible metabolites of the test substance in the fish. The BCF calculated on the basis of these values therefore represents a worst-case assumption and might be lower if only the unmetabolized parent test substance is considered. Metabolite identification would certainly help to discriminate between metabolites, which may be slowly depurated (and thus contribute to the B-potential of the parent) and those that are rapidly excreted (e.g., glucuronide or sulfate derivates) from the body via liver, gall bladder or kidney (Arnot et al., 2018). UV 326 has an hydroxy group, which is relevant for phase II metabolism (i.e., conjugation with glucuronides and/or sulfates). This hydroxy group is less accessible as it forms a hydrogen bond to the nitrogen atom of the benzotriazole moiety. For UV 326 this hydroxy group may be hindered by large side chains next to it, preventing a fast metabolization (Leubner et al., 2023). Substituted compounds may be less metabolized compared to unsubstituted phenolic benzotriazoles in rats (Waidyanatha et al., 2021). UV-326 is disubstituted and metabolism in fish is expected to be in general lower than in rats. In conclusion, using the BCF values based on total radioactivity analysis for the B/vB assessment of UV-326 is considered acceptable.

Estimated results:

Since there was a statistically significant difference between the slopes of the growth rate, the test and control data were not pooled and a separate fish growth rate constant (k_g) of 0.0148 (± 0.004) day^{-1} for test group was calculated and used for "growth corrected" calculations. The lipid content of 2.8% was used for lipid correction.

The concentration in fish reached 95% steady-state within 44 days based on the kinetic calculations. Based on uncentrifuged test solutions, overall, the measured steady-state bioconcentration factor (BCF_{ss}) value (3559±561) was very similar to the calculated kinetic

(BCF_K) value (3580) indicating that steady-state was reached, and that uptake and depuration follow first order kinetics. When normalised to a 5% lipid content in fish (using the mean lipid), the steady-state bioconcentration factor (BCF_{ssL}) was 6355 L/kg for the uncentrifuged test solution. Based on uncentrifuged test solutions, the lipid-normalised growth corrected bioconcentration factor BCF_{KgL} was 7093 for the whole fish based on total radioactive residues of the test substance. Based on centrifuged test solutions the BCF_{ss} was 7136±1124 L/kg. When normalised to a 5% lipid content in fish (using the mean lipid), the steady-state bioconcentration factor (BCF_{ssL}) was 12743 L/kg for centrifuged test solution and the bioconcentration factor BCF_{KgL} was 14225 L/kg for the whole fish based on total radioactive residues of the test substance.

This study is considered as reliable with restrictions.

Conclusion:

Based on this study, it can be concluded that UV-326 is very bioaccumulative with an estimated lipid-normalised and growth-corrected kinetic BCF value in the range 7093—14 225 L/kg (BCF>5 000, whole fish BCF back calculated from edible and non-edible portions and based on total radioactive residues of the test substance).

OECD TG 305 with UV-329 (aqueous exposure)[60]

Study description and test conditions:

This study determined the bioconcentration potential of UV-329 in juvenile rainbow trout (*Oncorhynchus mykiss*) according to the guideline OECD 305-I (aqueous exposure). The fish were exposed via water in a flow through system at test concentration 0.2 µg/L and a dilution water control (no solvent control as all acetone was evaporated prior to adding water) over an uptake period of 28 days followed by a depuration period in clean water of 28 days. In the interest of animal welfare, this study used only one concentration of test substance to determine bioconcentration as recommended in the 2012 revised OECD 305 test guideline for non-polar organic chemicals. Scientific publications (Creton et al. 2013, Burden et al. 2014) provide compelling evidence that BCF values do not differ when multiple concentrations are tested. Concentrations in fish and water were determined on 7 occasions during uptake by measuring the total radioactivity. During depuration the concentrations in water were measured on 3 occasions and in fish on 6 occasions. No toxic effects (i.e. mortality) or changes in behaviour or appearance were observed in the test treatment organisms in comparison to the control group. The registrant resumes that over the entire test all water quality parameters were maintained within acceptable limits. However, differing from the guideline as TOC was only measured in the control group. The mean measured concentrations of the test substance during the uptake period in water was 0.19 ±0.01 µg/L. The water concentration was kept constant within ±20% of the nominal concentration, except on day 7 when the concentration briefly dropped to 0.079 µg/L due to a pump malfunction. As the test concentration drop was very brief it was not included in the mean measured calculation (Table 31). Total radioactive residues in fish were measured separately in edible (e.g., fillet) and non-edible (e.g., remaining carcass) portions and the whole-fish value was calculated from the weight-normalised sum of the individually measured portions. Measuring the concentrations in separate portions add uncertainties to the whole body BCF value. The bioconcentration factor was based on analyses of total radioactive residues in water and fish tissue thus also includes residues of possible metabolites of the test substance in the fish. The BCF calculated on the basis of these values therefore represents a worst-case assumption and might be lower if only the unmetabolized parent test substance is considered. Metabolite identification would certainly help to discriminate between metabolites, which may be slowly depurated (and thus contribute to the B-potential of the parent) and those that are rapidly excreted (e.g., glucuronide or sulfate derivates) from the body via liver, gall bladder or kidney (Arnot et al., 2018). UV 329 has a hydroxy group, which is relevant for phase II

[60] ECHA Dissemination website and study report

metabolism (i.e., conjugation with glucuronides and/or sulfates). This hydroxy group is less accessible as it forms a hydrogen bond to the nitrogen atom of the benzotriazole moiety. Substituted compounds may be less metabolized compared to unsubstituted phenolic benzotriazoles in rats (Waidyanatha et al., 2021). UV-329 is monosubstituted and metabolism in fish is expected to be in general lower than in rats. In conclusion, using the BCF values based on total radioactivity analysis for the B/vB assessment of UV-329 is considered acceptable as a worst-case-scenario.

Table 31: Test substance concentration in water and whole fish during uptake phase

Sampling time (day)	Concentration in water, mean value (µg/L)	Concentration in whole fish, mean value (µg/L)
0	0.181	-
3	0.188	20.0 ±4.7
7	0.218	46.8 ±12.0
10	0.188	46.2 ±6.3
14	0.181	32.1 ±6.1
21	0.201	35.8 ±2.4
24	0.180	46.8 ±4.0
28	0.181	71.8 ±5.2

Estimated results:

There was no statistically significant difference in fish growth rate between control and treatment group during the experiment, therefore data from both groups were combined to determine the overall growth rate (k_g) of 0.0132 day^{-1} for "growth-corrected" calculations. The lipid content of control fish sampled over the test period remained constant considering the variability of individual values and the lipid content from the end of the uptake period (4.1%) was used for lipid normalisation calculations.

The registrant concluded that the steady-state criterion in OECD TG 305 is fulfilled after 24 days and derived a lipid-normalised BCF_{ssL} of 461. According to the OECD TG 305 guidance a steady-state is reached in the plot internal body concentration (C_f) of the test substance in fish against time when the curve becomes parallel to the time axis and three successive analyses of C_f made on samples taken at intervals of at least two days are within ±20% of each other, and there is no significant increase of C_f in time between the first and last successive analysis. All this is only true if C_f of the last sampling point of the uptake period (day 28) is disregarded. However, the registrant concluded that the value must be accepted as plausible and therefore needs to be considered for steady-state derivation. Consequently, steady-state was not reached at the end of the uptake period as (1) there was an extreme intermediate drop in C_f between day 10 and day 20, (2) the three last C_f values of the uptake phase (day 21, 24, 28) are not within ±20% of each other, and (3) there is a significant increase between day 21 and day 28 curve. Therefore, the derived steady-state value is considered as not reliable.

The kinetic derived growth and lipid corrected BCF_{kgL} given in the study report is 458 L/kg. The corresponding experimentally derived uptake rate constant k_1 of 64 L/kg/day was below model expectation (Table 32) by more than an order of magnitude. Experimental artefacts were expected for the uptake period as there were problems maintaining solute concentration (further discussed by Goss & Ebert, 2023). TOC was only measured in the control group and not in the treatment group. Consequently, TOC concentration of the treatment group is unknown, which is not in accordance with the OECD TG 305 guideline. As UV-329 is a very hydrophobic substances TOC concentration has a strong influence on freely dissolved test concentration. Therefore, monitoring of TOC concentration during uptake phase is essential. Sorption of the test substance to organic matter may reduce its bioavailability and therewith result in an underestimation of the BCF. Consequently, a bioavailability issue could explain the extreme intermediate drop in C_f between day 10 and day 20. Therefore, the fitted k_1 value is considered as unreliable.

The depuration phase is considered to be reliable and subsequently derived k_2 values were used for BCF estimation together with estimated uptake rate k_1 (Goss *et al.*, 2018) using the OECD-

BCF-Estimation-Tool. According to OECD 305 guidance document (OECD, 2017), it is recommended to use the tool to evaluate the results of fish feeding studies. The BCF estimation methods, however, are based on the depuration rate constant and are independent of the uptake rate and uptake route. Therefore, the tool can also be used to calculate BCF using depuration rates constants from studies with aqueous exposure. It should be noted that these calculated BCFs may be more uncertain than experimental BCFs due to the uncertainty in the k_1 prediction. The log Kow values of UV-329 (see section 3.4.1.1) are in the given range of the indicative applicability domain of method 1 (3.5 – 8.3) and method 2 (3 – 8.2) of the OECD-BCF-Estimation-Tool. Also, the used fish species is within the training set. For the prediction of a BCF it is not appropriate to take the mean value from all estimates derived in different ways. Therefore, the results of the OECD BCF estimation Tool (Version 2) are used in a weight of evidence approach by considering all results in a more general comparison with BCF trigger values. Growth corrected k_{2g} value of 0.168 day^{-1} (one compartment model) and 0.267 day^{-1} (two compartment model) were given in the study report. Despite the explanation "Since the depuration data demonstrate a biphasic pattern, the data were fit to a two-compartment kinetic model.", no further justification was given by the authors. In the two-compartment model, additional parameters are used which leads to over-parametrisation if the sample size is not considerably increased. Therefore, the the data were only used for comparison. Based on the raw data k_2 was refitted and a k_2 value of 0.119 day^{-1} (one compartment, BoxCox transformation) was calculated. In dependence of the used k_2 lipid normalised and growth-corrected BCF_{kgL} values ranged between 243 and 10592 (Table 32), whereas most values are >2000. When using the recalculated k_2 value some BCF_{kgL}s are >5000. The log kow value 6.91 (Do *et al.*, 2022) was used for the calculation presented in Table 32. When using the remaining log K_{ow} values (Table 28) as input parameter the general picture did not change.

Table 32: k_1 and BCF_{kgL} estimates using OECD BCF Estimation Tool (Version 2) and experimentally derived k_2 values

(Input parameter: mean weight at test start 2.24 g, uptake phase duration 28 days, Log K_{OW} 6.91 (Do *et al.*, 2022), growth rate 0.0132 day^{-1}, Mean fish lipid uptake end or depuration start (fraction) 4.1%, Mean fish lipid depuration end (fraction) 4.5%, Depuration phase duration 28 days).

K_{2g} (day^{-1})		**0.168***	**0.267****	**0.119*****	**Reference**
inputs for K_1	**K_1**	**BCF_{kgL}**			**Method 1**
weight	427	**2957**	1859	**4174**	Hayton and Barron (1990)
weight	589	**4079**	2565	**5759**	Erickson and McKim (1990a)
weight	584	**4043**	2542	**5707**	Barber *et al.* (1991)
weight	377	**2610**	1641	**3685**	Barber (2003) - observed
weight	605	**4189**	2634	**5914**	Barber (2001)
weight	115	793	499	1120	Streit and Sire (1993)
weight	470	**3255**	2047	**4595**	Erickson and McKim (1990b)
weight	397	**2750**	1729	**3883**	Sijm *et al.* (1995)
weight	477	**3300**	2075	**4658**	Barber (2003) - calibrated
log K_{ow}	1084	**7501**	4717	**10592**	Tolls and Sijm (1995)
log K_{ow}	990	**6854**	4310	**9677**	Spacie and Hamelink (1982)
weight, log K_{ow}	104	718	452	1014	Hendriks *et al.* (2001)
weight, log K_{ow}	56	386	243	544	Thomann (1989)
K_{2gl}					**Method 2**

0.168*	380	**2631**			Brookes and Crooke (2012)
0.267**	343		1493		
0.119***	410			**4011**	

* one compartment model, untransformed, source: study report ** two compartment model, source: study report *** one compartment model, BoxCox transformed, source: recalculation, see Figure 11

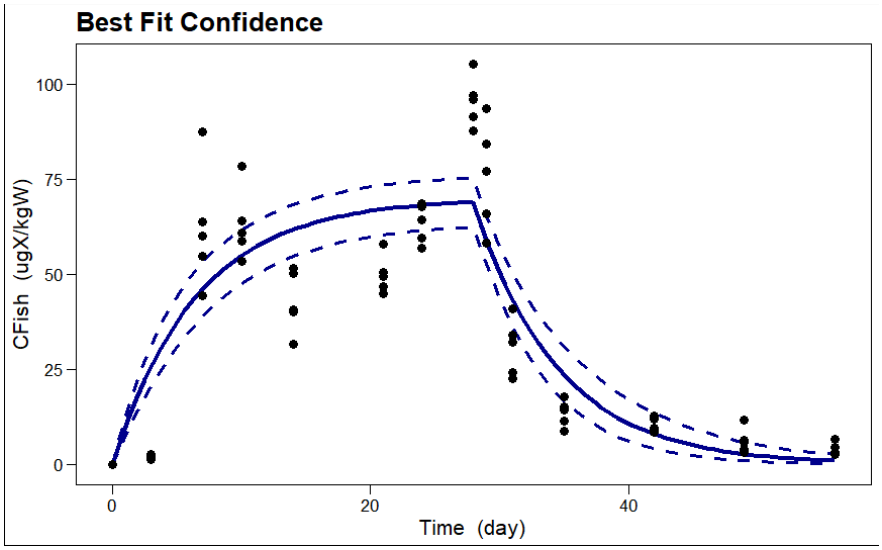


Figure 11: Best fit confidence of BoxCox transformed data (Gaus-Newton algorithm, R^2=0.56, RMSE = 18.82)

Conclusion:

This study is considered as reliable with restrictions.

