Substance Name:
Bis(4-chlorophenyl) sulphone

EC Number: 201-247-9

CAS Number: 80-07-9

MEMBER STATE COMMITTEE SUPPORT DOCUMENT FOR IDENTIFICATION OF

BIS(4-CHLOROPHENYL) SULPHONE

AS A SUBSTANCE OF VERY HIGH CONCERN BECAUSE OF ITS VPVB (ARTICLE 57E) PROPERTIES

Adopted on 12 May 2023

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ABBREVIATIONS

AMAP	Artic Monitoring and Assessment Programme
AR	Applied radioactivity
B	Bioaccumulative
BAF	Bioaccumulation factor
BCF	Bioconcentration factor
BCFss	Bioconcentration factor, steady-state
BCPS	Bis(4-chlorophenyl) sulphone
BMF	Biomagnification factor
BROD	Benzoylresorufin O-dealkylase
CoRAP	Community rolling action plan
CTD	Characteristic travel distance
CYP	Cytochrome P450
DDT	Dichlorodiphenyltrichloroethane
DDE	Dichlorodiphenyldichloroethylene
DFOP	Double first-order in parallel
DOC	Dissolved organic carbon
DS	Dry substance
DT_{50}	Disappearance half-life time, time to reach 50% disappearance/dissipation
$DT_{50, deg}$	Degradation half-life time
DM	Dry matter
EC	European Commission
ECHA	European Chemicals Agency
EI-GC-MS	Electron ionization gas chromatography mass spectrometry
ECNI	Electron-capture negative ionization
EOGRTS	Extended One Generation Reproductive Toxicity Study
EROD	Ethoxyresorufin-O-deethylase
eMSCA	Evaluating Member State Competent Authority
EU	European Union
GC-ECD	Gas chromatography with electron capture detection
GPC	Gel permeation chromatography
GST	Glutathione S-transferase
HCH	Hexachlorocyclohexane
HL	half-life
HL_B	biotransformation half-life
HL_T	total elimination half-life
HPLC	High performance liquid chromatography

LC-MS	Liquid chromatography–mass spectrometry
LRTP	Long-range transport potential
LSC	Liquid scintillation counting
LOD	Limit of detection
LOQ	Limit of quantification
l.w.	Lipid weight
MDL	Method detection limit
MROD	Methoxyresorufin O-demethylase
NER	Non-extractable residue
NOAEL	No observed adverse effect level
NOEL	No observed effect level
OECD	Organisation for Economic Co-operation and Development
P	Persistent
PBPK	Physiologically based pharmacokinetic
PBT	Persistent, bioaccumulative and toxic
PCB	Polychlorinated biphenyls
POP	Persistent organic pollutant
Pov	Overall environmental persistence
PROD	Pentoxyresorufin O-dealkylase
REACH	Registration, Evaluation and Authorisation of Chemicals
SD	Standard deviation
SEV	Substance evaluation
SFO	Single first-order
SMILES	Simplified Molecular Input Line Entry System
SS	Surrogate Standard
SVHC	Substances of very high concern
TE	Transfer efficiency
TG	Test Guideline
UDPGT	Uridine 5'-diphospho-glucuronosyltransferase
vB	very bioaccumulative
vP	very persistent
vPvB	very persistent, very bioaccumulative
w.w.	wet weight

IDENTIFICATION OF A SUBSTANCE OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance name: bis(4-chlorophenyl) sulphone (BCPS)

EC number: 201-247-9

CAS number: 80-07-9

- The substance is identified as very persistent and very bioaccumulative (vPvB) according to Article 57 (e) of Regulation (EC) No 1907/2006 (REACH).

Summary of how the substance meets 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 is used to identify bis(4-chlorophenyl) sulphone (referred to hereinafter as BCPS) as vPvB. All available relevant information (such as the results of standard tests, monitoring and modelling, and (Q)SAR results) was considered together in a weight-of-evidence approach.

According to the ECHA guidance (ECHA 2017a, R.11), the weight-of-evidence determination by expert judgement enables the use of all (screening and assessment) information types listed in Section 3 of Annex XIII of the REACH Regulation in the PBT/vPvB assessment for comparing with REACH Annex XIII criteria, although not all of these information types can be directly (numerically) compared with the criteria.

Persistence

Based on the weight-of-evidence assessment of all available relevant information BCPS fulfils the P and vP criteria of REACH Annex XIII.

The following lines of evidence were considered in the assessment:

- BCPS is considered as hydrolytically stable. Furthermore, photodegradation in air for BCPS is unlikely to be a significant degradation pathway in the environment (atmospheric half-life is expected to be higher than 54.7 days).

- BCPS is not readily biodegradable according to a reliable OECD TG 301C study and meets the screening criteria P and vP. BIOWIN predictions are in line with the experimental data as they also indicate that BCPS screens as potentially P or vP.

- Based on a water-sediment simulation test according to OECD TG 308 (reliable without restrictions), the vP criterion is fulfilled for the sediment. Under aerobic conditions at 20°C, the $DT_{50,\ deg}$ values were 1287.2 and 394.3 days in the Tilft and Goose water-sediment systems, respectively. Temperature corrected $DT_{50,\ deg}$ values at 12°C are between 842 – 2748 days.

- In the OECD TG 308 study no degradation products of BCPS ≥5% of applied radioactivity (AR) at two consecutive sampling intervals were observed and $^{14}CO_2$ formation was ≤ 0.5 % of AR.

- Monitoring data showed the presence of the substance in environmental media (e.g., data from UK).

For the persistence assessment of BCPS, most weight is given to half-lives measured from reliable and well documented GLP and OECD conforming studies. Half-lives from such tests can be directly compared with the P/vP criteria and clearly result in very high persistence. Screening tests, QSAR data and monitoring data support the findings from the simulation test.

As an overall conclusion, based on the above information used in a weight-of-evidence approach, it is concluded that BCPS meets the 'persistent' 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 its persistent and very persistent (P/vP) properties in sediment (degradation half-lives > 180 days).

Bioaccumulation

Using a weight-of-evidence assessment of all the data available, BCPS meets the B and vB criteria according to Annex XIII of REACH.

The assessment is based on the following lines of evidence:

- The screening criterion for bioaccumulation for aquatic organisms based on measured log K_{OW} of 3.9 (OECD TG 107) is not fulfilled. Additionally, the predicted BCF values indicate a low to moderate bioaccumulation potential of BCPS in fish. An experimentally derived BCFss value of 82 (NITE, 2001) is considered to be reliable with restriction. There is no evidence for a significant bioaccumulation in fish.

- Screening criteria for air-breathing organisms have been established based on log K_{OW} > 2 and log K_{OA} > 5. The measured log K_{OW} for BCPS is 3.9 and the estimated log K_{OA} value is 9.2 (KOAWIN v.1.10), indicating, despite the low to moderate bioaccumulation potential in fish, a biomagnification potential for BCPS in air-breathing terrestrial and marine wildlife, as well as humans.

- BCPS is taken up by organisms and humans and detected in various wildlife species.

- High BCPS levels were detected in fish-eating bird eggs (geometric mean: 1118 ng/g l.w. period: 1971 -2003) and seals (liver median: 200 ng/g l.w.; blubber median: 60 ng/g l.w.).

- Results from toxicokinetics studies in rats demonstrate, that BCPS is readily adsorbed and rapidly distributed to lipid-rich tissues. The substance is very slowly excreted and exhibits a very long terminal half-life of 12 days in adipose tissue (after single intra-venous application in rats) which is indicative that BCPS is very bioaccumulative in adipose tissue. Based on this observation a biomagnification factor (BMF) value higher than 1 is anticipated for air-breathing mammals.

- A BMF value significantly higher than 1 can be considered as an indication for very high bioaccumulation. Field BMF values significantly higher than 1 have been found for BCPS. In total, three food chains (fish – guillemot, fish – cormorants, fish – seals) were identified with BMFs >1. The locations of these food webs are in the Baltic region and in Austria.

- In a benchmark approach, the concentrations of known structurally unrelated POP substances (with known vB properties) were compared with BCPS in species at the top of the food chain. Results for BCPS are in the range of known POPs.

- BCPS was investigated in post-mortem human liver samples and detected in all of them while liver is a target organ of BCPS toxicity in rats and mice.

- The applied QSAR predictions for half-lives in humans, birds and fish are considered more uncertain for the B assessment than experimental or monitoring data and they are given a low weight.

To conclude, while screening information and a measured BCFss value indicate a low to moderate bioaccumulation potential for fish, there is sufficient evidence that BCPS bioaccumulates in air-breathing organisms. Rat toxicokinetic data demonstrate that BCPS is rapidly distributed out of the blood into tissues, with adipose tissue as major storage site and the elimination is slow. Based on the derived terminal half-life in adipose tissue a BMF higher than 1 is anticipated for air-breathing mammals.

Monitoring data further supports findings from toxicokinetic data by the fact that the substance has been found in above Limit of Quantitation (LOQ) and partly very high concentrations in predatory organisms at the top of food-chains (e.g., fish-eating birds) and also in human liver samples. Further but lower line of evidence comes from field BMF values in three food-webs (fish – guillemot, fish – cormorants, fish – seals), which show BMF values significantly higher than 1 and BCPS in biota concentrations, which are in the range of known POPs.

Overall, taking all available information together in a weight-of-evidence determination, thereby considering high concentrations of BCPS in biota with a potential of biomagnification in certain food chains and a long half-life in rats, a high bioaccumulation potential of BCPS has been identified. Annex XIII, points 3.2.2. (b) and (c) of the REACH Regulation require that: detection of elevated levels in biota compared to levels in their surrounding environment, data from the toxicokinetic behaviour of the substance and information on the ability of the substance to biomagnify in the food chain are considered. Therefore, it is concluded that the 'bioaccumulation' criterion (B) and the 'very bioaccumulative' criterion (vB) of REACH Annex XIII are fulfilled.