BCF_{kgL} values for UV-329 were estimated based on experimental derived k_2 values and calculated k_1 values. Most BCF exceed the B criterion of 2000 irrespective of the used k_2 value (source: study report or recalculation). Some of the calculated BCF_{kgL} also exceed the vB criterion of 5000. Finally, it can be concluded that based on the study results the B criterion is fulfilled. The results may furthermore indicate a concern for vB (BCF_{kgL}>5000).

3.4.1.2.3.2 "Development of a bioaccumulation test using *Hyalella azteca*" - Bioconcentration test with UV-329

Study description and test conditions:

This study by Schlechtriem et al., 2022 determined the bioconcentration potential of UV-329 in freshwater amphipods *Hyalella azteca* (HYBIT) using the test protocol as described by Schlechtriem et al. (2019). Male amphipods older than 2 months were exposed via water in a flow-through set-up. Solvent facilitated application of UV-329 was performed using a test media performed with a nominal concentration of 1 µg/L at a flow rate of 6 L/h. Uptake and depuration phases lasted 7 days. The test with solvent facilitated application was disregarded in the assessment due to significant mortality of the test animals. In addition, a solvent free column-generated application of UV-329 was performed with a test substance concentration (time weighted average) of 0.208 µg/L at flow rate of 6 L/h, an uptake phase of phase of 5 days, and a depuration phase of 6 days. Concentrations in amphipods and water were determined on 9 occasions during uptake phase and on 6 occasions during the depuration phase for the solvent-free application and analysed by LC-MS/MS.

The lipid content of the amphipods was determined at test start, end of the uptake phase and end of the depuration phase. A mean lipid content of 2.1 % was used for lipid normalisation calculations. In contrast to the BCF determination in fish, growth can be neglected in *H. azteca* BCF calculation due to the short duration of the study. The time-weighted average (TWA) concentrations of the test substance during the uptake period in water was 0.208±0.055 µg/L for UV-329.

Results:

The measured values of UV-329 in amphipods were within ±20% of each other from days 2 – 5, thus steady-state concentration was reached and a BCF_{ss} of 7744 was derived. Normalised to 3% lipid the BCF_{ssL} was 11063. The kinetic derived BCF_k value was 8352, normalised to 3% lipid BCF_{kL} was 11876. The corresponding experimentally derived uptake rate constant k_1 was 8288 L/kg/day and the derived depuration rate k_2 was 0.992 day^{-1}.

The test concentration in water was uncertain during the test as it was not always within the ±20% range (day 1: -27 %, day 5: +50 %). Even though, the tissue concentration reached steady-state (±20 % from day 2-5). To address these uncertainties especially for k_1 estimation from HYBIT test the project "Bioaccumulation assessment of superhydrophobic substances" was initiated (see study summary of Goss and Ebert (2023) below).

Conclusion:

This study is considered as reliable with restrictions.

According to the draft PBT guidance[61], BCFs from *H. azteca* bioconcentration tests can be compared against the REACH Annex XIII criteria on B and vB properties.

The experimentally derived BCF_{ssL} and BC_{FkL} values for *Hyalella azteca* are in the range of 11063—11876 L/Kg and thus exceed the vB criterion of 5000 in accordance with REACH Annex XIII.

3.4.1.2.3.3 Study summaries of supporting studies

"Bioaccumulation assessment of superhydrophobic substances"

Bioconcentration tests with the freshwater amphipod *Hyalella azteca* (HYBIT) have been proposed as alternatives to fish tests, which is desirable in terms of reducing the number of vertebrates used for testing under the 3R principles of Replacement, Reduction and Refinement (de Wolf *et al.*, 2007). The respective BCFs show promising correlations. It is still unclear though whether HYBIT is also suitable for highly hydrophobic chemicals, such as UV stabilisers UV-234 and UV-329. These chemicals have been tested in *H. azteca* for their bioaccumulative potential (Schlechtriem *et al.*, 2022), yet strong variations in the uptake rate constants k_1 were observed, not only between fish and *H. azteca*, but also between different experiments conducted in *H. azteca* for the same chemical. In *H. azteca*, k_1 for UV-329 ranged from 8288 Lw/kgorg/d to 66085 Lw/kgorg/d. Yet, Goss and Ebert (2023) believe the second value to be an experimental artefact due to the strong growth of biofilm, which might have led to the uptake of contaminated diet. It will therefore not be discussed any further. To assess whether the increased k_1 as compared to fish are realistic, they developed a model to predict k_1 from the K_{ow} and molecular weight MW in work package 1. In work package 2, the authors evaluated the suitability of HYBIT for superhydrophobic substances.

[61] https://echa.europa.eu/support/guidance/consultation-procedure/ongoing-reach

A detailed literature search was undertaken to gather the physiological data necessary for model development, and to determine the relevant uptake/elimination processes. Data regarding the respiration rate and uptake efficiency of O_2 allowed the estimation of the ventilation rate constant, which resulted in quite similar values as estimated empirically for fish of the same weight. Empirical correlations developed for amphipods were used, or physiological data from similar amphipods were scaled down to estimate organ surface areas. Estimates for unstirred water layer thickness in water and blood correspond to assumptions made in literature, in case of blood assumed for fish. Although data on protein content in amphipods exist, binding kinetics and partition coefficients are yet unknown. For the calculations, the authors thus assumed proteins similar to albumin in fish, which might act as a carrier across the unstirred layer in blood for superhydrophobic compounds and thus facilitate transport. Having no data on bloodflow in *H. azteca*, the authors simply assumed it to be insignificant for superhydrophobic chemicals due to facilitated transport by the albumin-like protein.

The authors also collected information on the test chemicals UV-234 and UV-329. Predicted octanol/water partition coefficients varied widely between different prediction methods, resulting in a broad uncertainty in k_1 prediction. The authors decided to use the mean log K_{ow} for calculations. The physiological data allowed the determination of relevant uptake processes: The amphipods were fed uncontaminated diet; therefore, the diet was excluded as a possible uptake path. The authors had a closer look at uptake via skin, because the area to volume ratio is higher for smaller animals. Yet, the total body area was estimated to be only marginally higher than gill area. Considering the chitin shell, additional cell layers, and an increased unstirred water layer as compared to the gills, this possible uptake path was deemed irrelevant. The authors thus identified uptake via gills as the important uptake path.

For the uptake via gills, another effect must be considered. The influence of chemical binding to organic matter (TOC) in water is very high for superhydrophobic chemicals. The bioavailable fraction may decrease by orders of magnitude, decreasing k_1 in turn. It is not yet clear whether for superhydrophobic chemicals, some fraction of chemical bound to TOC might still be bioavailable, i.e., whether de-/sorption kinetics are fast enough for the chemical to diffuse across the ventilation volume or unstirred water layer bound to TOC and then desorb before being absorbed by the gills. Yet, the authors assumed all chemical bound to TOC as not-bioavailable, which is the usual approach (Arnot and Gobas, 2004).

Modelling k_1 revealed the unstirred layer in water and the ventilation rate as the main resistances for the uptake via gills. Within uncertainties, modelled k_1 values corresponded well to experimental values from literature, except for a slight overestimation of k_1 for chemicals with log K_{ow} below 6.5, which could be due to the absence of blood flow in our modelling, which might be a limiting factor for low K_{ow}. The resulting k_1 are indeed higher than expected for fish, due to the increased ventilation rate per body weight in *H. azteca*.

Yet, the authors consider the extremely low k_1 value measured in fish for UV-329 to be an experimental artefact. There were problems maintaining solute concentration, resulting in an extreme intermediate drop in internal body concentration. Also, steady-state was never reached, and the value lies well below predicted k_1 for fish. The authors thus conclude that experimentally measured k_1 in *H. azteca* are quite plausible. Yet, data in the superhydrophobic range are too sparse and K_{ow} uncertainties too high to conclusively validate the prediction method or the experimental data.

Conclusion:

The project results support the reliability of the experimentally derived BCF values for for UV-329 with *Hyalella azteca* which are > 5000.

3.4.1.2.3.3.1 Field Data

Table 33 summarises several field studies providing measured organism concentration of UV-329. This non-exhaustive overview shows that UV-329 is found in several fish and some vertebrate species in different regions of the world. Partial high concentrations in muscle tissues give evidence, that UV-329 accumulate in fish in the environment. This is supported by BAF and TMF values summarised in Table 34. The study list is not complete and more studies are available. Partially, these studies did not detect UV-329 (e.g., Langford *et al.*, 2015), what is no contradicting evidence but rather indicates that UV-329 may so far not entered every region of the world. Further explanation for absence of detection can be that LOD/LOQ values may set too high or analytical issues.

Uncertainties of these studies are considered to be medium and sometimes high mainly due to: (1) sampling of different species with differences in habitat, feeding, digestion, metabolism, age, sex, size, weight and lipid content (2) different locations with different fluctuating and unknown exposure scenarios under different environmental conditions (3) methodical differences in sampling, extraction and analysis (4) incomplete documentation. Therefore, the measured values are not directly comparable with each other and therefore only used in a more general way as supporting evidence in the weight-of-evidence assessment

Table 33: UV-329 concentrations in aquatic biota samples from different field studies

Reference	Species	Location	Date	Age	Sex	Size & weight	Sampling	Storage, extract, analysis,	Lipid content [%]	Concentration of UV-329	Frequency of detection [%]
Castilloux *et al.* (2022)	Lake sturgeon (n=15),	Lake St. Louis (LSL), Montreal	06/ 2018	16-25 years	M & F	94-129.5 cm, 4.2-12.5 kg	Fish tissues, on-sight (liver, muscle)	Frozen in field (-20 °C), ultrasonic assisted extraction with hexane/ dichloromethane, GC-MS	Liver: 1.9±1.1, muscle: 0.11-14.1	[ng/g ww] liver: ND, muscle: ND-41	Liver: 0 muscle: 20
	Northern pike (n=32)	Iles des Boucherville (IB), Iles Vert (IV) -> upstream and downstream of Montreal's WWTP	05/ 2016	2-7 years	M & F	43.5-93.0 cm, NA	Fish tissue, on-sight (liver, muscle, brain, blood plasma)		Liver (IB): 1.9±1.1, muscle (IB): 0.75±0.8, brain (IB): 1.65±1.3, Liver (IV): 2.29±1.55, muscle (IV): 0.27±0.2, brain (IV): 1.58±0.4	[ng/g ww] Liver (IB): ND-214, muscle (IB): ND-<MQL, brain (IB): 0, blood (IB): ND-19 (median: 5.5), liver (IV): ND, muscle (IV): ND-<MQL (median: 4.5), brain (IV): ND, blood (IV): ND-17 (median: 7.5)	Liver (IB): 38, muscle (IB): 44, brain (IB): 0, blood (IB): 88, liver (IV): 0, muscle (IV): 64, brain (IV): 0, blood (IV: 86
Kim *et al.* (2011)	20 fish species (n=58)	Manila Bay (local fish markets)	01 & 06/2008	N/A, juvenile, adult	N/A	8.5-31.0 cm, 3.4-531 g	Fish tissues (muscle)	polyethylene bags, transported on dry ice, frozen (-25 °C), High Speed Solvent Extractor, hexane/acetone, ultra-fast LC-MS/MS	0.13-2.6	[ng/g lw] Muscle: ND-39.4	muscle: 41
Lyu *et al.* (2022)	17 fish species	Lake Chaohu, China	09/2016	N/A	N/A	7.8-63.3 cm, 10.8-4178	Fish tissue (back muscle), whole	Aluminium foil, frozen in field, stored in low-temperature box for transport, freeze-dried,	7.6-18.0	[ng/g dw, mean] Muscle: 0.64	100

						g	body for small species	stored (-20 °C), extract in an ultrasonic bath, GC		– 6.65	
	2 shrimp species					N/A	Head and shell removed, rest reserved		9.2-10.4	[ng/g dw, mean] 1.03 – 2.19	
Langford *et al.* (2015)	Atlantic cod (n=15), northern shrimp (n=15 bulk samples of 50-60 individuals), common shore crab (n=15 bulk samples of 10-13 individuals)	Oslofjord, Norway	08/2016	N/A	Fish: M & F	Cod: 43-82 cm, 0.76-8.5 kg	Fish tissue (liver), shrimps were peeled	Frozen within 4 h of collection, stored at -20 °C, accelerated solvent extraction, hexane/dichloromethane, LC-HRMS & GC-HRMS	N/A	ND (LOQ: 25 ng/g ww)	0
	burbot (n=15), perch (n=15), whitefish (n=15)	Lake Mjøsa, Norway	06-08/2016		N/A	N/A	Fish tissues (muscle, stomach, intestine, liver)		4.4, 1.6, 1.3	ND (LOQ: 25 ng/g ww)	0
Montesdeoca-Esponda *et al.* (2020)	3 fish species	3 different marine outfalls in Grand Canaria Island (Spain)	07/2016, 10/2026, 04/2017, 07/2017, 01/2018, 04/2018	N/A	N/A	N/A	Fish tissues (muscle, viscera	Freeze dried, microwave extraction, acetonitrile, UHPLC-MS/MS		[ng/g dw] Muscle: ND Viscera: 1.34-10.7	
Peng *et al.* (2017)	17 fish species	Pearl River Estuary, south China	04/ & 10/ 2013	N/A	N/A	8.4-49.3 cm, 5-206 g	Fishes were skinned, only	aluminium foil and ziplock polyethylene bags, on ice during transport, freeze-dried,	Muscle: 1.36-4.21	[ng/g lw] muscle: ND-	Muscle: 88

							muscles used, 2-3 individuals were pooled for each species	stored at -20 °C, ultrasonic assisted extraction with ethyl acetate/ cyclohexane, ultra-high liquid C-MS, stabile isotopes abundance of carbon & nitrogen		27.6	
Tang *et al.* (2019)	6 fish species (n=43)	Lake Chaohu, China	09/ 2016	N/A	N/A	24.6-68.0 cm, 0.32-5.45 kg	Fish tissue (gill, liver, muscle) samples from 2-3 individuals were pooled	Aluminium foil, frozen in field, thaw naturally in laboratory, freeze-dried, stored at -20 °C, ultrasonic assisted extraction with acetone/n-hexane, GC-MS	muscle7.6-18 liver: 9.2-25 gill: 16.8-30.4	[ng/g dw] muscle: <0.19-15.86 liver: 0.92-12.1 gill: 0.85-4.54	Muscle: 88
Vimalkumar *et al.* (2018)	6 fish species (n=14)	2 rivers (Kaveri (K), Vellar (V)), India	11/2015 (wet season), 05/2016 (dry season)	N/A	N/A	N/A	muscle	Frozen (-20 °C), liquid-liquid extraction, hexan/ dichloromethan, GC-MS	N/A	[ng/g ww] muscle: 0.6-28 (7.4±3.6)	K: 100 V: 100

Table 34: Selected bioaccumulation factors (BAF) and trophic magnification factor (TMF) of UV-329. For more study details see Table 33.