Conclusion on vPvB properties

In conclusion, BCPS is identified as a vPvB substance 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 substance: Yes

Justification

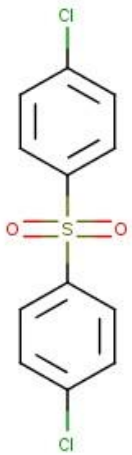
1. Identity of the substance and physical and chemical properties

1.1 Name and other identifiers of the substance

Table 1: Substance identity

EC number:	201-247-9
EC name:	bis(4-chlorophenyl) sulphone
CAS number (in the EC inventory):	80-07-9
CAS number:	80-07-9
IUPAC name:	1,1'-sulfonylbis(4-chlorobenzene)
Index number in Annex VI of the CLP Regulation	-
Molecular formula:	$C_{12}H_8Cl_2O_2S$
Molecular weight range:	287.1617 g/mol
Synonyms:	1,1'-Sulfonylbis(4-chlorobenzene) 4,4'-Dichlorodiphenyl sulfone 4,4'-Dichlorodiphenyl sulphone 4-Chlorophenyl sulfone Benzene, 1,1'-sulfonylbis(4-chloro-) Bis(4-chlorophenyl) sulfone Bis(4-chlorophenyl) sulphone Di-p-chlorophenyl sulfone *p,p*'-Dichlorodiphenyl sulfone *p*-Chlorophenyl sulfone Sulfone, bis(*p*-chlorophenyl) BCPS DCDPS

Structural formula:



1.2 Composition of the substance

Name: bis(4-chlorophenyl) sulphone

Description: solid, white

Substance type: mono-constituent

No impurities and additives are listed for the substance on the ECHA dissemination site (accessed 07/2022).

Table 2: Constituents other than impurities/additives

Constituents	Typical concentration	Remarks
bis(4-chlorophenyl) sulphone EC 201-247-9	≥80% w/w	The substance is a mono-constituent.

1.3 Identity and composition of degradation products/metabolites relevant for the SVHC assessment

No relevant degradation products / metabolites have been identified. The vPvB assessment is based on the parent substance only.

- A reliable OECD 308 water / sediment simulation test is available for BCPS (Unpublished study report, 2014). No degradation products ≥5% at two consecutive sampling intervals were observed.

- In toxicokinetic studies (Mathews *et al.*, 1996; Poon *et al.*, 1999) using BCPS, the substance was nearly completely adsorbed and rapidly distributed, especially to adipose tissue. The excretion of BCPS is dependent on metabolism to more polar compounds (mono-hydroxy-BCPS and its glucuronide), and relatively little parent compound was excreted before metabolism.

1.4 Identity and composition of structurally related substances (used in a grouping or read-across approach)

No structurally related substances were used for the assessment in a grouping or a read-across approach.

Related substances are DDT (dichlorodiphenyltrichloroethane, CAS No. 50-29-3) and DDT metabolites (e.g., 4,4´-dichlorodiphenyldichloroethylene (4,4´-DDE), CAS No. 72-55-9), dapsone (4,4′-diaminodiphenylsulfone, CAS No. 80-08-0) and certain polychlorinated biphenyls. These related substances have been used along BCPS either in cited efficacy studies, phototransformation studies or in monitoring studies.

To support the identification of BCPS as vB, a benchmark approach was used to compare concentrations of known structural unrelated persistent organic chemicals (POPs) with BCPS in biota. POPs in the benchmark approach, which are proven to fulfil the vB criteria were identified by the OECD tool[1] to model the long-range transport potential. Chemicals behaving similar in the LRTP-tool to BCPS (e.g., Lindan (ɣ-HCH), among others) were used

[1] http://www.oecd.org/document/24/0,3343,en_2649_34379_45373336_1_1_1_1,00.html

as reference chemicals. The concentrations in biota were extracted from these reference chemicals from respective POP risk profiles or published studies available at the Stockholm Convention Website[2]. Concentrations of known vB POPs were compared to concentrations of BCPS in respective biota.

1.5 Physicochemical properties

Table 3: Overview of physicochemical properties

Property	Description of key information	Value [Unit]	Reference / source of information*
Physical state at 20°C and 101.3 kPa	Substance is a white, odourless solid.		ECHA's dissemination site
Melting point		147 °C - 150 °C	ECHA's dissemination site
Boiling point	Decomposition closely to boiling temperature	397°C at 101325 Pa	ECHA's dissemination site
Density		1.504 ± 0.001 g/cm³ (= 1504 kg/m³) at 20.2°C	ECHA's dissemination site
Vapour pressure	Experimental values were obtained in a guideline study under GLP according to OECD TG 104 or EU TG A.4. In application of the gas saturation method the vapour pressure was measured at 50, 60 and 70 °C. By extrapolation the values of 1.50x10-5 Pa at 25 °C, 5.1x10-6 Pa at 20 °C and 1.2x10-6 Pa at 12 °C were derived.	5.1x10-6 Pa at 20°C	ECHA's dissemination site
Henry´s Law constant	Henrys Law Constant (25 deg C) [HENRYWIN v3.20]: User entered water solubility, log K_{OW}, melting and boiling point.	Bond Method: 1.37E-007 atm-m³/mole (1.39E-002 Pa-m³/mole) Group Method: 2.496E-007 atm-m³/mole (2.529E-002 Pa-m³/mole)	Estimated values, Epi Suite, vers. 4.11
Water solubility	Water solubility has been determined under GLP according to OECD TG 105 with the column elution method. A value of 0.86 mg/L at 20 °C at a pH from 5.5 to 6 was measured.	0.86 mg/L at 20°C	ECHA's dissemination site
Partition coefficient n-octanol/water (Log Kow)	Based on an experimental result from study under GLP using the shake flask	3.9 at 20°C	ECHA's dissemination site

[2] Stockholm Convention - Home page (pops.int)

	method according to OECD TG 107 the log K_{OW} of BCPS is determined to be 3.9.		
Solubility in organic solvents / fat solubility		n-octanol: 6831 mg/L; aceton: 94 g/L at normal conditions	ECHA's dissemination site
Flammability		Non flammable	ECHA's dissemination site
Explosive properties		Non explosive	ECHA's dissemination site
Oxidising properties		No oxidising properties	ECHA's dissemination site
Granulometry	The particle size distribution of BCPS powder was determined similar to OECD TG 110 and ISO 13320-1 methods under non-GLP conditions. About 7.5% of BCPS belongs to inhalable fraction. No respirable fraction was identified. The dustiness of the powder is classified as "medium" due to the particle size distribution (D10=115 µm, D50=240 µm, D90=561 µm). The dustiness of the pellets is classified as "low" because the pellets are not dusty.	particles <100µm approximate 7.5% particles <10µm approximate 0% particles <4µm approximate 0%	ECHA's dissemination site
Stability in organic solvents and identity of relevant degradation products		Stable	ECHA's dissemination site
Dissociation constant		BCPS does not contain an ionisable functionality. Therefore, dissociation is not expected to be relevant.	ECHA's dissemination site

**Values are taken from ECHA's dissemination site (accessed 18.07.2022).*
https://echa.europa.eu/de/registration-dossier/-/registered-dossier/14560/4/3

2. Harmonised classification and labelling

No harmonised classification is available for BCPS according to Annex VI of Regulation (EC) No. 1272/2008 (CLP Regulation).

3. Environmental fate properties

3.1 Degradation

3.1.1 Abiotic degradation

3.1.1.1 Hydrolysis

The available hydrolysis study with BCPS was performed according to OECD TG 111 and GLP (Unpublished study report, 2007) and is considered reliable. The hydrolysis rate of BCPS was studied in purified water and aqueous buffer solution with pH 4.0, 7.0, and 9.0 during 21 days at 50°C. No hydrolysis (≤ 10%) of BCPS was observed after 21 days at 50°C. Therefore, the substance is considered to be hydrolytically stable. According to OECD TG 111 a preliminary test should be conducted at 50°C if the hydrolysis is unknown. In higher tier studies three temperatures should be carried out, but only if the substance is unstable in the screening study. At 50°C no hydrolysis occurred and no further studies were conducted. Hydrolysis is not expected to be a relevant fate process for the environment.

3.1.1.2 Oxidation

There is no information available regarding abiotic oxidation in environmentally relevant conditions (with the exception of atmospheric reactions described in 3.1.1.3).

3.1.1.3 Phototransformation/photolysis

No information on the substance is available. According to the registrant(s), the manufactured polymers are not suitable for outdoor use, as UV exposure provokes chain scission.

3.1.1.3.1 Phototransformation in air

No experimental data regarding atmospheric degradation have been measured. The half-life of BCPS in the atmosphere was calculated with the AOPWIN program (v.1.92). The calculated rate constant is 5.8 $\times 10^{-11}$ cm^3 / molecule-sec. The half-life in the gas phase of air is 27.3 days (24-hours day) or equal to 54.7 days (12-hours day) using an average atmospheric hydroxyl radical concentration of 5×10^5 OH/cm^3. The used radical concentration refers to the concentration of OH radicals of the Northern hemisphere and not to the default values in EPISuite. AOPWIN indicated that a part of the substance can be sorbed to airborne particulates. Two sorbed fractions were calculated: 2.7% (Koa method) and 8.3% (Junge-Pankow, Macay avg). This fraction (2.7-8.3% sorbed) may be resistant to atmospheric oxidation by hydroxyl radicals, thus the estimated half-life by AOPWIN in the gas phase is an underestimation of the real/total half-life in air (gas and particle phase of BCPS). This is further supported by Norström *et* al., 2010 as BCPS was measured in vapour and particulate phases. The half-life was also cited by the registrant(s), who quoted the reference Meylan and Howard (1993). The calculated DT_{50} for BCPS in air is >2 days, which shows a potential for long-range environmental transport according to Annex D of the Stockholm Convention.

3.1.1.3.2 Phototransformation in water

No data are available in the registration dossier[3] on the monomer. Data on a similar substance (dapsone, CAS No. 80-08-0) indicate increased photoinduced toxicity to bacteria under UV-B radiation, which might be due to toxic transformation products (Kawabata *et al.*, 2013).

3.1.1.3.3 Phototransformation in soil

No data are available in the registration dossier. According to the registrant(s) BCPS is assumed to be stable and relevant degradation in soils is not expected by direct photolysis.

3.1.1.4 Summary on abiotic degradation

There is no information regarding abiotic oxidation under environmental relevant conditions. Hydrolysis is not considered a relevant route, as BCPS is considered hydrolytically stable. The QSAR predicted atmospheric half-lives with hydroxyl radicals are between 27 and 54 days. No experimental phototransformation studies that investigated direct or indirect photolysis in air, soil or water are available for BCPS.

In summary, based on all information available, abiotic degradation in compartments relevant for determining a degradation half-life for P/vP assessment is not expected to occur and it is not considered a relevant route for degradation. Reaction with hydroxyl radicals in the atmosphere is very slow based on a QSAR prediction that may indicate a potential for long- range atmospheric transport.

3.1.2 Biodegradation

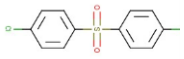
3.1.2.1 Biodegradation in aqueous media or aqueous environment

3.1.2.1.1 Estimated data

Estimated data on BCPS using BIOWIN models

According to BIOWIN v4.11 estimation (EPI Suite™), BCPS fulfils the screening criteria for persistence. The various sub-modules of this QSAR model provide the following quantitative predictions:

Table 4: BIOWIN (Epi Suite, vers. 4.11) estimations for BCPS

	BCPS
Structure	
Smiles	O=S(=O)(c(ccc(c1)Cl)c1)c(ccc(c2)Cl)c2
Biowin1	0.2460
Biowin2	0.0061
Biowin3 (ultimate biodegradation time)	2.1514
Biowin4	3.1028
Biowin5	-0.0641
Biowin6	0.0053
Biowin7	-0.7319
Ready Biodegradability Prediction	NO

[3] https://echa.europa.eu/de/registration-dossier/-/registered-dossier/14560/5/2/4

Comparison to PBT screening criteria based on BIOWIN

The guidance on PBT assessment (ECHA, 2017, Chapter R.11, Table R.11-4: Screening information for P and vP) states that a combination of the estimated values of Biowin 2, 3 and 6 provides an indication of the persistent character of a substance.

For BCPS, the estimated values with Biowin 2 and 6 are < 0.5; the estimated value of Biowin 3 is also lower than the cut-off value of 2.25. Based on the combination of BIOWIN 2 and 3 results and also BIOWIN 3 and 6 results, BCPS fulfils the screening criteria and can be considered as potentially P or vP.

Whereas the aromatic chlorides and aromatic hydrogens of the substance are covered by the training set of the structure, the sulfonyl group is not represented in these sets and no fragment coefficients are available for this group. In this case, the model considers molecular weight of the group only. Nevertheless, there are no indications, that the sulfonyl group is sensitive to degradation.

Table 5: Molecular fragments recognised by BIOWIN models and conclusion on model reliability

Substance	BIOWIN models 1,2,3, and 4		Conclusion on model applicability	BiOWIN models 5 and 6		Conclusion on model applicability
	Fragments recognised by the models	Remarks on fragments recognised by the model		Fragments recognised by the models	Remarks on fragments recognised by the model	
BCPS	2	2x Aromatic chloride	Reliable with restrictions	10	2x Aromatic chloride 8x Aromatic H	Reliable with restriction

3.1.2.1.2 Screening tests

A ready biodegradability test was conducted with BCPS according to a modified MITI Test (I), (NITE, 1999). After 28 days, 1% degradation measured as O_2 consumption was observed. Thus, BCPS is not readily biodegradable. The identity of the test item was confirmed by mass, nuclear resonance spectroscopy. Additionally, the stability of the test item was confirmed. A mix of soil, sludge and activated sludge was obtained from ten different wastewater treatment plants across Japan, recycled sludge and sediment samples were used as inoculum. Aniline was used as positive control and revealed 78.6% BOD on day 28. No toxicity controls were included, but abiotic controls and an inoculum blank were included in the test.

Table 6: Screening level biodegradation test on BCPS

Method	Results	Reliability	Remarks	Reference
Inoculum: activated sludge (return sewage sludge or topsoil of beach) Test conc.: 100 mg/L Activated sludge conc.: 30	Degradation: 0%; 3%; 0% based on BOD Average: 1% 0% based on	Klimisch 1, reliable without restrictions	Test material: 4,4´-dichloro diphenylsulfone K-1200 Adaptation of the sluge was	NITE, 1999

mg/L Temp.: 25°C Test duration: 28 days Purity: 100.1% Method: OECD 301C and modified MITI Test (I), 1992 GLP	HPLC analysis BCPS is not readily biodegradable under the test conditions.		not specified.	

3.1.2.1.3 Simulation tests

3.1.2.1.3.1 Biodegradation in water

No data are available in the registration dossier.

3.1.2.1.3.2 Biodegradation in sediment

A reliable without restrictions OECD TG 308 water / sediment simulation test is available with BCPS (Unpublished study report, 2014; Klimisch score of 1).

The biodegradation of radiolabelled BCPS was studied in two water-sediment systems (Tilft and Goose water-sediment systems, USA) under aerobic conditions at 20°C in the dark. The properties of the water-sediment systems are indicated in the table below.

Table 7: Properties of the water-sediment system

	Sediment				Water
	Textural class	% Clay	pH	% organic matter	pH
Tilft River	Sandy loam	17	6.6	3.2	7.6
Goose River	Clay loam	29	7.8	5.1	8.4

The radiolabelled test substance (phenyl-U-14C)-4,4-BCPS was synthesized and frozen when not in use. The radiochemical purity was 98.3%. The test vessels consisted of 1-L polypropylen bottles (biomass samples only), 250 mL (Tilft), or 500 mL (Goose River) glass vessels. In total 20 test vessels were prepared per sediment (14 for time points and reserve vessels). 51.0 or 66.5 g dry weight of Tilft or Goose River sediment were put into each bottle and then water was added to bring the total water content to 150 (Tilft) or 300 mL (Goose). The water:sediment ratios were between 3:1 and 4:1 with a sediment layer of 2.5 cm or > 50 g sediment on a dry weight basis for each test system, which is in line with OECD TG 308. No sterile controls were used in the study.

Both sediment test systems were allowed to acclimate to the test temperature and achieved stabilized aerobic conditions (dissolved oxygen > 2 mg O_2/L) by incubating for 27 (Tilft River) and 5 (Goose River) days before the test substance was applied to the main study samples.

Tilft water had a pH of 7.6 and the sediment was characterised as sandy loam with a pH of 6.6 and an organic carbon content of 1.1%, while the Goose River water had a pH of 8.4, the sediment was characterised as clay loam with a pH of 7.8 and an organic carbon content of 3.2%.

The redox potential in the Tilft system ranged from 97 to 196.9 mV in the water and from -382.2 to -279.6 mV in the sediment. In the Goose River system, the redox potential ranged from 107 to 181.1 mV in the water and -241.1 to -163 mV in the sediment.

In more detail, the redox potential of the sediment was at day 0 -279.6 mV and -240.2 mV and after 100 days study duration –382.2 mV and -229.9 mV, for Tilft System and the Goose River System respectively, indicating anaerobic conditions. The redox potential of water was at day 0 153 mV and 128.4 mV and after 100 days study duration 196.9 mV and 181.1 mV, for Tilft System and the Goose River System. Aerobic conditions were maintained in both systems over the course of the experiment by drawing humidified air through the series containing the water sediment samples. The dissolved oxygen concentration in water at day 0 was 8.73 mg/L and 7.94 mg/L and after 100 days 8.4 mg/L and 8.36 mg/L, for Tilft and Goose River System, which is consistent with Annex I of OECD TG 308 as the values are in the range of the stated oxygen concentration of 7 – 10 mg/L. Further, the guideline mentions that the sediment layer is aerobic at the surface and anaerobic below the surface (typical average redox potentials (Eh) in the anaerobic zone of the sediment range from –80 to – 190 mV). The redox potential from the sediment used within this study is below the values mentioned in the guideline. Lower redox values indicate anaerobic and reduced conditions. The redox potential in sediments decreases with depth. It is unknown in which depth the redox potential was measured in the probe. But the redox measurements were performed in flasks, which were equipped with a permanently installed redox probe that was positioned in the undisturbed sediment, so no physical disruption occurred. Under aerobic conditions potentially degradable substances are generally faster degraded than under anaerobic conditions. BCPS dissipated to the sediment gradually, so there was also enough time under aerobic conditions in water that degradation could happen. During the dissipation of BCPS from water to sediment, only negligible CO_2 formation occurred indicating that negligible mineralisation occured.

The substance was dosed into the water at nominal concentrations of 0.37 and 0.30 µg a.i./g water for the Tilft and Goose River test systems, respectively. HPLC / UV / RAM analysis of the water layer throughout the study showed that the radioactivity was almost entirely BCPS as the radioactivity, recovered in the water layer, compared well with the % applied radioactivity (AR) for BCPS. One significant peak (HPLC profile) in water and sediment was confirmed by GC/MS-EI analysis as BCPS. No metabolites were observed that required characterisation.The results for both water-sediment systems are presented in the tables below:

Table 8: % applied radioactivity (AR) for Tilft water-sediment systems

	% AR						
	0 d	**7 d**	**14 d**	**30 d**	**50 d**	**75 d**	**100 d**
in sediment							
extractable fraction	10.3	53.9	64.5	70.9	71.5	81.0	82.4
non-extractable fraction	0.5	1.4	1.2	2.2	2.4	3.5	4.4
BCPS (mean)	9.3	52.6	61.1	69.9	70.4	79.7	81.8
Unassigned (mean)	1.0	1.3	3.4	1.1	0.4	0.1	0.3
$^{14}CO_2$	N/A	0.0	0.0	0.1	0.2	0.3	0.4
in water							

BCPS (mean)	88.8	44.6	33.6	26.6	22.3	16.2	12.4
unassigned (mean)	3.1	1.0	1.1	0.3	0.2	0.1	0.3
total in water	91.9	45.6	34.8	27.0	22.4	16.3	12.7
mass balance	102.7	101.0	100.5	100.2	95.8	101.1	99.9

Table 9: % applied radioactivity (AR) for Goose River Water / sediment systems

	% AR						
	0 d	**7 d**	**14 d**	**30 d**	**50 d**	**75 d**	**100 d**
in sediment							
extractable fraction	12.8	52.4	68.1	81.0	72.7	77.9	81.1
non-extractable fraction	0.3	6.2	6.9	15.5	13.7	17.4	15.2
BCPS (mean)	11.8	51.2	65.5	79.8	72.7	75.3	79.8
unassigned (mean)	1.0	1.2	2.6	1.1	0.0	2.7	1.2
$^{14}CO_2$	N/A	0.0	0.0	0.1	0.2	0.3	0.5
in water							
BCPS (mean)	85.1	38.5	22.9	9.9	8.0	5.9	2.4
unassigned (mean)	2.1	0.1	0.0	0.1	0.1	0.0	0.1
total in water	87.2	38.6	22.9	9.9	7.5	3.8	2.6
mass balance	100.3	97.3	98.3	105.0	94.8	100.8	99.8

From the data it can be concluded that degradation of BCPS was very low in water and in sediment. The concentration of BCPS decreased from the water layer from above 88.8 and 85.1% AR at day 0, to 12.4 and 2.4% AR at the end of the study, indicating partitioning to sediment. No degradation products were detected in the water phase. CO_2 formation was negligible in both systems. In contrast, in the sediment the concentration of BCPS steadily increased from 10.3 and 12.8% AR at day 0, to 82.4 and 81.1% AR at day 100. Non-extractable residues (NERs) increased over time in both systems (max. 15.2%). No degradation products ≥5% at two consecutive sampling intervals were observed.