Referenz	Species	C_w [ng/L]	BAF [L/kg]	BAF lipid normalised to 5%	TMF
Castilloux *et al.* (2022)	Northern pike (n=32)	IB: ND-31 IV: ND-4	Liver: 15848 Muscle: 2512 Plasma: 3162	Liver: 37733 Muscle: 23287	N/A
Peng *et al.* (2017)	17 fish species	N/A	N/A	N/A	1.70
Vimalkumar *et al.* (2018)	6 fish species (n=14)	1.7-29.3 (13.7±8.1)	Muscle (mean): 552	N/A	NA

3.4.1.2.4 Integration and Weight of Evidence (WoE) analysis and Application of Level of Confidence

3.4.1.2.4.1 UV-326

Table 35: Conclusion for aquatic bioaccumulation potential of UV-326

Type of Evidence	Consistency & Specificity	Likelihood/ Biological Plausibility	Temporality	Confidence / Strength of Evidence	Remaining Uncertainty
OECD TG 305-I with UV-326	Results are consistent with screening results, high specificity as substance specific BCF value is the result of the study and enables direct comparison with B/vB criteria of Annex XIII	Plausible	Not relevant	High	Low
Conclusion from overall confidence	As a standard OECD 305 BCF is available a direct comparison with the Annex XIII criteria for bioaccumulation is possible. The available BCF data give high confidence that UV-326 fulfills the B and vB criteria of REACH Annex XIII.				

3.4.1.2.4.2 UV-329

Table 36: Conclusion for aquatic bioaccumulation potential of UV-329

Type of Evidence	Consistency & Specificity	Likelihood/ Biological Plausibility	Temporality	Confidence / Strength of Evidence	Remaining Uncertainty
OECD TG 305-I with UV-329	Consistent with the other evidence if uptake period is disregarded and replaced by applicable estimation, high specificity as substance specific BCF value is the result of the study and enables direct comparison with B/vB criteria of Annex XIII	Plausible, if uptake phase disregarded and replaced by applicable estimations	Not relevant	High for B conclusion, Medium for vB conclusion	Low for B conclusion, Medium for vB conclusion (some of the used estimation methods end up with BCF values > 5000 most values are >2000)
HYBIT BCF	Consistent with the other evidence, high specificity as substance specific BCF value is the	Plausible	Not relevant	Medium to high for B/vB conclusion	Low/medium (new test system and uncertainties regarding k_1 -> to address these

with UV-329	result of the study and enables direct comparison with B/vB criteria of Annex XIII				uncertainties the project "Bioaccumulation assessment of superhydrophobic substances." was initiated)
Project report "Bioaccumulation assessment of superhydrophobic substances."	Consistent with the other evidence, high specificity as substance specific calculated HYBIT BCF values enable direct comparison with B/vB criteria of Annex XIII	Plausible	Not relevant	Supporting evidence for B/vB conclusion	Low/medium (further validation with experimental data necessary)
Several field studies **UV-329**	Consistent with the other evidence, high specificity as substance specific results can be used in WoE to conclude on B/vB	Plausible	Not relevant	Supporting evidence for B/vB conclusion	Medium to high
Conclusion from overall confidence	The conclusion for UV-329 is based on a weight-of-evidence assessment using different pieces of information. The HYBIT BCF is given the highest weight. BCFs derived from HYBIT test are directly comparable with the numerical B and vB criteria of REACH Annex XIII. Considering all evidence together especially the HYBIT test in combination with the related model predictions, fish BCFs and the field data the confidence that UV-329 fulfills the B and vB criterion for aquatic organisms is high.				

3.4.2 Bioaccumulation in terrestrial organisms (soil dwelling organisms, vertebrates)

Both substances might screen as potentially B in terrestrial organisms. This potential is, however, not fully assessed as it is not crucial for the B/vB conclusion of the substances. In the following, some studies are summarised as supporting evidence for the B/vB conclusion.

Each of the many steps involved in the process of performing environmental studies described below will have an impact on the overall uncertainty of the final results. This uncertainty begins with the design of the sampling regime and is compounded through the entire process to storage of samples, chemical analysis and data treatment. As it is difficult to estimate the absolute uncertainty for all steps in the process the results are used in a more general way as supporting evidence in the bioaccumulation assessment.

3.4.2.1 Detection in breast milk

Lee *et al.* (2015)

Breast milk samples (n=208) were collected from 87 lactating women in the Children's Health and Environmental Chemicals in Korea Panel, or CHECK Panel. In this study, breast milk samples were collected from five Korean university hospitals located in four cities including Seoul, Pyeongchon, Ansan and Jeju, from February to December in 2011. The breast milk samples were divided into four groups at the following timepoints after delivery: <7, 15, 30, and 90 days postpartum. Participants completed questionnaire about current and previous pregnancy histories, medical history, and demographic parameters (age, BMI, parity, gestational age at delivery, sex of newborn, and delivery mode). Breast milk samples were collected in polypropylene tubes and were frozen and transported on ice to the laboratory. Samples were stored in the laboratory at −70 °C until analysis. Breast milk samples (10 mL) were extracted with 2.5 mL of 8% potassium oxalate solution, 10 mL of ethanol, and 5 mL of diethyl ether for 30 min by mechanical shaking and analysed with GC/MS. Among the BUVSs [benzotriazole UV stabilisers] analysed, UV-328 was dominant in all the samples, with a detection rate of 98%. The concentrations of UV-329 and UV-326 ranged from <5 to 178 and <2 to 53.1 ng/g lipid wt. in human breast milk with detection rate of 8.7 and 9.1%.

Kim *et al.* (2019)

Human breast milk samples (n=87) from primipara and multipara mothers were collected from Kanagawa Prefecture, Japan (n=20) in 2009–2011, Malate (n=19) and Payatas (n=22), the Philippines in 2008, and Hanoi (n=7), Bui Dau (n=10), and Trang Minh (n=9), Vietnam in 2008. Informed consent was obtained from all the donors. The general information in the questionnaire included each mother's age, height, occupation, dietary habits, body mass index, birth procedure, and breastfeeding period, as well as the age and weight of the baby (Table 1). From each participant, about 100 mL of breast milk was collected using a breast pump to express milk into prewashed glass containers prepared for every individual. The collected milk samples in the Philippines and Vietnam except for Japan were shipped frozen to Japan and were stored at −25 °C in the Environmental Specimen Bank (es-BANK) of Ehime University until chemical analysis. Approximately 10 g of human breast milk samples were freeze-dried and then were extracted by High Speed Solvent Extractor (hexane/acetone, 1:1, v/v). Total concentrations of the 8 benzotriazoles in breast milk ranged from MDL (method detection limit) to 1100 ng/g lipid wt. in present study. Among the 8 benzotriazoles compounds targeted, the highest concentration of UV-9 was found in breast milk samples collected from Vietnam. The concentrations of UV-329 and UV-326 ranged from <MDL to 26 and <MDL to 210 ng/g lipid wt. in human breast milk. In the samples from the Philippines the detection frequency of UV-329 was 0% and in Hanoi 100%.

3.4.2.2 Detection in predators

Schlabach *et al.* (2018)

In this screening study about 90 different compounds with an array of physiochemical properties were measured in environmental samples. These samples included a selection of biota from localised hot-spot areas and from the most remote Arctic species. Biota samples were stored frozen (−20 °C) and extracted with organic solvents in an ultrasonic bath. UV-329 was detected in eggs of European shag (0.35 ng/g w.w., n=5, DF: 100%), blood of polar bear (0.5 ng/g w.w., n=5, DF: 10%), liver of American mink (0.35 ng/g w.w., n=5, DF: 100%). UV-326 was detected in eggs of kittiwake (0.13 ng/g w.w., n=5, DF: 20%), blood of polar bear (0.31 ng/g w.w., n=5, DF: 10%), liver of American mink (0.37 ng/g w.w., n=5, DF: 100%). The UV filters UV-326 and UV-329 were found in Arctic hotspot biota. These findings suggest a potential to bioaccumulate and support earlier conclusions.

Lu *et al.* (2019)

Ringed seals were collected at Resolute Bay (n=3), Arviat (n=3), Sachs Harbour (n=3), and Lake Melville (n=5) by local hunters in 2016 and 2017 during subsistence harvesting. The livers of ringed seals were used for the present study. A mixture solvent of 5 mL 1:1 (v:v) hexane:dichloromethane was used to extract the sample. An ultra-performance liquid chromatography tandem mass spectrometer (UPLC-MS/MS) system was used for sample analysis. UV-329 was detected in all samples from Resolute Bay and Sachs Harbour, while UV-326 was occasionally detected in the seal samples from Arviat, Sachs Harbour, and Resolute Bay regions. The concentrations of UV-329 and UV-326 ranged from <580 to 9411 and <4100 to 6621 pg/g ww. in seal liver samples with detection rate of 0-100 and 0-33%. The detection suggests the presence of these contaminants in remote regions and resident species.

3.4.3 Summary and discussion of bioaccumulation

UV-326 and UV-329 both screen as potentially B/vB due to log Kow values above the screening trigger value of 4.5.

As a standard OECD 305 BCF is available for UV-326 a direct comparison with the Annex XIII criteria for bioaccumulation is possible. The available BCF data give high confidence that UV-326 fulfils the B and vB criteria of REACH Annex XIII (BCF>5000).

The conclusion for UV-329 is based on a weight-of-evidence assessment using different pieces of information. The HYBIT BCF of >5000 is given the highest weight. HYBIT is a new test system and therefore is connected to some uncertainties regarding less experience in judging the results especially k_1 values. To address these uncertainties especially for k_1 estimation from HYBIT test the project "Bioaccumulation assessment of superhydrophobic substances" was initiated which supports the HYBIT BCF. *H.azteca* is an aquatic organism to which the B and vB criteria of REACH annex XIII refers to. Considering all evidence together especially the HYBIT test in combination with the related model predictions, recalculated fish BCF >2000 and the field data as supporting evidence, it is concluded that UV-329 fulfils the B and vB criterion of REACH Annex XIII for aquatic organisms.

Furthermore, UV-326 and UV-329 are detected in human breast milk and predators. As it is difficult to estimate the absolute uncertainty for the results of these studies they are used in a more general way as supporting evidence for the B/vB conclusion.

4 Human health hazard assessment

Not assessed

5 Environmental hazard assessment

Not assessed.

6 Conclusions on the SVHC Properties

6.1 vPvB assessment

6.1.1 Assessment of vPvB properties

A weight of evidence determination according to the provisions of Annex XIII of REACH is used to identify the substances as vPvB substances. All available information (such as the results of standard tests, monitoring and modelling, information from the application of the category and analogue approach (grouping, read-across) and (Q)SAR results) was considered together in a weight of evidence approach.

6.1.1.1 Persistence

The screening criterion for persistence (P) is fulfilled for both, UV-326 and UV-329. The results from the available screening studies showed that these substances are not readily biodegradable. This is confirmed by the available (Q)SAR results.

Hydrolysis of the substances is not expected due to the absence of functional groups susceptible to hydrolysis.

In a water sediment simulation study at 20 °C, no degradation was observed after 100 days. At an environmentally relevant temperature of 12 °C this corresponded to a half-life significantly larger than 212 days.

Faster dissipation in an aquifer test may be related to the different sediment type tested. Simulation test results for a structurally related substance (M1) support both very high persistence in sediment and the impact of different sediment types on dissipation.

UV-P (a structurally related substance to UV-329), UV-326 and further phenolic benzotriazoles have been detected in sediment sections that date back years and even decades, both in samples downstream from a former point source and in samples from urban estuaries.

UV-326 and UV-329 are persistent (and potentially very persistent) in two soil dissipation studies.

As an overall conclusion, based on the above information used in a weight-of-evidence-approach, it is concluded that UV-326 and UV-329 meet the 'persistence' criterion (P) and the 'very persistent' criterion (vP) in accordance with Annex XIII, points 1.1.1 and 1.2.1, of the REACH Regulation on the basis of their persistent and very persistent (P/vP) properties in sediment (DegT50 > 180 days). Furthermore, UV-326 and UV-329 meet the 'persistence' criterion (P) and potentially the 'very persistent' criterion (vP) in accordance with Annex XIII, points 1.1.1 and 1.2.1, of the REACH Regulation on the basis of their persistent and potentially their very persistent (P/vP) properties in soil (at least DegT50 > 120 days).

6.1.1.2 Bioaccumulation

UV-326 and UV-329 both screen as potentially B/vB due to the available log K_{ow} values above the screening trigger value of 4.5.

As a standard OECD 305 BCF is available for UV-326 a direct comparison with the Annex XIII criteria for bioaccumulation is possible. The available BCF data give high confidence that UV-326 fulfils the B and vB criteria of REACH Annex XIII (BCF>5000).