Non-extractable residue extraction was performed by excess solvent, which was left in the extracted sediment samples. The samples (3 x 0.5 g) were evaporated under nitrogen, homogenised and then analysed by combustion followed by liquid scintillation counting (LSC) to determine the amount of non-extractable radioactivity (NER).

The endpoints, which need to be addressed for P assessment are the primary or ultimate degradation rate and degradation half-lives ($DT_{50,deg}$) or dissipation/disappearance half-lives ($DT_{50,diss}$). The definitions for $DT_{50,deg}$ and $DT_{50,diss}$ are given below:

$DT_{50,deg}$: Degradation half-life time; only degradation processes are subsumed into this term. A $DT_{50,deg}$ value is equal to or higher than a $DT_{50,diss}$ value, because $DT_{50,deg}$ comprises mere degradation processes, only, whereas $DT_{50,diss}$ takes into account additional dissipation mechanisms.

$DT_{50,diss}$: Disappearance half-life time; all processes which contribute to the disappearance of a substance are subsumed in this term, i.e. shift to other compartments through, e.g. adsorption or volatilisation, as well as degradation processes.

In this case, the DT_{50} for the total system is used as an estimate for the DT_{50} in sediment, which is in line with ECHA Guidance R.11, as for adsorptive substances, the half-life in the sediment can reasonably be estimated from the half-life for the total water-sediment system.

The predicted half-lives are used and compared with the P/vP criteria. It is recommended to use single-first order kinetics. If not possible then bi-phasic kinetic models are used.

The DT_{50} values were re-calculated with the kinetic software CAKE v3.3. The FOCUS guidance (2014) recommends that a t-test (or examination of the confidence intervals) is used in order to assess the reliability of the individual rate parameter estimates of each model. If a parameter is not significantly different from zero, then the parameter is either very uncertain due to variability in the data or the model is not adequate with respect to the data. The parameter is considered significantly different from zero if the probability is smaller than 0.1 (i.e. considering a 10% significance level for water-sediment studies; FOCUS, 2014). Similarly, if zero is not included in the confidence interval, the parameter is significantly different from zero. Both, the t-test and the confidence interval give the same answer.

At day 0 the sum of parent and unassigned metabolites were used for the kinetic evaluation according to the Generic Guidance Document for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration (FOCUS, 2014). For the whole system $DT_{50,deg}$ values were derived. In addition, Chi2 and t-test outcomes were reported using the four kinetics models: Single First Order (SFO) and three bi-phasic models: First Order Multi Compartment (FOMC), Double First Order in parallel model (DFOP) and the Hockey Stick model (HS). The degradation kinetics was performed using the whole system (water and sediment). Results are summarised below.

Table 10: Kinetic modelling for Tilft water-sediment systems (whole system)

model	DT_{50}[4]	χ^2	r^2 (Obs v Pred)	Parameter value		Prob. > t
SFO	1.37E+03	1.88	0.3507	k: 5.07E-004		0.0805
FOMC	>10 000	1.07	0.82	α: 0.008816 β: 0.01023		n.a.
DFOP	>10 000	1.13	0.8346	k1: 0.1921 k2: 5.74E-005 g: 0.07032		k1: 0.188 k2: 0.4374 g: n.a.
HS	9.5E+03	1.09	0.84	k1: 0.007165 k2: 7.30E-005 tb: 10.05		k1: n.d. k2: 0.3876 tb: n.a.

Table 11: Kinetic modelling for Goose River water-sediment systems (whole system)

model	DT_{50}[4]	χ^2	r^2 (Obs v Pred)	Parameter value		Prob. > t
SFO	398	3.39	0.6531	k: 0.001741		0.01426
FOMC	>10 000	2.02	0.8948	α: 0.04364 β: 0.8782		n.a.
DFOP	625	2.29	0.8884	k1: 0.3561 k2: 0.001109 g: 0.01044		k1: 0.3303 k2: 0.08082 g: n.a.
HS	619	2.29	0.8883	k1: 0.006867 k2: 5.66E-004 tb: 7.6		k1: 0.05439 k2: 0.07122 tb: n.a.

[4] For DFOP and HS the DT_{50}-value from the slow phase (k2) is reported.

All predicted DT_{50} values indicated a DT_{50} well above the vP criteria (degradation half-life >180 days).

DT_{50} values were also calculated by the registrant(s) using ModelMaker® 4.0 and the results can be obtained from Table 12.

The study showed that BCPS dissipated from water into the sediment with a nearly similar $DT_{50,diss}$ value of 7.1 and 6.2 days in the Tilft and Goose River system, respectively. Within the first 30-days negligible ultimate degradation occurred, as the $^{14}CO_2$ level was very low (0.1%) and the amount of transformation products was low. Therefore, the DT_{50} calculated is attributed to dissipation mainly to dissipation process other than degradation.

At 20°C, negligible mineralisation (max. 0.5% $^{14}CO_2$ at 100 days) in the whole system was observed and the $DT_{50,deg}$ values were 1287.2 and 394.3 days in the Tilft and Goose River water-sediment systems, respectively. The best visual fit and statistics for the data was obtained using the SFO model, whereas for the dissipation from the water, the DFOP model provided the best fit.

The composition of non-extractable residues (NER) in sediment is unknown. In this particular case, when calculating the $DT_{50,\ deg,}$ NER was not added to the parent substance concentration (i.e., it was assumed that NER represented irreversibly bound residues), as it would not change the vP conclusion.

Noteworthy, the amount of NER increased over time and reached a maximum of 15.2% of the applied radioactivity. Assuming intact BCPS as part of NER would increase the half-lives.

Table 12: Kinetics of parent compound BCPS

Water-sediment type	**layer**	**BCPS rate const. 1 (day -1)**	**BCPS rate const. 2 (day-1)**	**BCPS DT_{50}** (days);**	**R^2**
Tift (Sandy Loam)	Water	0.223	0.011	7.1**	0.994
	Total System	0.001	N/A	1287.2*	0.31
Goose River (Clay)	Water	0.147	0.016	6.2**	0.994
	Total System	0.002	N/A	394.3*	0.64

* $DT_{50,\ deg}$ in water-sediment system, extrapolation beyond the 100 day study duration; ** $DT_{50,\ diss}$ in water;

Temperature correction of $DT_{50,deg}$:
For comparing with the P/vP criteria the experimental obtained $DT_{50,deg}$ were converted to 12°C in accordance with EFSA, 2007 (p. 7-32 (Eqn 3).

$$DT50_{,deg(12^{o}C)}=DT50_{,deg(20^{o}C)} \exp (65.4/0.008314*((1/285.15)-(1/293.15)))$$

Values used:
activation energy, E_a: 65.4 kJ/mol
gas constant, R: 0.008314 (kJ K^{-1} mol^{-1})
temperature 1: 285.15 K
temperature 2: 293.15 K

Table 13: Temperature corrected $DT_{50,deg}$ of BCPS

Substance	Water-sediment system	**$DT_{50,deg}$** in days at 20°C	**$DT_{50,deg}$** in days at 12°C
BCPS	Tilft System	1287	2748
BCPS	Goose River System	394	842

Under aerobic conditions at 20°C, the $DT_{50,deg}$ values were greater than the study duration of 100 days (1287 and 394 days in the two studied water-sediment systems).
The results suggest that it is unlikely that ≥50% mineralisation or primary degradation would occur over a subsequent 80-day period at 20°C.

Based on this study it can be concluded that BCPS is very persistent in sediment (degradation half-lives >180 days).

3.1.2.2 Biodegradation in soil

3.1.2.2.1 Simulation tests in soil

No data are available in the registration dossier.

3.1.2.3 Summary and discussion on biodegradation

BCPS is not readily biodegradable and fulfils the criteria for "very persistent" in the sediment based on the OECD TG 308 study.

3.1.3 Field data

No data are available in the registration dossier.

Herein, only a brief summary of BCPS concentration ranges in various media is given, detailed information is provided under section 3.2.4 (field data in the environment) and 3.4.3 (field data in biota).

BCPS concentration ranges, including sampling date and location are summarised:

Table 14: BCPS in water

Matrix	Range of BCPS conc.	Date	Location	Reference
Surface water	0.004 – 0.4 µg/L	2012-2017	England, UK	UK Environment Agency's National Laboratory Service (unpublished)
Ground-water	0.007 – 0.3 µg/L	2012-2017	England, UK	UK Environment Agency's National Laboratory Service (unpublished)
Lake	detected, but not quantified	1991 1992	Maggiore, Garda, Como, Italy	Guzzella and Sora, 1998
Raw water	0.01 – 0.11 µg/L	2003	Sweden	Arner *et* al., 2004

Table 15: **BCPS in landfill leachates**

Matrix	Range of BCPS conc.	Date	Location	Reference
Landfill Leachates	0.01 – 1 µg/L	2012-2017	England, UK	UK Environment Agency's National Laboratory Service (unpublished)

Table 16: BCPS in estuarine/seawater

Matrix	Range of BCPS conc.	Date	Location	Reference
Estuarine water	0.003 – 0.32 µg/L	2012-2017	England, UK	UK Environment Agency's National Laboratory Service (unpublished)
Estuarine water	0.68 ng/L	1990	River Elbe estuary, Germany	Bester *et* al., 2001

Seawater	0.33 – 0.45 ng/L	2010	Sweden	Norström *et al*., 2010
Seawater	0.18 – 2.2 ng/L	1990 1995	German Bight and North Sea; highest conc. Near Island of Helgoland	Bester *et al*., 2001
Seawater	Detected in 20/24 samples, not quantified	2016	Black Sea	unpublished, projects: Seawater and sediment from Black Sea Survey 2017
Seawater	0.08 to 0.12 ng/L	2017	Black Sea	unpublished, projects: Seawater and sediment from Black Sea Survey 2017

Table 17: BCPS in sediment

Matrix	Range of BCPS conc.	Date	Location	Reference
Sediment	8.1 – 14 ng/g	2017	Danube delta	unpublished, projects: Seawater and sediment from Black Sea Survey 2017
Sediment (marine and surface water)	< LOD (4 ng/g d.w.)	2009	North Sea (background); Baltic Sea (background) ; and Stockholm Långholmen, Sweden	Norström *et al*., 2010
Sediment	< LOQ (0.01 mg/kg TS)	2003	Sweden	Arner *et al.*, 2004

BCPS was detected in sediment samples collected in the Danube delta. Concentration levels ranged from 8.1 to 14 ng/g in sediment (unpublished, projects: Seawater and sediment from Black Sea Survey, 2017).

Table 18: BCPS in wastewater

Matrix	Range of BCPS conc.	Date	Location	Reference
Influent	0.01 – 3.9 µg/L	2003	Sweden	Arner *et* al., 2004
Influent	0.4 – 11.8 ng/L	2017	Zilina, Budapest, Ljublijana, Sabac, Zagreb	unpublished data, project: ITN, Answer, Solutions
Influent	17 ng/L	2009	Estonia	Norström *et al*., 2010
Influent	n.d.	2009	Poland, Sweden, Finland, and Lithuania	Norström *et al*., 2010
Influent	0.25 ng/L - 2.00 ng/L	2020	Austria	Unpublished report, Umweltbundesamt 2020
Influent [summary]	**n.d. – 17 µg/L**			
Effluent	<0.05 ng/L - 0.87 ng/L	2020	Austria	Unpublished report, Umweltbundesamt 2020

Table 19: BCPS in sewage sludge

Matrix	Range of BCPS conc.	Date	Location	Reference
Sludge	0.01 – 2 mg/kg DM	2003	Sweden	Arner *et al.,* 2004

Table 20: BCPS in soil

Matrix	Range of BCPS conc.	Date	Location	Reference
Soil	*No data available*	-	-	-

Table 21: BCPS in air

Matrix	Range of BCPS conc.	Date	Location	Reference
Air	0.05 - 0.3 ng/m^3	2003	Sweden	Arner *et al.,* 2004

3.1.4 Summary and discussion of degradation

BCPS is hydrolytically stable. The QSAR calculations indicate a half-life of BCPS in the atmosphere (gas-phase) of 54.7 days (12-hours) with OH radicals, this value might be an underestimation considering that a fraction is sorbed to airborne particles and resistant to atmospheric oxidation by hydroxyl radicals. For phototransformation in other media no data are available. Abiotic degradation is not expected to occur and it is not considered a relevant route for degradation.

For the persistence assessment of bis(4-chlorophenyl) sulphone, most weight is given to half-lives measured within the water-sediment simulation test according to OECD TG 308 and GLP (Unpublished study report, 2014). Based on a water-sediment simulation test according to OECD TG 308 (reliable without restrictions), the vP criterion is fulfilled for the sediment. Under aerobic conditions at 20°C, the $DT_{50,deg}$ values were greater than the study duration of 100 days (1287 and 394 days in the two studied water-sediment systems). Temperature-corrected $DT_{50,\ deg}$, 12°C were 842 and 2748 days. Based on this water-sediment simulation study (OECD TG 308), it can be concluded that BCPS is very persistent in sediment (degradation half-lives >180 days).
The composition of non-extractable residues (NER) in sediment is unknown. In this particular case, when calculating the $DT_{50,deg}$, NER was not added to the parent substance concentration (i.e., it was assumed that NER represented irreversibly bound residues), as it would not change the vP conclusion.

It is noteworthy that the amount of NER increased over time and reached a maximum of 15.2% of the applied radioactivity. Assuming intact BCPS as part of the NER would increase the half-lives.

In the OECD TG study 308 no degradation products of BCPS ≥5% of applied radioactivity (AR) at two consecutive sampling intervals were observed.

The negligible degradability of BCPS in the simulation test is substantiated by the very low mineralisation rate (volatile CO_2) of max 0.5% AR after 100 days.

Results from a ready biodegradability screening test (NITE, 1999) are used as supporting information, which show negligible degradation. BIOWIN predictions are in line with the experimental data as they indicate that BCPS fulfils the screening criteria and it can be considered as potentially P or vP. Further monitoring data show the presence of the substance in various environmental media (e.g., Norström, 2010; UK Environment Agency's National Laboratory Service, unpublished).

3.2 Environmental distribution

3.2.1 Adsorption/desorption

The adsorption coefficient was determined according to OECD TG 121 (Unpublished report, 2010). The test is GLP compliant. The log K_{OC} of 3.5 was interpolated with the HPLC method at 23°C and at pH 6.2 using several reference compounds. The results are considered reliable and they indicate an intermediate sorption of the substance.

3.2.2 Volatilisation

Information on volatilisation is included in chapter 1.5. The estimated Henry´s law constant (0.0139 Pa m^3/mol) of BCPS indicates little tendency to volatilise from water to air.

3.2.3 Distribution modelling

Environmental distribution of BCPS was predicted by Level III fugacity model in EPI Suite v.4.11 (Table 22). The model predicts the relative distribution of a compound in the model environment at steady state.

BCPS showed a partitioning of 6.4% to the air compartment, 15.5% to water, 76.3% to soil, and 1.75% to sediment, if the substance is released with identical initial release rate to the compartments air, water and soil. The reliability of the results from EPI Suite calculation is rated Klimisch 2. If the emission of BCPS takes only place via water, then the distribution changes to mostly water with 89.9% and sediment with 10.1%. In the water-sediment simulation study, a rapid dissipation of BCPS to sediment was observed (Unpublished study report, 2014). However, these water-sediment ratios coming from a laboratory simulation test are not representative for the environment, because the ratios of the compartment volumes are very different in a simulation study in comparison to the field situation.

Table 22: Environmental distribution of BCPS predicted by Mackay Level III fugacity model in EPI Suite v.4.11.

	Air	Water	Soil	Sediment
Scenario 1: Calculation based on max. half-lives in sediment 65,852 hours (at 12°C), water solubility = 0.86 mg/L, Koc = 3162, half-life in air = 13,104 hours, melting and boiling point according to Section 1.5 Phys. chemical parameters, other input parameters were according to the default settings of the software including the emission values air 1000 kg/hr, water 1000 kg/hr, soil 1000 kg/hr				
Mass amount in %	6.4	15.5	76.3	1.75
Scenario 2: Similar input parameters as above, but including the emission values air 0 kg/hr, water 1000 kg/hr, soil 0 kg/hr				
Mass amount in %	0.000411	89.9	0.0183	10.1

3.2.4 Field data

The conclusion of the distribution modelling is further supported by monitoring data, as BCPS is found in various aquatic environments such as surface water, groundwater, estuarine water, seawater and sediment.

Data from UK, 2012 - 2017

Unpublished monitoring data originate from analyses undertaken by the UK Environment Agency's National Laboratory Service. The data comprise a large number of different sample points from across England. Measurements are compiled in Table 23. All of the results from this method should be treated with caution as they are from a semi-quantitative analysis method that is not accredited.

Table 23: Semi-quantitative GC/MS target based screen data for BCPS (CAS Number 80-07-9) in UK

Media	Year	Country	No. of positive detections	Approx. min. conc. [µg/L]	Approx. max. conc. [µg/L]	Approx. detection frequency	Limit of detection
Surface water	2012 - 2017	England, UK	59	0.004	0.4	0.4%	Not evaluated
Ground-water	2012 - 2017	England, UK	11	0.007	0.3	0.1%	Not evaluated
Estuarine/coastal water	2012 - 2017	England, UK	46	0.003	0.32	1.1%	Not evaluated
Landfill leachate	2012 - 2016	England, UK	2	0.01	1	1.1%	Not evaluated

Method: Targeted GC/MS screening for organic substances was carried out following sample pre-concentration. A double liquid-liquid extraction was employed, using acid-neutral dichloromethane, to extract non-polar substances. The GC/MS target based (multi-residue) screening method allows for over 850 substances to be identified from a single sample, including both volatile organic compounds (VOCs) and semi-volatile organic compounds (SVOCs).

Semi-quantitative data: All of the results from this method should be treated with caution as they are from a semi-quantitative analysis method that is not accredited.

Sample points: The data come from a large number of different sample points from across England.

Distribution of the concentrations: Maximum and minimum concentrations are presented in Table 23. The data are typically skewed towards the minimum concentration with most values being below 0.05 µg/L.

Potential source: Analysis of groundwater quality data (ref. Table 23) suggests that a possible source of this chemical could be plastic pipe fittings at the groundwater abstraction. These fittings may leach BCPS into the water as the groundwater sample is being taken. This potential source has not been confirmed.

Data from Italy, 1991 and 1992

BCPS was detected, but not quantified, in all water samples from the three Italian lakes, Maggiore, Garda and Como in 1991 and 1992 (Guzzella and Sora, 1998).

Data from Germany, 1990 and 1995

Sampling from the German river Elbe and the German Bight in the North Sea shows BCPS contamination (Bester *et al.*, 2001). 100 L water samples were taken at a depth of 5 m. Water samples were spiked with surrogates and extracted with n-pentane, extracts dried over sodium sulfate and analysed by LC-MS/MS. LOD (BCPS) = 0.10 ng/L due to blank problems observed: blank (BCPS) = 0.052 ng/L. Recovery = 56 %. The recovery rate was not taken into account for calculating the final concentrations.

The BCPS concentrations ranged from 0.18 – 2.2 ng/L in seawater (Figure 1). In 1995, the highest and maximum concentration of BCPS of 2.2 ng/L was found near the Island of Helgoland., while the concentration in the river Elbe estuary was 0.68 ng/L. No significant changes in BCPS concentrations were detected between 1990 and 1995. LOD was 0.1 ng/L

(due to blank problems), recovery rate was 56%. The pattern points towards the main input most probably being due to the Rhine River (Bester, 2022 personal communication).