The conclusion for UV-329 is based on a weight of evidence assessment using different pieces of information. The HYBIT BCF of >5000 is given the highest weight. HYBIT is a new test system and therefore is connected to some uncertainties regarding less experience in judging the results, especially k_1 values. To address these uncertainties especially for k_1 estimation from HYBIT test the project "Bioaccumulation assessment of superhydrophobic substances" was initiated, which supports the HYBIT BCF. *H.azteca* is an aquatic organism to which the B criteria of REACH Annex XIII refers to. Considering all evidence together especially the HYBIT test in combination with the related model predictions, recalculated fish BCF_{kgL} >2000 and >5000 and the field data as supporting evidence UV-329 fulfils the B and vB criterion for aquatic organisms. Furthermore, UV-326 and UV-329 are detected in human breast milk and top predators. This information is used in a more general way as supporting evidence for the B/vB conclusion.

6.1.2 Summary and overall conclusions on the vPvB properties

A weight of evidence determination according to the provisions of Annex XIII of REACH has been used to identify UV-326 and UV-329 as vPvB substances. All available relevant information (such as the results of standard tests, monitoring and modelling, information

from the application of the read-across and (Q)SAR results) was considered together in a weight-of-evidence approach.

Persistence

The screening criterion for persistence (P) is fulfilled for both UV-326 and UV-329. The results from the available screening studies (reliable with or without restrictions) showed that these substances are not readily biodegradable. This is confirmed by the available (Q)SAR results with BIOWIN and CATALOGIC which indicate that UV-326 and UV-329 screen as potentially P or vP. The outcomes of the screening tests and the (Q)SARs predictions have been assigned a low weight in the weight-of-evidence approach (WoE) for the P assessment.

Hydrolysis of UV-326 and UV-329 is not expected due to the absence of functional groups susceptible to hydrolysis. As a conclusion, abiotic degradation of UV-326 and UV-329 is not considered to be a significant degradation pathway in the environment.

In a water-sediment simulation study for UV-326 and UV-329 at 20 °C (reliable with restrictions), no degradation was observed after 100 days. At an environmentally relevant temperature of 12 °C this corresponded to a half-life significantly larger than 212 days for UV-326 and UV-329 thus indicating their very persistent properties in sediment (DegT50>180 days). The outcome of this higher tier study is given a high weight in the WoE approach as it provides information directly comparable with the P and vP criteria set out in Annex XIII, points 1.1.1 (d) and 1.2.1 (b) of the REACH Regulation.

Faster dissipation of UV-326 and UV-329 in an aquifer test (reliable with restrictions) may be related to the different sediment type tested. This study has been assigned a low weight in the WoE approach considering its deviating test conditions and the difficulty to derive an appropriate DT50. Simulation test results (reliable with restrictions) for a structurally related substance 3-[3-(2*H*-benzotriazol-2-yl)-5-*tert*-butyl-4-hydroxyphenyl]propionicacid (M1) *H*-support both very high persistence in sediment (DegT50 in sediment >180 days) for UV-326 and the impact of different sediment types on dissipation. This study on a structurally related substance is assigned a medium weight in the WoE approach.

UV-P (a structurally related substance to UV-329), UV-326 and further phenolic benzotriazoles have been detected in sediment cores that date back years and even decades (starting from the 1960s), both in samples downstream from a former point source and in samples from urban estuaries. This information provides indirect evidence that UV-326 and potentially UV-329 (as a structurally related substance to UV-P) can persist in sediments for several decades. Monitoring data in sediment cores are used as supporting information in the WoE approach for UV-326 and UV-329. They are in line with the outcome of the water-sediment simulation study, the screening studies and the QSAR predictions as they point towards the persistence of UV-326 and potentially UV-329 (based on results of the structural analogue UV-P) in sediments.

UV-326 and UV-329 are persistent (and potentially very persistent) in two soil dissipation studies (reliable with restrictions) (at least DegT50>120 days).

As an overall conclusion, based on the above information used in a weight-of-evidence-approach, it is concluded that UV-326 and UV-329 meet the 'persistence' criterion (P) and the 'very persistent' criterion (vP) in accordance with Annex XIII, points 1.1.1 and 1.2.1, of the REACH Regulation on the basis of their persistent and very persistent (P/vP) properties in sediment (DegT50 > 180 days). Furthermore, UV-326 and UV-329 meet the 'persistence' criterion (P) and potentially the 'very persistent' criterion (vP) in accordance with Annex XIII, points 1.1.1 and 1.2.1, of the REACH Regulation on the basis of their persistent and potentially their very persistent (P/vP) properties in soil (at least DegT50 > 120 days).

Bioaccumulation

Both UV-326 and UV-329 screen as potentially B/vB due to the available log K_{ow} values above the screening trigger value of 4.5.

An OECD TG 305 study (aqueous exposure; reliable with restrictions) with rainbow trout (*Oncorhynchus mykiss*) performed on UV-326 indicates a high bioaccumulation potential with a lipid-normalised growth corrected kinetic bioconcentration factor (BCF_{kgL}) value in the range of 7093—14225 L/kg (whole fish BCF back calculated from edible and non-edible portions and based on total radioactive residues of the test substance). This study is given a high weight and its results are used to conclude that UV-326 has B/vB properties (BCF>5000 L/kg) in accordance with REACH Annex XIII. Monitoring data tend to confirm this prediction as UV-326 has been found in human breast milk and in biota including in top predators such as the polar bears which are listed as vulnerable to extinction, according to the International Union for Conservation of Nature (IUCN) Red List. Based on the weight of evidence of the data available, it is concluded that UV-326 meets the 'bioaccumulation' criterion (B) and the 'very bioaccumulative' criterion (vB) in accordance with Annex XIII, points 1.1.2 and 1.2.2, of the REACH Regulation.

The conclusion for UV-329 is based on a weight-of-evidence assessment using different pieces of information. The outcome of the *Hyalella azteca* bioconcentration test (HYBIT; reliable with restrictions) for UV-329 is given a high weight in the WoE approach with 3 %-lipid-normalised steady-state bioconcentration factor (BCF_{ssL}) and 3%-lipid-normalised kinetic bioconcentration factor (BCF_{kL}) values in the range of 11063—11876 L/Kg. This study provides information directly comparable with the B (BCF>2000) and vB criteria (BCF>5000) set out in Annex XIII. Re-calculated fish BCF_{kgL} >2000 and >5000 derived from an OECD TG 305 study (aqueous exposure; reliable with restrictions) with rainbow trout (*Oncorhynchus mykiss*) are all supporting the vB conclusion for UV-329. Monitoring data tend to confirm this prediction as UV-329 has been found in human breast milk and in biota including in top predators such as the polar bears which are listed as vulnerable to extinction, according to the IUCN Red List. Based on the weight of evidence of the data available, it is concluded that UV-329 meets the 'bioaccumulation' criterion (B) and the 'very bioaccumulative' criterion (vB) in accordance with Annex XIII, points 1.1.2 and 1.2.2, of the REACH Regulation.

Conclusion

In conclusion, UV-326 and UV-329 are proposed to be identified as vPvB substances according to Art. 57(e) of REACH by comparing all relevant and available information listed in Annex XIII of REACH with the criteria set out in the same Annex, in a weight-of-evidence determination.

Part II

7 Registration and C&L notification status

7.1 Registration status

Table 37: Registration status

From the ECHA dissemination site[62,63]	
Registrations	☒ Full registration(s) (Art. 10) ☒ Intermediate registration(s) (Art. 17 and/or 18)

7.2 CLP notification status

Table 38: CLP notifications

	CLP Notifications for UV-326[64]	**CLP Notifications for UV-329[65]**
Number of aggregated notifications	12	13
Total number of notifiers	2143	736

8 Total tonnage of the substance

Table 39: Tonnage status for UV-326 and UV-329

	UV-326	UV-329
Total tonnage band for each of the registered substances (excluding the volume registered under Art 17 or Art 18)[66]	1 000-10 000 t/pa	1 000-10 000 t/pa

[62] Substance entry on UV-326, https://echa.europa.eu/de/registration-dossier/-/registered-dossier/5785 (accessed 26.06.2023)
[63] Substance entry on UV-329, https://echa.europa.eu/de/registration-dossier/-/registered-dossier/13220 (accessed 26.06.2023)
[64] C&L Inventory database on UV-326, https://echa.europa.eu/de/information-on-chemicals/cl-inventory-database/-/discli/details/44804 (accessed 23.06.2023)
[65] C&L Inventory database on UV-329, https://echa.europa.eu/de/information-on-chemicals/cl-inventory-database/-/discli/details/68877 (accessed 23.06.2023)
[66] *https://echa.europa.eu/substance-information/-/substanceinfo/100.021.315*,

9 Information on uses of the substance

Table 40: Uses of UV-326

	Use(s)	**Registered use** *(If not, specify the source of the information)*	**Use <u>likely</u> to be in the scope of Authorisation**
Uses as intermediate	-	-	
Formulation or repacking	Release to the environment can occur from formulation in mixtures and materials during preparation of masterbatches, compounds and additive mixtures. Activities include charging and discharging of substances, material transfers, mixing, large scale and small scale packing, sampling, maintenance and associated laboratory activities. Formulations are further used for coatings, inks and toners, textile dyes and impregnation products, perfumes and fragrances, cosmetics and personal care products, production of polymers like rubber production and processing and rigid foams and flexible foams, Adhesives and sealants manufacture, lubricants and greases, metalworking fluids and hydraulic fluids	Yes	Yes
Uses at industrial sites	Release to the environment can occur from formulation of mixtures and/or repacking, compounding and conversion of masterbatches for production of polymers; manufacture of plastic products; use of coating formulations and masterbatches of compounds in roll coating, spreadcoating or dip coating, resulting in inclusion into a matrix; use of adhesives and sealants, use of additive in plastics and printing inks (spray, roller or dipping application) Uses include open, semi-open, semi-closed and closed processes The substance is used in the manufacture of plastic products, the recycling of plastics, for polymers like foams and resins, adhesives and sealants, in coatings, in photo-chemicals, for lubricants and greases, for textile application, and in industrial cleaning agents	Yes	Yes
Uses by professional workers	Release to the environment can occur from formulation of mixtures and/or repacking, and wide dispersive outdoor an indoor use resulting in inclusion into a matrix, including application in coatings, adhesives/sealants, printing inks, and plastics. Further emissions can occur by use plastics, use of processing aids and	Yes	Yes

	functional fluids, professional use of textile dyes, use in cleaning agents and use in plant protection products.		
Consumer uses	The substance is used indoor and outdoor in applications resulting in inclusion into a matrix, including application in coatings, adhesives, sealants, printing inks, polishes and wax blends, textile dyes, finishing and impregnation products. It is used in washing and cleaning products, fillers, putties, plasters, modelling clay, cosmetics, fragrances, air care products, biocidal products, photo-chemicals, and metal and non-metal surface treatment. Further release to the environment can occur during indoor and outdoor use of long-life articles and materials with low release, including coatings, adhesives and plastics and the use of functional fluids.	Yes	Yes
Article service life	Release to the environment can occur from the processing of plastic articles at industrial sites, the finishing of plastic articles by professionals indoor and outdoor, and the use and processing of rubber and plastic articles both indoor and outdoor by consumers and professionals. Further emissions might occur from consumer use of articles containing H4EDTA (applies to a variety of articles, including vehicles, machinery, mechanical appliances, electrical/electronic articles, electrical batteries and accumulators, stone, plaster, cement, glass and ceramic articles, fabrics, textiles and apparel, leather articles, metal articles, paper articles, rubber articles, wood articles, plastic articles, scented clothes, scented eraser, scented toys, scented paper articles, scented CD, packaging materials for metal parts, releasing grease/corrosion inhibitors), Service life of textiles both indoor and outdoor, and service life of Coatings, Adhesives and sealants both indoor and outdoor in articles like vehicles, metal articles and rubber articles for furniture.	Yes	No, but if the substance is subject to authorisation for the incorporation into articles, this can also affect its presence in articles. However, this does not cover imported articles.

Table 41: Uses of UV-329

	Use(s)	**Registered use** *(If not, specify the source of the information)*	**Use <u>likely</u> to be in the scope of Authorisation**
Uses as intermediate	-	-	-
Formulation or repacking	Release to the environment can occur from formulation in mixtures and materials during preparation of masterbatches, compounds, additive mixtures and fragranced endproducts.	Yes	Yes

	Formulations are further used for coating, ink, fragranced endproducts like washing and cleaning products, production of polymers like rubber production and processing and rigid foams and flexible foams, Adhesives and sealants manufacture.		
Uses at industrial sites	Release to the environment can occur from formulation of mixtures and/or repacking, compounding and conversion of masterbatches for production of polymers; use of coating formulations, masterbatches of compounds in roll coating, spreadcoating or dip coating, resulting in inclusion into a matrix; use of adhesives and sealants Uses include open, semi-open, semi-closed and closed processes The substance is used in the manufacture of plastic products, the recycling of plastics, for polymers like foams and resins, adhesives and sealants	Yes	Yes
Uses by professional workers	Release to the environment can occur from formulation of mixtures and/or repacking, and wide dispersive outdoor an indoor use resulting in inclusion into a matrix, including application in coatings, adhesives/sealants, polymer preparations and compounds, and plastics	Yes	Yes
Consumer uses	This substance is used in the following products: air care products, coating products, adhesives and sealants, lubricants and greases, polishes and waxes and washing & cleaning products. Other release to the environment of this substance is likely to occur from: indoor use (e.g. machine wash liquids/detergents, automotive care products, paints and coating or adhesives, fragrances and air fresheners), outdoor use, indoor and outdoor use in closed systems with minimal release (lubricants as processing aid and functional fluid)	Yes	Yes
Article service life	Release to the environment can occur from the processing of plastic articles at industrial sites and the use and processing of rubber and plastic articles, both indoor and outdoor, by consumers and professionals.	Yes	No, but if the substance is subject to authorisation for the incorporation into articles, this can also affect its presence in articles. However, this does not cover imported articles.