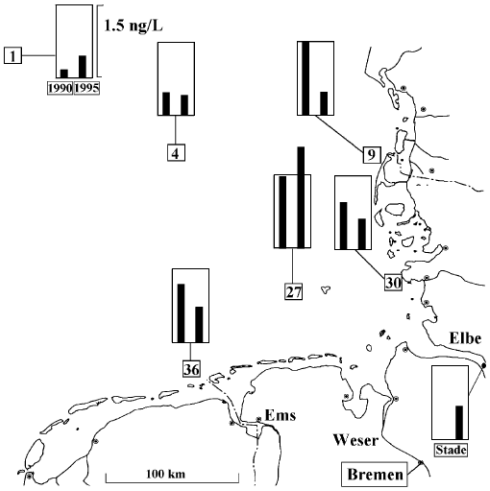


Fig. 5. Concentrations of bis (4-chlorphenyl)-sulfone in the water of the German Bight of the North Sea (ng/l). Values for 1990 and 1995 are given in comparison. Maximal values within the fields are 1.5 ng/l.

Figure 1: Concentration of BCPS in the German river Elbe and the German Bight in the North Sea (Figure taken from Bester *et* al., 2001, with permission from author), maximum values within the fields are 1.5 ng/L.

Data from Sweden, 2003

On behalf of the Swedish Environmental Protection Agency, the occurrence of bisphenol A (BPA), bis(4-chlorophenyl) sulphone (BCPS) and 2,2',6,6'-tetra-butyl-4,4'-methendiphenol (TBMD) has been investigated in sludge, wastewater, raw water, air, fish (perch) and sediment (Arnér *et al.*, 2004). Results are summarised for each matrix in Table 24. Sampling has been carried out in 12 different provinces throughout Sweden. Recovery rates and details of the analytical method for the analysed substances were not reported, but sample preparation, location and LOD were presented.

BCPS was found only in few samples, suggesting that the substance was either not ubiquitously present or the LOQ was too high to determine BCPS in a quantitative way. In Norström *et* al. (2004), the LOQ for BCPS was 0.2 ng/g fat and not 2 µg/g fat as reported in this study (Arnér *et al.*, 2004).

Local and industrial emissions were suggested as the substance was detected in few sludge samples. BCPS was also occasionally detected in raw water, which originated from Lake Mälaren, which probably stems from a local pollution source. From all investigated matrices, the highest detection frequency (82.3%) was obtained for sewage sludge samples.

Table 24: Highest BCPS concentration in various matrices, Sweden, 2003

Matrix	Unit	Total No. of samples[1]	No. of positve detections > LOQ	Detection frequency in %	Range of BCPS min. – max.	LOD	LOQ
Fish (perch)	µg/g fat	49	0	0.00	<2.00	0.01	2.00
Sediment	mg/kg DM	28	0	0.00	<0.01	0.01	-

Air	ng/m^3	21	3	14.28	<0.30	1 ng/filter	-
Raw water	µg/L	30	3	6.70	0.01 - 0.11	0.01	-
Sludge	mg/kg DM	79	65	82.30	0.01 – 2.00	0.01	-
Influent	µg/L	49	3	6.10	0.01 – 3.9	0.01	-
Effluent	µg/L	2	-		-	-	-
Groundwater	µg/L	1	-		-	-	-
Lake water	µg/L	2	-		-	-	-

Adapted from Arner *et* al. (2004), DM dry matter – sample freeze-dried or oven-dried (105°C); [1]total number of samples where BCPS was investigated

Data are further explained in more detail for each matrix; tables were taken from Arner *et al.* (2004).

Analytical data from sludge, Sweden, 2003

In the following wastewater treatment plants (WWTP) BCPS was detected: Henriksdal WWTP in Stockholm County (in sludge: 0.13 mg/kg DM), Slottshagen WWTP in Östergötland County (2 mg/kg DM) and Sjöstadsverket WWTP in Värmland County (0.011 mg/kg DM). There was no significant difference in the BCPS levels between the sampling areas. In addition, there was also no significant difference in BCPS levels between primary and digested sludge, suggesting that BCPS is very stable. Sludge samples are of particular relevance, as sludge acts as a soil improver and is used as fertiliser in fields in some regions and soil and food might get contaminated with BCPS. Exposure of man via the environment might therefore also be a relevant route. In total, in 65 samples out of 79 investigated samples BCPS was detectable in sludge (Table 25).

Table 25: Data of BCPS from sludge samples, Sweden, 2003

Sludge		Unit
Total number of samples investigated	79	-
Positive detections	65	-
Detection frequency	82.3	%
Max. value	2	mg BCPS/kg DM
90th percentiles	0.01	mg BCPS/kg DM
Min. value	0.01	mg BCPS/kg DM
Mean	0.05	mg BCPS/kg DM
Median	0.01	mg BCPS/kg DM
Standard Deviation	0.2	mg BCPS/kg DM
Confidence, 90% level	0.1	mg BCPS/kg DM
LOD	0.01	mg BCPS/kg DM
Impact level environment / health	not known	-

Analytical data from wastewater influent, Sweden, 2003

The highest concentrations of BCPS were found in Uddebo ARV in Norrbotten County with concentrations of 3.9 µg/L. Other BCPS concentrations found were taken from Sjölunda ARV in Skåne and Henriksdal wastewater treatment plant in Stockholm (0.21 and 0.16 µg/L, respectively).

Table 26: Data of BCPS from wastewater influent, Sweden, 2003

Wastewater		Unit
Total number of samples investigated	49	-
Positive detections	3	-
Detection frequency	6.1	%
Max. value	3.9	µg BCPS/L
90th percentiles	0.1	µg BCPS/L

Min, value	0.01	µg BCPS/L
Mean	0.2	µg BCPS/L
Median	0.1	µg BCPS/L
Standard Deviation	0.5	µg BCPS/L
Confidence, 90% level	0.13	µg BCPS/L
LOD	0.01	µg BCPS/L
Impact level environment / health	not known	-

Analytical data from raw water, Sweden, 2003

Raw water was sampled three times per waterworks during seven months, starting in summer 2003. In total, a number of 30 samples were analysed. BCPS was detected in only two samples at one location, at the Hässlö waterworks in Västmanland County. The waterworks (Hässlö) takes its water from Lake Mälaren and had the highest concentration of BCPS at 0.11 µg/L.

Table 27: Data of BCPS from raw data, Sweden, 2003

Raw water		Unit
Total number of samples investigated	30	-
Positive detections	2	-
Detection frequency	6.7	%
Max. value	0.11	µg BCPS/L
90th percentiles	0.1	µg BCPS/L
Min. value	0.01	µg BCPS/L
Mean	0.1	µg BCPS/L
Median	0.1	µg BCPS/L
Standard Deviation	0.02	µg BCPS/L
Confidence, 90% level	0.01	µg BCPS/L
LOD	0.1	µg BCPS/L
Impact level environment / health	not known	-

It is difficult to compare raw water data as there are too few previous studies on water containing BCPS. When compared to the Elbe River (estuary) in Bester *et al.* (2001) with measured BCPS concentrations of 0.68 ng/L and to the German Bight with measured concentrations of 0.18 - 2.2 ng/L, the concentration from raw waters in this study (concentrations of 20 and 110 ng/L) is higher. The detection of the substance in raw water may be of concern as it could possibly be an important route of human exposure, even though the levels currently appear to be low.

Analytical data from air, Sweden, 2003

Two to three air samples per sampling area (ten) were taken over a period of seven months. Out of a total of 21 air samples, 3 samples showed detectable levels of BCPS. The highest measured concentrations of BCPS in ambient air were found in Västerås in Västmanland County and in Skåne (Perstorps Industri) with concentrations up to 0.3 ng/m^3.

Table 28: Data of BCPS from air, Sweden, 2003

Air		Unit
Total number of samples	21	-
Positive detections	3	-
Detection frequency	14.28	%
Max. value	0.3	ng BCPS/m^3
90th percentiles	0.2	ng BCPS/m^3
Min. value	0.05	ng BCPS/m^3
Mean	0.1	ng BCPS/m^3
Median	0.1	ng BCPS/m^3
Standard Deviation	0.1	ng BCPS/m^3
Confidence, 90% level	0.03	ng BCPS/m^3
LOD	1	ng BCPS/filter*
Impact level environment / health	not known	-

*approximately 18 m^3 of air was sampled over a one-week period, giving LODs in the order of 0.05-0.1 ng/m^3.

According to Norström *et* al. (2010), BCPS was detected in one air sample in Aspvreten (2010) at a level of 1.1 pg/m^3 (LOD=0.3 pg/m^3). The authors stated that a contamination of the first sample from Aspvreten could not be excluded.

Analytical data from sediment, Sweden, 2003

BCPS was not quantified in 28 aggregated sediment samples. This might have been due to a very high LOQ (see Table 24).

Various other data from other countries in different matrices

Wastewater treatment plants (WWTPs)

Substances detected in wastewater effluents can provide information on actual emissions into the surface water. In a study from 2017 in Europe, BCPS was detected in effluents from WWTPs (Zilina, Budapest, Ljublijana, Sabac, Zagreb) at concentrations between 0.4 and 11.8 ng/L (unpublished data, project: ITN, Answer, Solutions)[5], indicating recent emissions, although the origin is unknown. Recent investigations of Austrian WWTP influents detected BCPS in all five samples, but only in three effluents (unpublished data, project 03702-17, Umweltbundesamt 2020). BCPS concentrations in the influent ranged from 0.25 ng/L to 2.00 ng/L, while concentrations in the effluent ranged from < 0.05 ng/L to 0.87 ng/L. The mean removal of BCPS from wastewater was approximately 63%. The calculated loads for Austria in the influent of municipal wastewater treatment plants are below 0.5 kg/year and for Europe about 11 kg/year. The calculated total amount in the effluent of municipal wastewater treatment plants results in a volume of about 5 kg / year for Europe, thus the amount is below the estimate of the registrant(s), whereby the number of examined wastewater treatment plants was small (n=5) and the estimates based on wastewater treatment plants did not include potential landfill leachates. It is noted that according to the information of registrant(s), landfill leachate is another possible input pathway of BCPS into the environment. Therefore, the calculated amount of 5 kg / year for Europe represents only a part of the total possible emittable amount.

Point sources for BCPS emissions in Latvia have been discussed in the study of Valters *et al.* (1999) as the BCPS levels (perch sampled in 1997) in fish increased with increasing river length. The involved point sources had not been identified.