10 Information on structure of the supply chain

Not assessed.

11 Additional information

11.1 Substances with similar hazard and use profiles on the Candidate List

Table 42: Substances with similar hazard and use profiles on the Candidate List[67]

Name	EC Number	CAS Number	Reason for inclusion in Candidate List	Use
2-(2*H*-benzotriazol-2-yl)-4-(*tert*-butyl)-6-(sec-butyl)phenol (UV-350)	253-037-1	36437-37-3	vPvB (Article 57e)	UV filter
2,4-di-*tert*-butyl-6-(5-chlorobenzotriazol-2-yl)phenol (UV-327)	223-383-8	3864-99-1	vPvB (Article 57e)	UV filter
2-benzotriazol-2-yl-4,6-di-*tert*-butylphenol (UV-320)	223-346-6	3846-71-7	PBT (Article 57d) vPvB (Article 57e)	UV filter
2-(2*H*-benzotriazol-2-yl)-4,6-ditertpentylphenol (UV-328)	247-384-8	25973-55-1	PBT (Article 57d) vPvB (Article 57e)	UV filter

[67] https://www.echa.europa.eu/candidate-list-table

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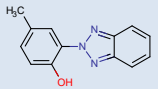
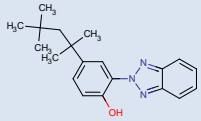
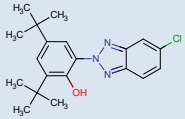
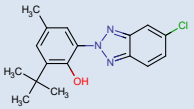
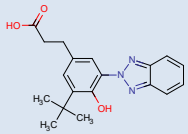
ANNEX I

Data matrix

Data matrix for UV-326, UV-329, UV-327, M1 and UV-P.

Chemical name	UV-P	UV-329	UV-327[68]	UV-326	M1
EC number	219-470-5	221-573-5	223-383-8	223-445-4	630-348-4
Chemical structure					
Molecular weight	225.25	323.44	357.89	315.81	339.4
Impurities	None registered	None registered	None known	None registered (2 conformers)	None registered
Octanol water partition log K_{OW}	4.2 (OECD TG 107) 3.95 (COSMOtherm)	≥ 6.5 (OECD TG 107) 6.91 (Do et al. 2022) 6.4 (COSMOtherm)	7.31 (Do et al. 2022) 7.85 (COSMOtherm)	≥ 6.5 (OECD TG 107) 7.38 (Do et al. 2022) 6.7 (COSMOtherm)	≥ 2.75 (OECD TG 107) 3.32 (COSMOtherm; log D)
Water solubility in µg/L	173 (OECD TG 105)	2 (OECD TG 105)	not available	4 (OECD TG 105)	< 1000 (OECD TG 105)
Estimated log K_{OC} (KOCWIN)	3.593	5.114	5.275	4.644	3.801
Vapour pressure at 20°C in Pa	1.47 E-4 (exp)	4.1 E-6 (exp)	not available	7.5 E-7 (exp)	2.9 E-10 (exp, 25°C)
HLC in atm-m3/mole (HENRYWIN)	6.12E-14	4.45E-13	2.74E-13	1.17E-13	1.56E-18
pK_a	9.53 (chemicalize) [69]	9.4 (chemicalize)	10.07 (chemicalize)	10.18 (chemicalize)	9.31 and 4.25 (chemicalize)[70]
Hydrolysis	not expected	not expected	not expected	not expected	not expected

[68] Data on UV-327 added here as supporting information
[69] 27.10. 2022, https://chemicalize.com/ developed by ChemAxon (http://www.chemaxon.com)
[70] 19.08. 2023, https://chemicalize.com/ developed by ChemAxon (http://www.chemaxon.com)

Chemical name	UV-P	UV-329	UV-327[68]	UV-326	M1
BIOWIN1 (Linear Model) Probability	0.8108	0.3415	0.1427	0.4013	0.6452
BIOWIN2 (Non-Linear Model) Probability	0.7851	0.016	0.0013	0.0235	0.197
BIOWIN3 numerical output	2.6829	2.1165	1.8338	2.0641	2.5832
BIOWIN4 numerical output	3.4939	3.1139	2.8989	3.0445	3.5614
BIOWIN5 (Linear MITI Model) Probability	0.2481	0.0704	-0.0095	0.065	0.4279
BIOWIN6 (Non-Linear MITI Model) Probability	0.1597	0.0081	0.002	0.0086	0.1056
CATALOGIC_301C_v12-17 BOD [28 days]	0	0.01	0	0	0
Ready biodegradability tests [28 days]	2% (OECD 301 B)	1% (OECD 301 B)	0% (OECD 301 C)	10-20% (OECD 301 B); 2-10% (OECD 301 B); 0% (OECD 301 C)	not available
Water sediment study (Wick et al 2016a, 2016b)	not tested	no degradation in 100 d	no degradation in 100 d	no degradation in 100 d	not tested
Aquifer system DT50	not tested	34 d	not tested	52 d	not tested
Rhode Island sediment cores (downstream Cranston chemical plant point source)	detected	not analysed	detected	detected	not analysed
Pear River Estuary sediment core (diffuse sources)	detected	not constantly detected, detections close to MQL	detected	detected	not analysed
Soil dissipation studies DT50	75-113 d; 85-157 d	98-129 d; 79-155 d	151-192 d; 112- 173 d	104-141 d; 81-135 d	not analysed

CATALOGIC results for M1
CATALOGIC 301C v12.17 is preferred because its training set contains the most phenolic benzotriazoles. The training set of CATALOGIC

301 C v12.17 contains UV-P and UV-327 and consequently, these substances are in domain. The automatic applicability domain check shows that this model is also the best for M1 while it is still denoted "out of domain"due to 5% unknown fragments. If the default settings of the structural domain for the model are changed to allow for unknown fragments with inert additions (meaning fragments that are not expected to have an impact), then also M1 would be 100 % within structural domain.

BIOWIN results for M1 and UV-P
Some BIOWIN results are contradicting; however, the reliability of these predictions is considered lower than the reliability of CATALOGIC 301C v12.17.

K_{OC}
The dossiers for UV-329 & UV-326 contain KOCWIN predictions. For the sake of comparison, KOCWIN predictions[71] are given for the other substances as well. However, these predictions are not documented according to REACH Annex XI and hence, the respective results should be considered with caution. All considered substances are in the molecular weight range of training set and validation set. Correction factors for carboxylic acid groups and phenolic hydroxy groups were derived from training set substances with these structural features, i.e. though being dependent on pH, the ionic interactions of these groups may be covered by the model to a certain extent.
The registration dossier of UV-P contains further K_{OC} estimations. These were not included as they cannot be directly compared with estimations from the same methods for the other substances.

Henry's Law Constant
To estimate the expected impact of volatility on degradation studies, HENRYWIN predictions[72] are given for the substances. Note that these predictions are not documented according to REACH Annex XI and hence, the respective results should be considered with caution. All considered substances are in the molecular weight range of training set. The range of Henry's Law constants in the training set is exceeded by M1 which has a much lower Henry's Law constant. All other substances are in the Henry's Law constant range of the training set.

[71]2010 U.S. Environmental Protection Agency. KOCWIN v2.01 in EPISUITE v4.11.
[72]2010 U.S. Environmental Protection Agency. HENRYWIN v3.21 in EPISUITE v4.11. Bond method was applied; no results were obtained for the group method.

ANNEX II

Kinetic modelling for aquifer study Liu et al. 2013: UV-329

CAKE Kinetic Evaluation Report

Experiment 1 (SFO)

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Fit step: Final

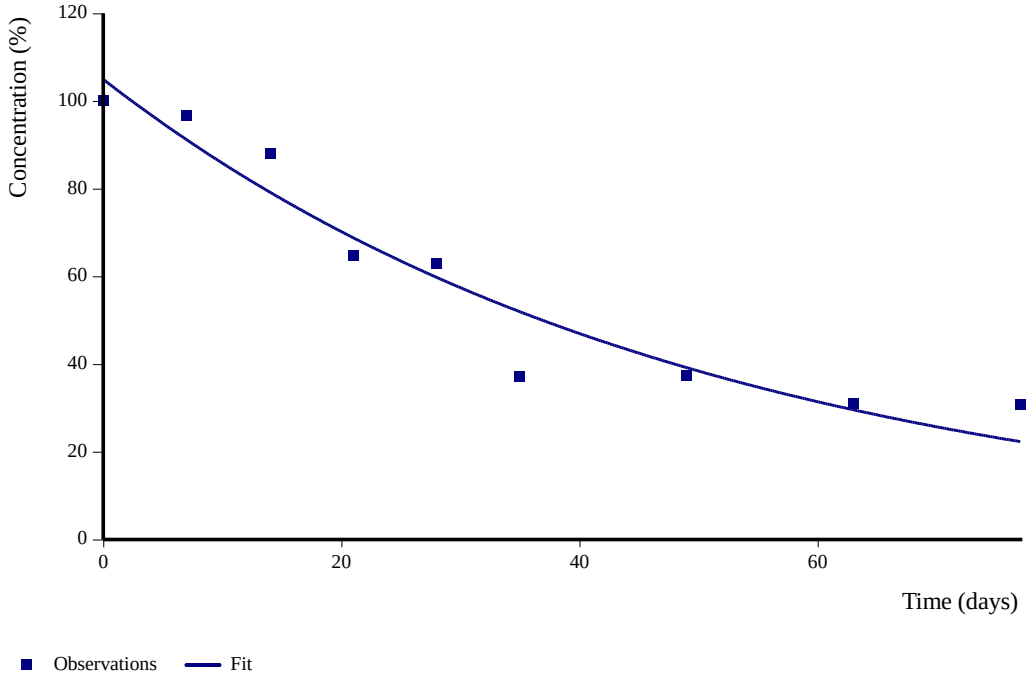
Used Extra Solver for SFO model fit: No

Reference Table:

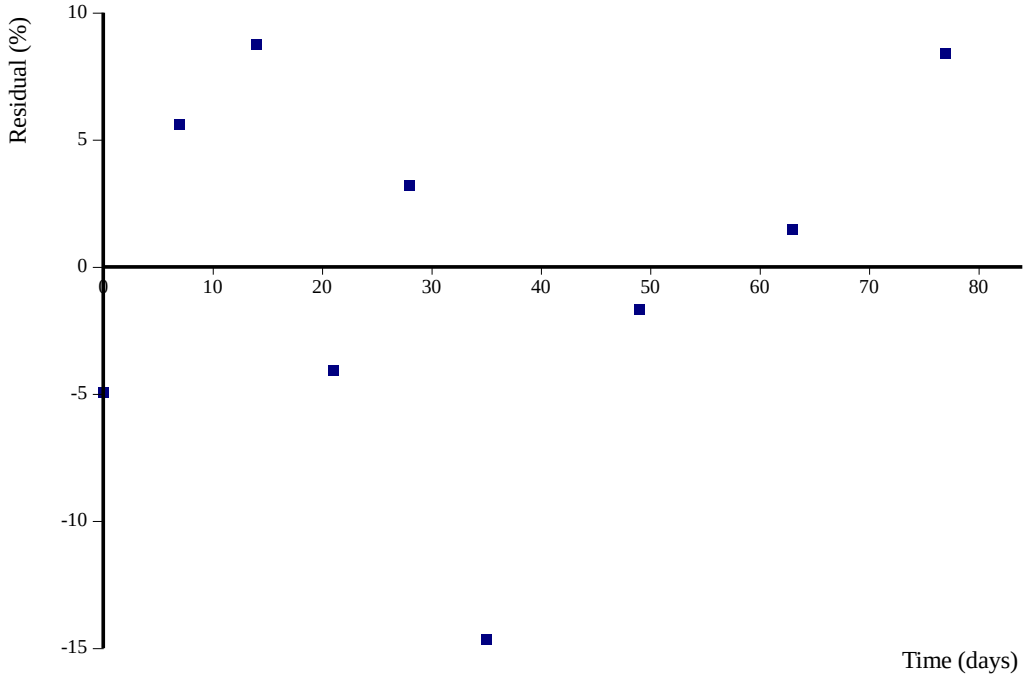
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Estimated Values:

Parameter	Value	□	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	104.9	5.812	N/A	93.93	116	91.2	118.7
k_Parent	0.0201	0.002465	4.04E-005	0.01543	0.02477	0.01427	0.026

Sum of Squared Residuals: 449.6

χ^2

Parameter	Error %	Degrees of Freedom
All data	9.27	7
Parent	9.27	7

Decay Times:

Compartment	DT50 (days)	DT90 (days)
Parent	34.5	115

Additional Statistics:

Parameter	r² (Obs v Pred)	Efficiency
All data	0.931	0.9306
Parent	0.931	0.9306

Parameter Correlation:

	Parent_0	k_Parent
Parent_0	1	0.6856
k_Parent	0.6856	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	100	104.9	-4.944
7	96.78	91.17	5.605
14	87.97	79.21	8.758
21	64.76	68.81	-4.056
28	62.98	59.78	3.194
35	37.27	51.94	-14.67
49	37.52	39.2	-1.686
63	31.05	29.59	1.461
77	30.71	22.33	8.379

Sequence Creation Information:
Fit generated by CAKE version 3.4 (Release)
running on R version 3.0.0 (2013-04-03)

Experiment 1 (DFOP)

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Fit step: Final

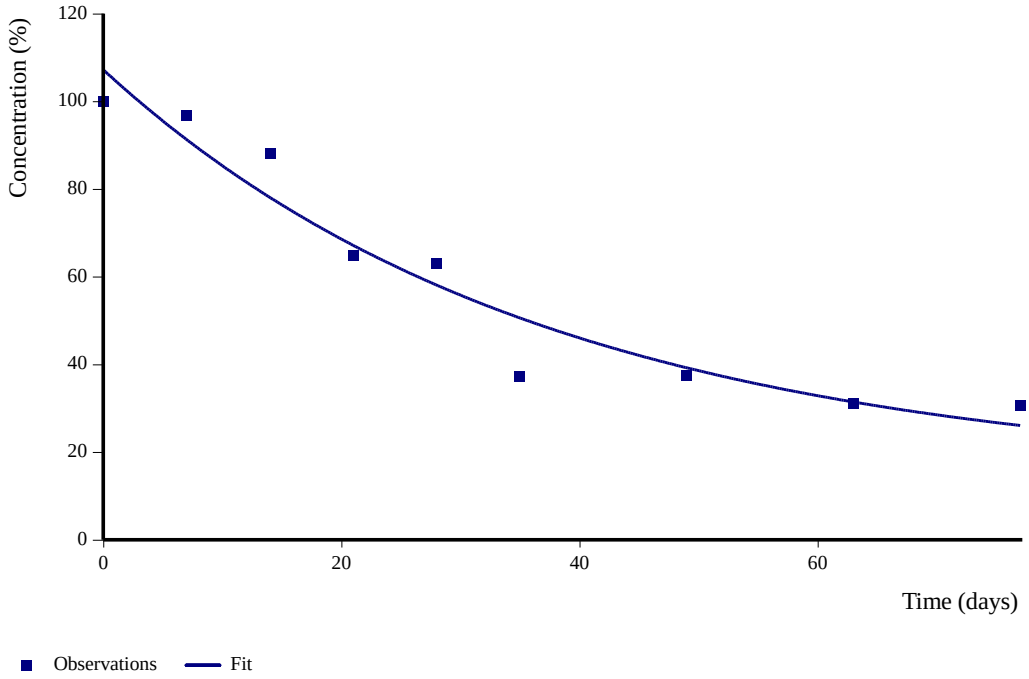
Used Extra Solver for DFOP model fit: No

Reference Table:

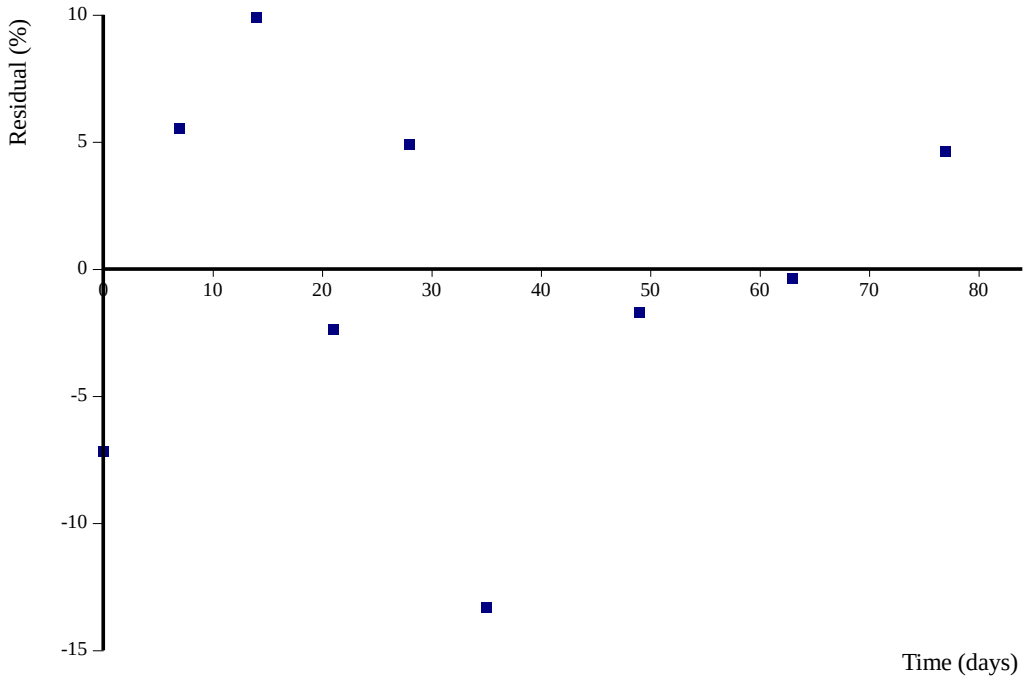
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Estimated Values:

Parameter	Value	□	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	107.2	8.368	N/A	90.33	124.1	85.68	128.7
k1_Parent	0.02691	0.0661	0.3504	-0.1063	0.1601	-0.143	0.197
k2_Parent	8.66E-009	0.1706	0.5	-0.3437	0.3437	-0.4385	0.438
g_Parent	0.8657	2.587	N/A	-4.348	6.079	-5.785	7.516

Sum of Squared Residuals: 411.5

χ^2

Parameter	Error %	Degrees of Freedom
All data	10	5
Parent	10	5

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	32	>10,000	25.8	>10,000

Additional Statistics:

Parameter	r² (Obs v Pred)	Efficiency
All data	0.9364	0.9364
Parent	0.9364	0.9364

Parameter Correlation:

	Parent_0	k1_Parent	k2_Parent	g_Parent
Parent_0	1	0.4743	0.3803	-0.4017
k1_Parent	0.4743	1	0.9838	-0.9924
k2_Parent	0.3803	0.9838	1	-0.998
g_Parent	-0.4017	-0.9924	-0.998	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	100	107.2	-7.192
7	96.78	91.26	5.517
14	87.97	78.06	9.904
21	64.76	67.13	-2.374
28	62.98	58.08	4.901
35	37.27	50.58	-13.31
49	37.52	39.22	-1.703
63	31.05	31.43	-0.3765
77	30.71	26.08	4.633

Sequence Creation Information:
Fit generated by CAKE version 3.4 (Release)
running on R version 3.0.0 (2013-04-03)

Experiment 1 (FOMC)

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Fit step: Final

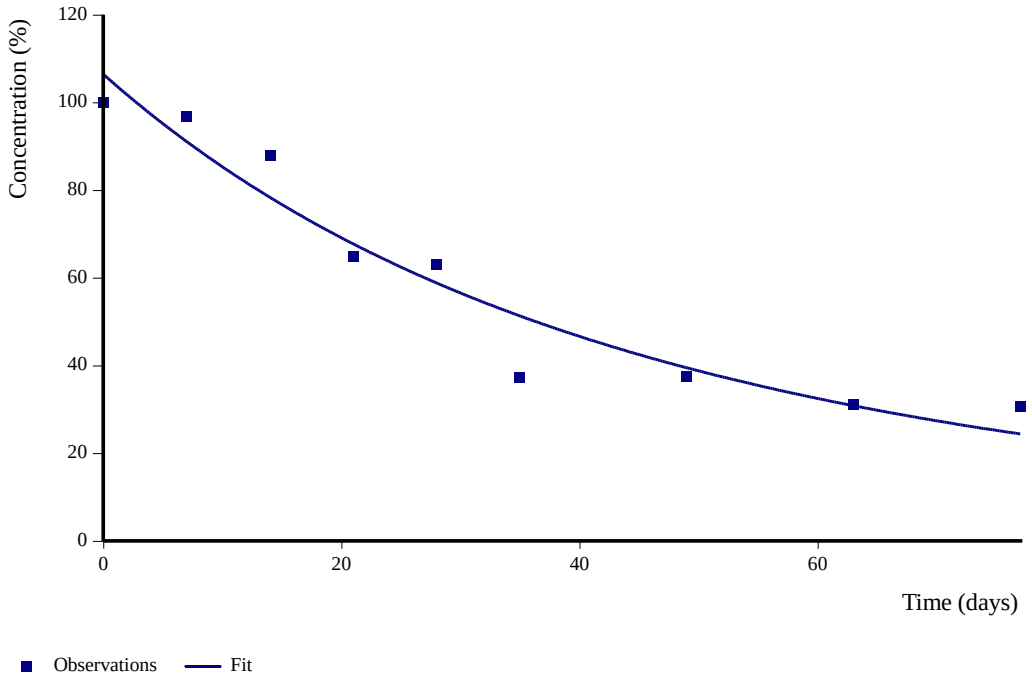
Used Extra Solver for FOMC model fit: No

Reference Table:

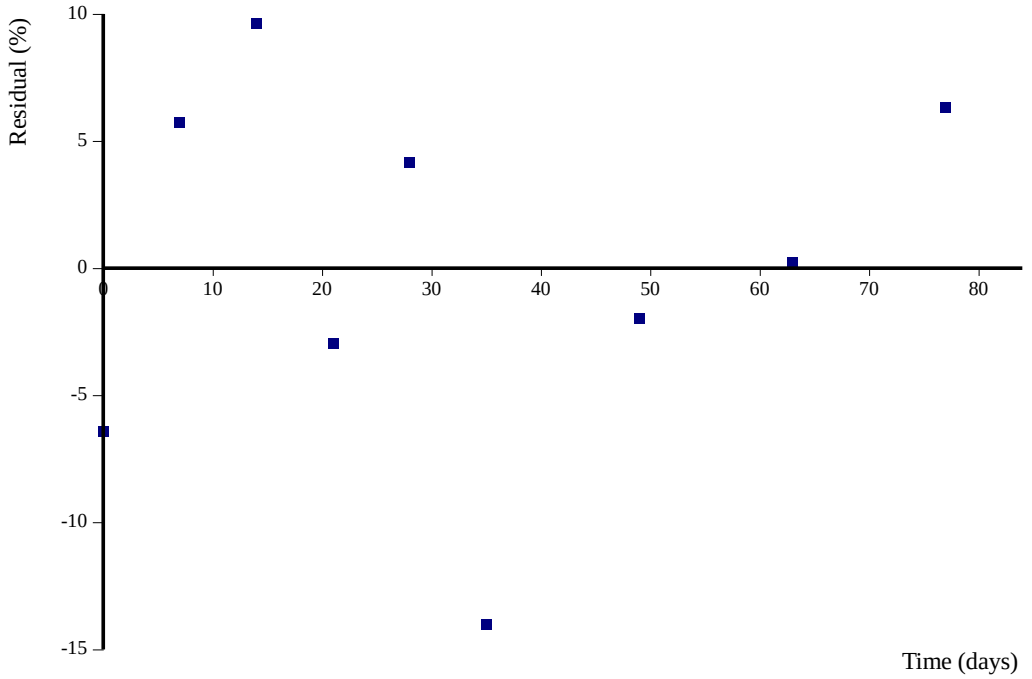
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Estimated Values:

Parameter	Value	□	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	106.4	7.508	N/A	91.83	121	88.05	124.8
alpha	4.48	11.59	N/A	-18.04	27	-23.87	32.83
beta	197.8	574.7	N/A	-919	1.31E+003	-1208	1.60E+003

Sum of Squared Residuals: 433.1

χ^2

Parameter	Error %	Degrees of Freedom
All data	9.61	6
Parent	9.61	6

Decay Times:

Compartment	DT50 (days)	DT90 (days)	DT90 / 3.32 (days)
Parent	33.1	133	40

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.9332	0.9331
Parent	0.9332	0.9331

Parameter Correlation:

	Parent_0	alpha	beta
Parent_0	1	-0.5105	-0.5399
alpha	-0.5105	1	0.9988
beta	-0.5399	0.9988	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	100	106.4	-6.418
7	96.78	91.07	5.712
14	87.97	78.34	9.63
21	64.76	67.72	-2.96
28	62.98	58.81	4.17
35	37.27	51.29	-14.02
49	37.52	39.48	-1.968
63	31.05	30.84	0.212
77	30.71	24.4	6.314

Sequence Creation Information:
Fit generated by CAKE version 3.4 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.4 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Runtime: .NET Framework 4.8.4300.0

Data set: Experiment 1 (HS)

Study date: Mittwoch, 14. April 2021
Report generated: Mittwoch, 14. April 2021

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	Automatic	0 to (unbounded)	No

Fit step: Final

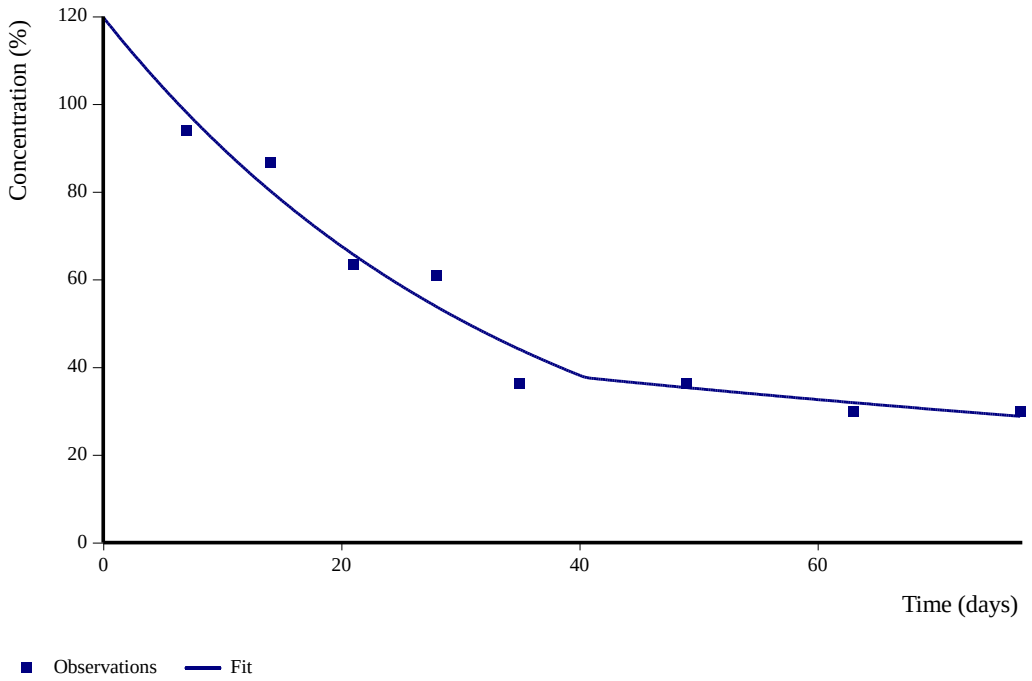
Used Extra Solver: Yes

Reference Table:

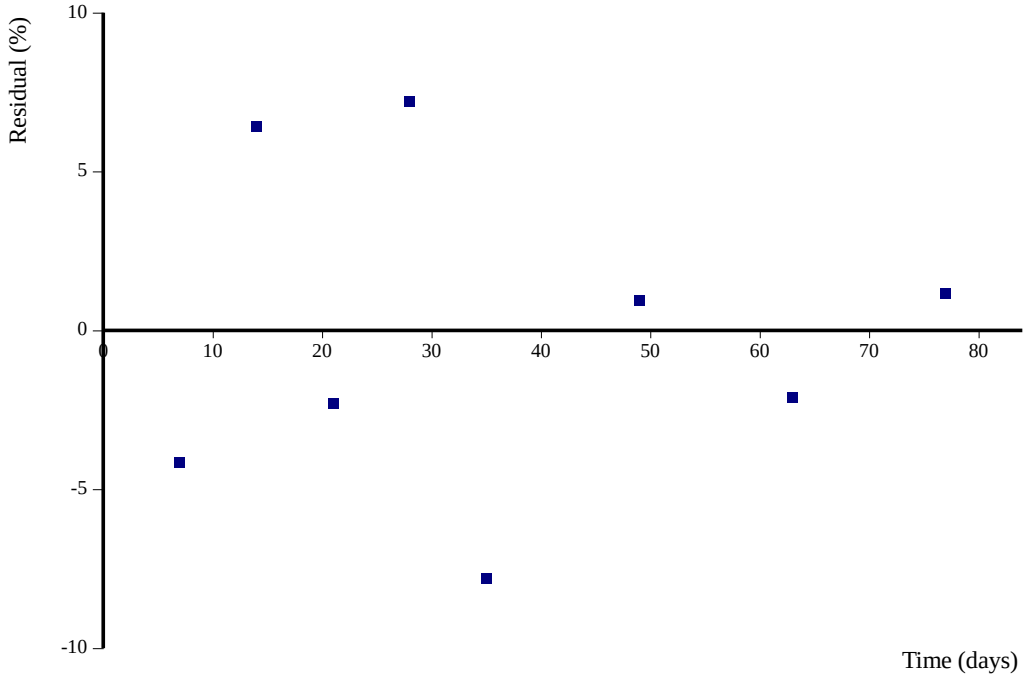
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	28	0 to (unbounded)	No

Estimated Values:

Parameter	Value	□	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	119.8	9.911	N/A	98.67	140.9	92.28	147.3
k1	0.0286	0.004435	0.001488	0.01915	0.03806	0.01629	0.041
k2	0.00728	0.01003	0.2541	-0.0141	0.02866	-0.02057	0.035
tb	40.52	11.3	N/A	16.42	64.62	9.138	71.9

χ^2

Parameter	Error %	Degrees of Freedom
All data	8.06	4
Parent	8.06	4

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	24.2	198	24.2	95.2

Additional Statistics:

Parameter	r² (Obs v Pred)	Efficiency
All data	0.9599	0.9599
Parent	0.9599	0.9599

Parameter Correlation:

	Parent_0	k1	k2	tb
Parent_0	1	0.8569	-0.1117	-0.1754
k1	0.8569	1	-0.1483	-0.2923
k2	-0.1117	-0.1483	1	-0.7477

tb	-0.1754	-0.2923	-0.7477	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
7	93.9	98.06	-4.164
14	86.7	80.27	6.43
21	63.4	65.71	-2.305
28	61	53.78	7.217
35	36.2	44.02	-7.824
49	36.3	35.35	0.9546
63	29.8	31.92	-2.121
77	30	28.83	1.172

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Kinetic modelling for aquifer study Liu et al. 2013: UV-326

CAKE Kinetic Evaluation Report

Experiment 1 (SFO)

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Fit step: Final

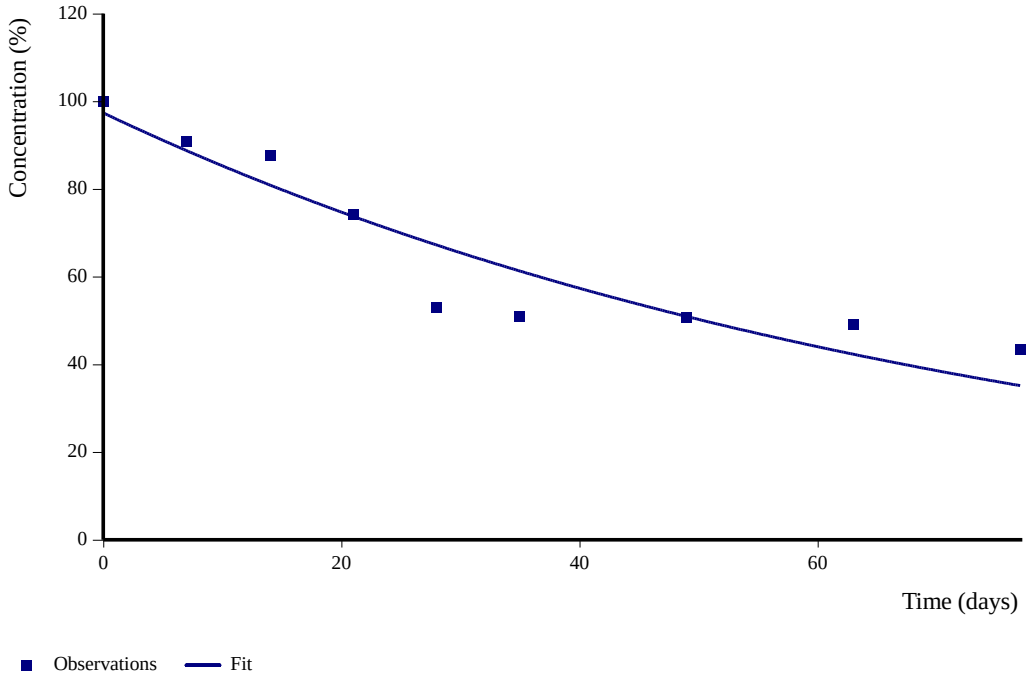
Used Extra Solver for SFO model fit: No

Reference Table:

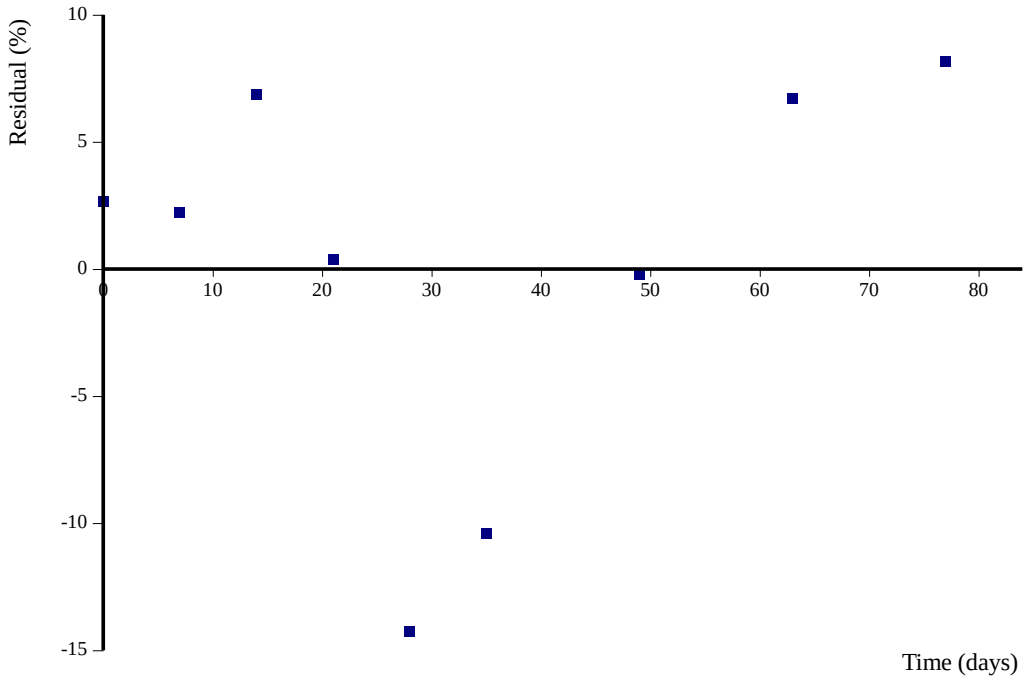
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Estimated Values:

Parameter	Value	□	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	97.34	5.57	N/A	86.79	107.9	84.17	110.5
k_Parent	0.01322	0.002075	1.89E-004	0.009292	0.01715	0.008316	0.018

Sum of Squared Residuals: 482.3

χ^2

Parameter	Error %	Degrees of Freedom
All data	8.79	7
Parent	8.79	7

Decay Times:

Compartment	DT50 (days)	DT90 (days)
Parent	52.4	174

Additional Statistics:

Parameter	r² (Obs v Pred)	Efficiency
All data	0.8729	0.8713
Parent	0.8729	0.8713

Parameter Correlation:

	Parent_0	k_Parent
Parent_0	1	0.7164
k_Parent	0.7164	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	100	97.34	2.66
7	90.95	88.73	2.211
14	87.74	80.89	6.851
21	74.1	73.74	0.3601
28	52.96	67.22	-14.25
35	50.86	61.28	-10.42
49	50.72	50.92	-0.1999
63	49.02	42.32	6.703
77	43.33	35.16	8.165

Sequence Creation Information:
Fit generated by CAKE version 3.4 (Release)
running on R version 3.0.0 (2013-04-03)

Experiment 1 (DFOP)

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Fit step: Final

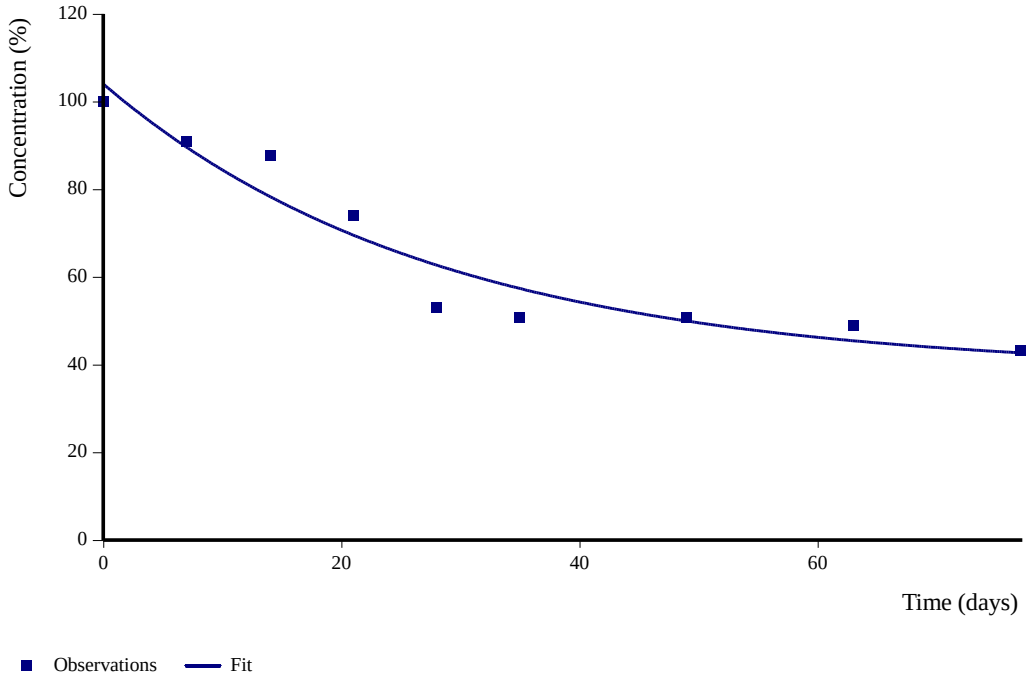
Used Extra Solver for DFOP model fit: No

Reference Table:

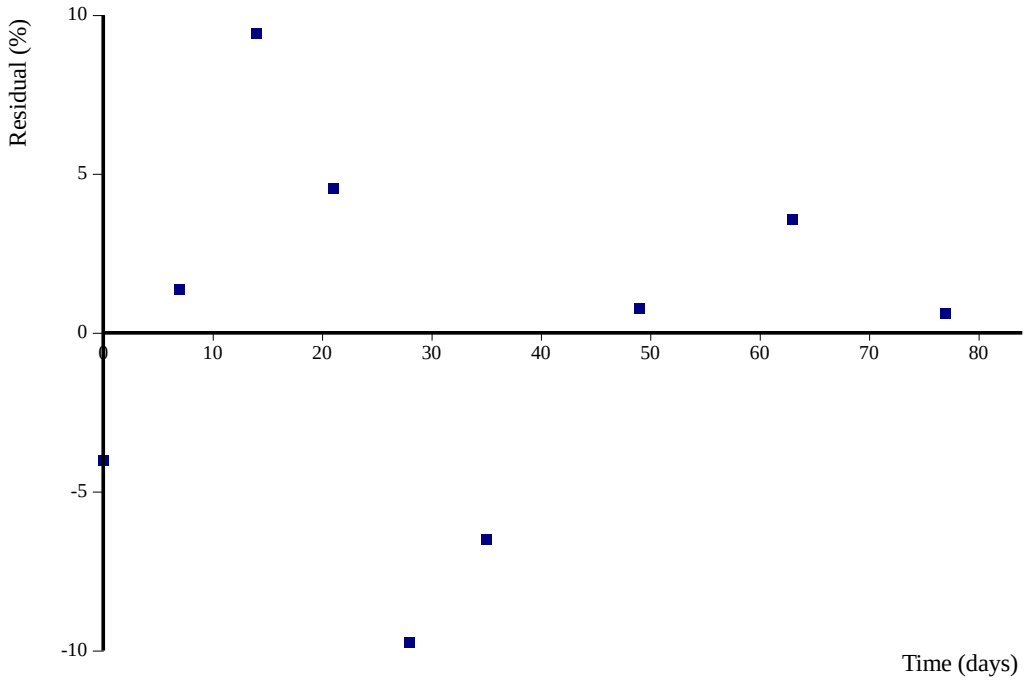
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No

k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Estimated Values:

Parameter	Value	□	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	104	6.97	N/A	89.98	118.1	86.11	121.9
k1_Parent	0.03554	0.05949	0.2881	-0.08434	0.1554	-0.1174	0.188
k2_Parent	5.09E-009	0.03152	0.5	-0.06352	0.06352	-0.08103	0.081
g_Parent	0.6302	1.104	N/A	-1.595	2.855	-2.208	3.469

Sum of Squared Residuals: 278.2

χ^2

Parameter	Error %	Degrees of Freedom
All data	7.52	5
Parent	7.52	5

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	44.4	>10,000	19.5	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.9258	0.9258
Parent	0.9258	0.9258

Parameter Correlation:

	Parent_0	k1_Parent	k2_Parent	g_Parent
Parent_0	1	0.4616	0.3439	-0.3507
k1_Parent	0.4616	1	0.9719	-0.9838
k2_Parent	0.3439	0.9719	1	-0.9968
g_Parent	-0.3507	-0.9838	-0.9968	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	100	104	-4.022
7	90.95	89.58	1.362
14	87.74	78.33	9.415
21	74.1	69.55	4.551
28	52.96	62.7	-9.738
35	50.86	57.37	-6.504
49	50.72	49.96	0.7624
63	49.02	45.46	3.563
77	43.33	42.72	0.6115

Sequence Creation Information:
Fit generated by CAKE version 3.4 (Release)
running on R version 3.0.0 (2013-04-03)

Experiment 1 (FOMC)

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No

alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Fit step: Final

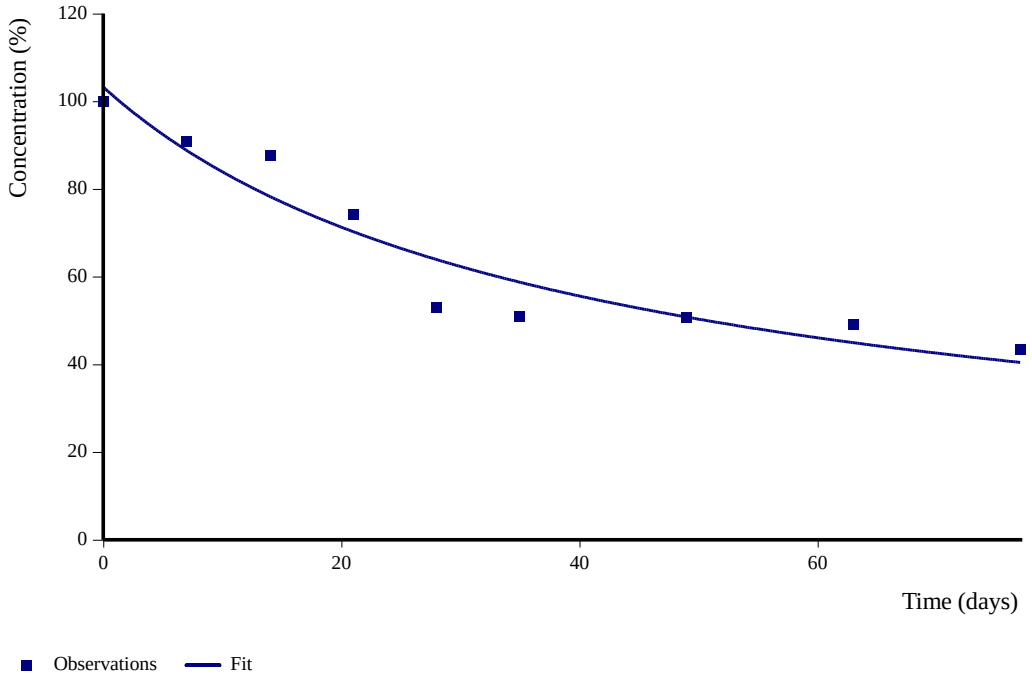
Used Extra Solver for FOMC model fit: No

Reference Table:

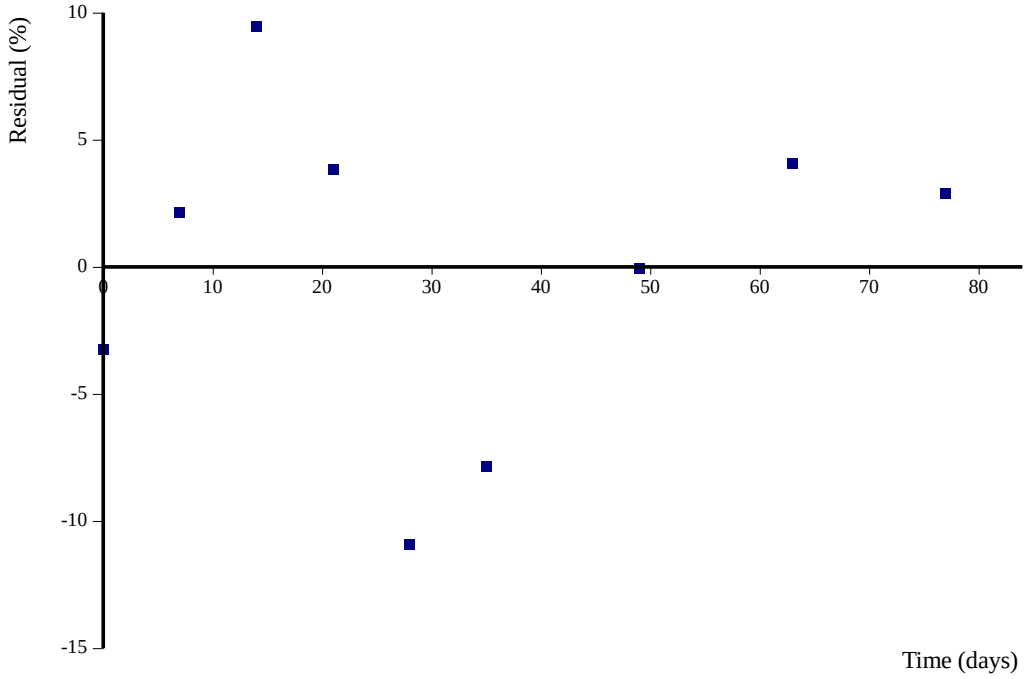
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Estimated Values:

Parameter	Value	□	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	103.2	6.867	N/A	89.91	116.6	86.45	120.1
alpha	0.7684	0.5806	N/A	-0.3597	1.897	-0.6522	2.189
beta	32.29	38.61	N/A	-42.73	107.3	-62.18	126.8

Sum of Squared Residuals: 325.6

χ^2

Parameter	Error %	Degrees of Freedom
All data	7.63	6
Parent	7.63	6

Decay Times:

Compartment	DT50 (days)	DT90 (days)	DT90 / 3.32 (days)
Parent	47.3	614	185

Additional Statistics:

Parameter	r² (Obs v Pred)	Efficiency
All data	0.9132	0.9131
Parent	0.9132	0.9131

Parameter Correlation:

	Parent_0	alpha	beta
Parent_0	1	-0.4618	-0.5772
alpha	-0.4618	1	0.985
beta	-0.5772	0.985	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	100	103.3	-3.249
7	90.95	88.8	2.147
14	87.74	78.29	9.454
21	74.1	70.26	3.841
28	52.96	63.9	-10.94
35	50.86	58.73	-7.867
49	50.72	50.79	-0.06763
63	49.02	44.95	4.068
77	43.33	40.46	2.873

Sequence Creation Information:
Fit generated by CAKE version 3.4 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.4 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Runtime: .NET Framework 4.8.4300.0

Data set: Experiment 1 (HS)

Study date: Mittwoch, 14. April 2021
Report generated: Mittwoch, 14. April 2021

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	Automatic	0 to (unbounded)	No

Fit step: Final

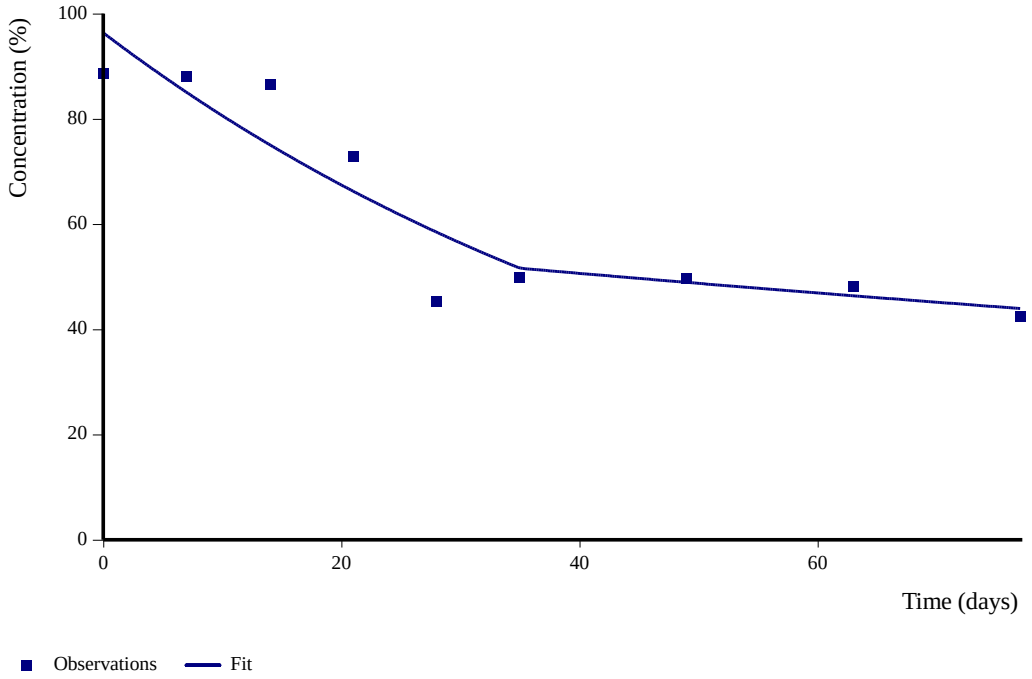
Used Extra Solver: Yes

Reference Table:

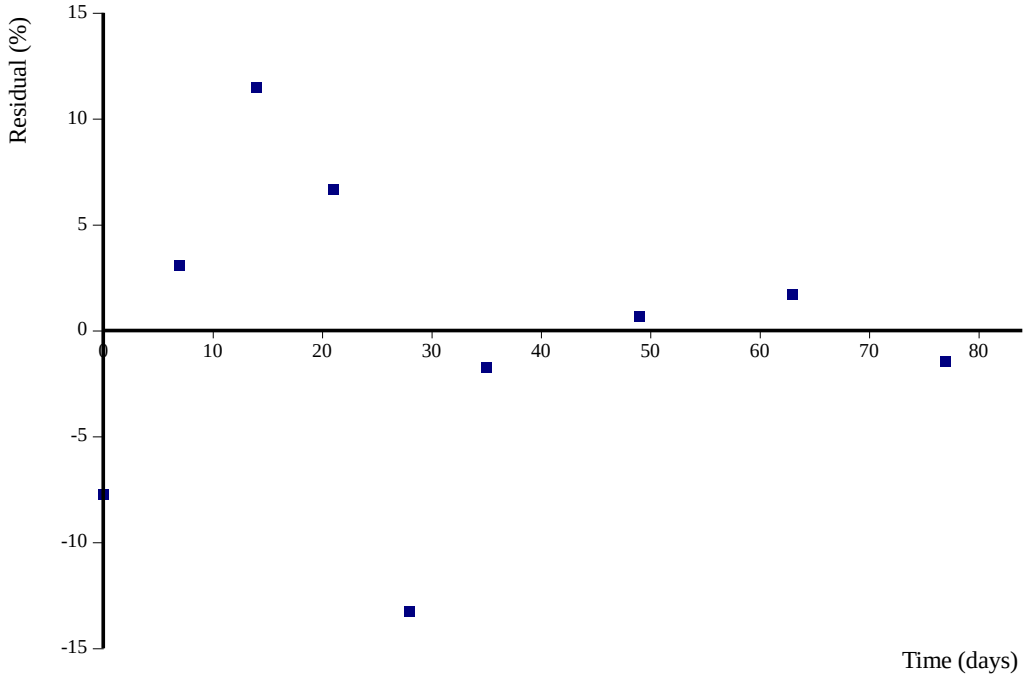
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	33.67	0 to (unbounded)	No

Estimated Values:

Parameter	Value	□	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	96.34	7.243	N/A	81.75	110.9	77.73	115
k1	0.01785	0.00428	0.004371	0.009222	0.02647	0.006844	0.029
k2	0.003816	0.005229	0.2492	-0.006721	0.01435	-0.009626	0.017
tb	34.98	5.378	N/A	24.14	45.82	21.15	48.8

χ^2

Parameter	Error %	Degrees of Freedom
All data	9.81	5
Parent	9.81	5

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	53	475	38.8	182

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.8678	0.8676
Parent	0.8678	0.8676

Parameter Correlation:

	Parent_0	k1	k2	tb
Parent_0	1	0.7354	-0.1761	-0.08203
k1	0.7354	1	-0.4723	-0.2256
k2	-0.1761	-0.4723	1	-0.2432
tb	-0.08203	-0.2256	-0.2432	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	88.6	96.34	-7.745
7	88.1	85.03	3.07
14	86.5	75.04	11.46
21	72.9	66.23	6.669
28	45.2	58.45	-13.25
35	49.9	51.66	-1.755
49	49.6	48.92	0.6797
63	48.1	46.38	1.724
77	42.5	43.96	-1.463

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000