Norström *et* al., 2010 investigated several sources among different effluents (n=4 from Sweden, n=6 from other Baltic countries) from WWTPs sampled from Poland, Sweden (Kalara, Henriksdal), Finland, Estonia and Lithuania. Only in one WWTP, the effluent from WWTP2 located in Estonia, 17 ng/L BCPS were detected in 2009. All other samples were below LOD (< 8 ng/L). BCPS in this study has likely not been detected as the LOD in this study is higher in contrast to other studies (e.g., LOD 0.1 ng/L in Bester *et al.*, 2001).

Surface water

Germany

BCPS has been detected in water samples in Germany (cited *in* Norström *et* al. 2010, originally from Müller *et* al., 1997).

Marine Surface Water

Sweden

In 2010, surface samples were analysed (Norström *et al*., 2010). The surface water sampled in Råö, Sweden contained 0.45 ng/L. The surface water concentration in Silviken, Ljusterö, Sweden revealed 1.3 ng/L and in Riddarfijärden, Sweden 0.33 ng/L BCPS, respectively.

[5] Samples were taken between 15th August 2017 – 1st Sept. 2017, more information on sampling locations is available under: https://www.sciencedirect.com/science/article/pii/S0160412019304052

Black Sea
BCPS was detected in 20 out of 24 samples collected in the Black Sea in 2016 (EC-UNDP funded projects EMLAS-II project[6]) and in seawater samples from five stretches of the Black Sea during the campaign that took place in 2017.

Sediment
Danube Delta
BCPS was detected in sediment samples collected in the Danube delta in 2017. Concentration levels ranged from 1.4 to 3.1 ng/L in seawater and from 8.1 to 14 ng/g in sediment (unpublished, project: Seawater and sediment from Black Sea Survey 2017).

Drinking water
USA
BCPS has been described in a Swedish report (Norström *et al*., 2010), where it was stated that BCPS was detected in drinking water in USA (Lucas *et* al., 1984). Substances were concentrated from large volumes (1,415 – 15,000 L) of finished drinking water (from US cities: Poplarville, Cincinnati, Miami, New Orleans, Ottumwa, Philadephiia and Seattle) and analysed by GC-MS. Samples were taken in 1976, 1979, and 1980.

3.2.5 Field data in Biota / Biomonitoring

All available data from biotamonitoring are summarised in section 3.4.3.

3.2.6 Summary and discussion of environmental distribution

Monitoring data indicate that BCPS is distributed to a wide variety of environmental media: WWTP influents and effluents, sewage sludge, surface water, ground water, estuarine/ coastal water, marine water, raw water, landfill leachate, sediment and air.

Physical chemical parameters indicate that there is little tendency for BCPS to escape from water to air, based on the Henry's Law constant. The registrant(s) classify BCPS as slightly mobile, based on a log K_{OC} of 3.5. Fugacitiy modelling showed, that if emission of BCPS takes place via water only, the main target compartment is water. Nevertheless, the final sink of BCPS might be according to the water-sediment simulation test (Unpublished study report, 2014) the sediment, where BCPS quickly dissipates from the water to the sediment phase where it persists. The detection and/or quantification of BCPS in sediment (unpublished, projects: Seawater and sediment from Black Sea Survey 2017) support findings from the OECD TG 308, asmore BCPS is found in sediment than in water.

3.3 Data indicating potential for long-range transport

Based on the vapour pressure and assuming BCPS is released to air, BCPS will exist in both the vapour and particulate phases in the ambient atmosphere (Norström *et* al., 2010) and the author further stated that BCPS may be removed from the atmosphere by wet and dry deposition. BCPS was measured in vapor and particulate phase in air (Norström *et al.,* 2010). The atmospheric concentrations of measured BCPS were below the LOD (LOD < 2 pg/m^3) at Råo, Pallas and Stockholm (Norström *et al.,* 2010). However, BCPS was detected in one air sample from the Swedish east coast (Aspvreten) in the same magnitude as individual PCB congeners, such as PCB 138 (Norström *et al*. 2010), the concentration was 1.1 pg/m^3 (LOD 0.3 pg/m^3) in August 2010. The authors stated that a contamination of the first sample could not be excluded.

[6] Joint Black Sea Surveys (2017) National pilot monitoring studies and joint open sea surveys in Georgia, Russian Federation and Ukraine, 2017. Available at: http:// emblasproject.org/publications-reports. Korotaev, G., Oguz, T., Nikiforov, A., Koblinsk, C

BCPS has a calculated DT_{50} in air (gas phase) of 27.3 days (24-hours) or 54.7 days (12-hours). The overall persistence in air considering the gas and particle phases is expected to be longer than the half-life calculated in gas phase alone, as BCPS sorbed to airborne particles might be resistant to OH reaction.

The DT_{50} in air (gas phase) indicates a potential for long-range atmospheric transport (AOPWIN v1.92), therefore a model was used to estimate the long-range transport potential (LRTP). The OECD "Pov and LRTP Screening Tool"[7] has been developed with the aim of using multimedia models for estimating overall environmental persistence (Pov) and long-range transport potential (LRTP) of organic chemicals at a screening level in the context of PBTs/POPs assessments. The tool calculates metrics of (overall environmental persistence) Pov, TE (Transfer Efficiency) and the Characteristic Travel Distance (CTD) from a multimedia chemical fate model and provides a graphical presentation of the results.

The result for BCPS is plotted against the reference chemicals α-HCH, Aldrin, c-octaBDE, PeCB, BDE-99 and γ-HCH. The criteria lines or boundaries for reference POP substances were not modified and taken as proposed in the tool (Pov limit: 195 days (for α-HCH), CTD limit: 5097 km (for PCB 28), TE limit: 2.248 % (for PCB 28)) according to Klasmeier *et* al. (2006). CTD (characteristic travel distance) is a transport-oriented LRT indicator and quantifies the distance from the point of release to the point at which the concentration has dropped to 1/e or about 38 % of its initial value. TE (transfer efficiency) estimates the percentage of emitted chemical that is deposited to surface media after transport away from the region of release (Wegmann, 2009).

Following input parameters for Kow and Kaw, half-lives for water and soil were used and are listed in Table 29. The input values DT_{50} water and soil are not derived from experimental findings but estimated with the Level III Fugacity model from EPISuite; the calculated DT_{50} in air is > 2 days (AOPWIN v1.92).

Table 29: Half-lives for air, water and soil (input parameters for the OECD Tool)

Half-Lives	Value (h)	Source
Air	1313	AOPWIN v1.92
Water	1440	Level III Fugacity
Soil	2880	Level III Fugacity
Log Kaw	-5.252	KOAWIN v1.10
Log Kow	3.9	KOWWIN v1.10

The multimedia OECD model results indicate a similar potential of LRT as the reference POP chemical γ-HCH (lindane).

Input parameter of a DT_{50} of 54.7 days (12-hours) resulted in a calculated CTD (characteristic travel distance) in air for BCPS of 2070 km and a CTD in water of 133 km. The calculated TE value is 8.5 %, Pov is 170 days (Figure 2). If the water solubility of 0.86 mg/L is used to calculate the log Kaw, the value of -5.252 is derived.

[7] AMAP Assessment 2009: Human Health in the Arctic | AMAP

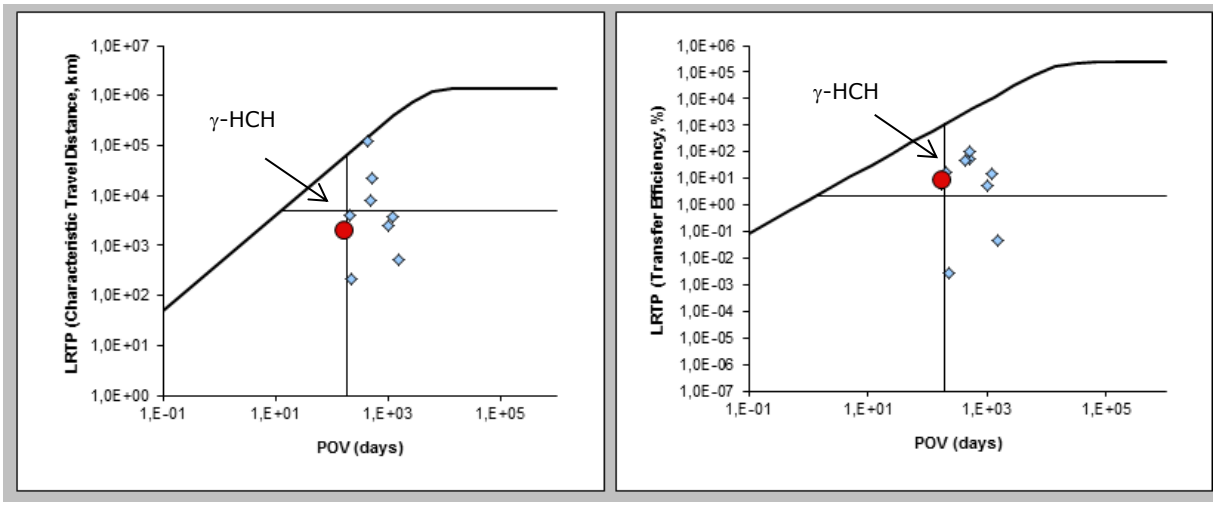


Figure 2: Results from the OECD Tool (CTD and TE) for BCPS (red point) and selected reference substances (α-HCH, Aldrin, c-octaBDE, PeCB, BDE-99 and γ-HCH).

Using the $DT_{50,diss}$ of 7.1 days (from OECD TG 308) instead of the estimated DT_{50} for water, following results are obtained: P_{OV} = 168 days, CTD in air = 2065 km, CTD in water = 18 km, TE = 8.4%, again BCPS is similar to the POP chemical γ-HCH (lindane).

The experimental derived vapor pressure is 5.1E-06 Pa and the calculated vapor pressure is 1.08E-4 (EPIWIN 4.1, Grain method). The value of the vapor pressure of 5.1E-06 Pa was derived according to OECD TG 104. Vapour pressure was measured at 50, 60 and 70 °C, by extrapolation value of 5.1E-6 was derived. (20°C). If the Henry's Law Constant is calculated using the experimentally determined values for vapor pressure (5.1E-06 Pa) and the water solubility of 0.86 mg/L, a log Kaw of -6.14 is derived (equation R.16-5 from REACH chapter R.16). Using the log Kaw of -6.14 for the calculation of the CTD, TE and Pov. results in: CTD in air (km): 585, CTD in water (km): 149, TE (%): 2.54, Pov (days): 171. Both log Kaw values (-6.14 and -5.252) lead to different CTDs in water and air.
According to Wegmann *et al.* (2009) compounds that are less problematic from an environmental exposure point of view are in the bottom-left corner (low Pov, low LRTP), while substances of environmental concern are found in the upper right region (high Pov, high LRTP).

However, no Monte Carlo Analysis for the given input parameter has been included in the calculation. Uncertainties concerning the input parameters include overestimation of photo-oxidative degradation in air (Scheringer, 2009) as well as CTD and TE might not yield in all cases a relevant LRTP description (see AMAP, 2009[8]).

There are some biomonitoring data from remote areas, which indicate potential for long-range transport potential of BCPS (see Annex I – Monitoring data in biota). Verreault *et al*. 2005 determined for the first time the occurrence of BCPS in the blood (plasma) and eggs of the Arctic bird from male and female glaucous gull (*Larus hyperboreus*). Blood samples and eggs were collected during 2002 and 2004. BCPS was analysed by ECNI-GC-MS. Mean recovery of the internal standards was 80.3%±1.96% and reported concentrations were recovery corrected. Method detection limit (MDL) for individual analytes was determined as 10 times the noise level, or in case where an analyte present in blanks, three times the standard deviation (SD) of the analyte blanks. MDL ranged between 0.001-0.35 ng/g wet weight, a specific value for BCPS is not disclosed. In both male (mean value: 26.5 ng/g and max. 143 ng/g l.w.) and female (mean: 19.5 ng/g and max. 58.8 ng/g lipid weight) plasma samples BCPS was detected. In the eggs, BCPS was not detected. It was the first time ever that this contaminant was found in Arctic biota. The sampling location was in the Norwegian Arctic at Bear Island (74°22´N, 19°05É), which is located in the Nordic Arctic

[8] AMAP Assessment 2009: Human Health in the Arctic | AMAP

Sea.

Another study detected BCPS in guillemot (*Uria aalge*) bird eggs (in the range of 3.3 to16 ng/g fat) from scarcely populated areas in Norway and in the Nordic Arctic (Bjørnøya or Bear Island and Sandøy, Faroe Islands) in 2005 (Jörundsdóttir *et al.*, 2008). Screening programme 2017 (AMAP, 2018) revealed a detection frequency for BCPS of 20% in Artic mink (Sommarøy, Norway; n= 5; in 2017). The concentration of BCPS in mink was 0.5 ng/g w.w. and in common gull 0.2 ng/g w.w.

3.3.1 Summary and discussion of the long-range transport

BCPS is predicted to be long-range transported via air with CTD in air, Pov- and TE-values comparable to the well-known POP substance lindane using the calculated log Kaw value of -5.252 (KOAWIN v1.10). Using the log Kaw (based on vapor pressure and water solubility) of -6.14 leads to much lower CTD values for air and water. Biomonitoring data from remote areas (cf. Arctic) indicate that the substance can be long-range transported far away from point sources.

3.4 Bioaccumulation

3.4.1 Bioaccumulation in aquatic organisms (pelagic & sediment organisms)

Screening data

Log K_{OW}

Estimated log K_{OW}

For the PBT and vPvB assessment a screening criterion has been established, which is log K_{OW} greater than 4.5 (ECHA, 2017). The substance BCPS does not screen as potential B/vB for aquatic organisms based on the predicted log K_{OW} of 3.9 (EPI Suite, EPI Web 4.1, KOWWIN v1.68). The used model is expected to be applicable for BCPS and the predictions to be valid. There are no indications in literature that this model is not applicable for this group of organic, aromatic substances containing a sulfone group and chlorine. Moreover, predicted and measured values are the same.

Measured log K_{OW}

The shake flask method (OECD TG 107) was used and the log K_{OW} of BCPS was determined to be 3.9 at 20°C (Unpublished study report, 2006a).

Summary on log K_{OW}

The screening criterion for bioaccumulation for aquatic organisms based on log Kow >4.5 is not fulfilled due to a measured and predicted log K_{OW} value of 3.9.

Estimated BCFs for BCPS

BCF values were estimated using the BCFBAF program (BCFBAF v3.01) within EPI Suite v4.11 using the following smiles code for BCPS O=S(=O)(c(ccc(c1)Cl)c1)c(ccc(c2)Cl)c2. The predictions have been carried out with the estimated log K_{OW} of 3.9 (KOWWIN v.1.68).

Estimated BCF values indicate a low to moderate bioaccumulation potential in fish (Table 30). The used model is expected to be applicable for BCPS and the predictions to be valid. There are no indications in literature that this model is not applicable for this group of organic, aromatic substances containing a sulfone group and chlorine.

Table 30: Estimated BCFs for BCPS (BCFBAF v3.01)

Name CAS No.	BCF (regression-based method)	BCF Arnot-Gobas Method (upper trophic)	BAF Arnot-Gobas
Bis (4-chlorophenyl) sulphone 80-07-9	172.8	675	692.3

The registrant(s) predicted BCF and BAF values with US EPA EPI Suite (ver. 4.1) BCFBAF v3.01 ($BCF_{Arnot-Gobas}$, 5% Lipid normalised = 309.8; BAF $BCF_{Arnot-Gobas}$, 5% Lipid normalised = 318) and the QSAR program CATALOGIC BCF LMC (Laboratory of Mathematical Chemistry, v. 02.09 - July 2017). For BCPS a BCF of 269 L/kg wet weight at steady-state was predicted (Personal communication, 2018).

Summary on estimated BCF values

Calculated BCF values are < 2000, indicating a low potential for aquatic bioaccumulation.

Experimental BCF data for BCPS

One experimental study on the aquatic bioaccumulation in carp is available (NITE, 2001; Table 31), which is considered as Klimisch 2, reliable with restriction. The study was performed with non-radiolabelled BCPS and without a depuration phase under flow-through conditions. As no depuration phase was conducted, no depuration rate constant and kinetic BCF were calculated. In the BCF study, the duration of exposure was 35 days and has been prolonged. . Steady-state was reached during the exposure phase. The study authors stated that the variation in the bioconcentration factors (mean) after 21, 28 and 35 days were within 20% of the mean value for the BCF in these 3 analyses from the 3 timepoints (NITE, 2001). The BCF at steady-state (BCFss) was calculated to be in the range of 75 – 83. A lipid normalisation was performed and a BCFss of 205 was calculated. The substance seemed to be stable under the test conditions. No fish abnormalities were observed.

Table 31: Experimental BCF data for BCPS

Method	Results	General comments on method	Reference	Validity/ Comments
Cyprinus carpio Yearling fish Body length: 6.9 – 8.1 cm aqueous (freshwater) flow-through uptake phase: 35 d depuration time: 0 d Based on Bioconcentration test of chemicals in fish and shellfish	BCFss: 75 L/kg (whole body weight) BCFss: 82 L/kg (whole body weight) BCFss normalised to 5% lipid content: 187.5 L/kg 205 L/kg	Test material name: "K-1200" bis(4-chlorophenyl) sulphone Two conc. used: 5 µg/L 50 µg/L well below water solubility of 0.86 mg/L, at 20°C Fish lipid content 2% (at start and end of exposure) Dispersant: Hydrogenated castor oil HCO-40	NITE, 2001 (Japan)	Registrant(s) ranked the study as Klimisch 2 (reliable with restrictions). Limitations: No depuration phase has been conducted, no lipid normalised BCFs are available, but they were re-calculated, test item was not radio-labelled. In the OECD guideline 305 it is stated "a depuration phase is always necessary, unless uptake of the substance during the uptake phase has been insignificant." This study is considered to be reliable with restriction

Method	Results	General comments on method	Reference	Validity/ Comments
				(Klimisch 2), but it is not in accordance with the recent OECD TG 305 guidance.

3.4.2 Bioaccumulation in terrestrial organisms

Screening criteria[9] for air-breathing organisms have been established and are based on log K_{OW} > 2 and log K_{OA} > 5 (ECHA, 2017). The measured log K_{OW} for BCPS is 3.9 (Unpublished study report, 2006a) and the estimated log K_{OA} value is 9.2 (KOAWIN v.1.10), indicating a biomagnification potential in terrestrial food chain and air-breathing marine as well as in humans.

The used model KOAWIN is expected to be applicable for BCPS and the prediction to be valid. According to Kelly *et al.* (2004) the substance belongs to polar non-volatiles, which do not biomagnify in aquatic organisms, but may substantially biomagnify in air-breathing (terrestrial) organisms. The substance itself has been mentioned as an example for a hydrophilic compound to exhibit a bioaccumulation potential (Kelly *et* al., 2004).

Toxicokinetic studies in rats (e.g., according to OECD TG 417) provide further information on the bioaccumulation potential of the substance. Toxicokinetics studies (summarised in chapter 4.1) demonstrate that BCPS is readily absorbed and distributed fast from blood into tissues, mainly to lipid-rich tissues such as adipose.

After intravenous administration of 10 mg/kg bw increasing accumulation of BCPS in adipose tissue was observed up to 24 hours, followed by slow elimination. A terminal half-life (rat, i.v. application) in adipose tissue of 12 days was estimated by the authors (Mathews *et al.* 1996). The tissue measurement data from this study are tabulated in NTP, 2001, and a half-life of ~10 days can be derived from adipose tissue concentrations between 3 and 21 days. The study author concludes that based on these observations BCPS has the potential to bioaccumulate in the tissues of higher animals and in the environment, if exposure occurs.

However, in the same publication (Mathews et al 1996) in a five-week repeated dose study via oral gavage at the same dose level of 10 mg/kg bw/day tissue concentrations peaked at week 3 and declined at week 5. Poon et al 1996 examined tissue content of BCPS after repeated dosing (75.6 mg/kg bw/day for 28 days, diet, vehicle: corn oil) in a rat study, in which the content of BCPS remained unchanged in adipose and liver between week 1 and 4, and even increased in kidneys.

The study of Mathews *et al.* (1996) directly measures the disappearance of radiolabelled BCPS from the body over a relevant time period after i.v. administration and provides a robust estimate of half-life. While it is possible to estimate half-life using other methods (such as the time to attain steady state), such methods have much greater uncertainty. Moreover, the repeated dosing studies in Mathews *et al.* (1996) and Poon *et al.* (1996) do not clearly reach steady-state and so cannot be used for estimating half-life.

The excretion of BPCS depends on metabolism to more polar compounds, thus the BCPS levels found in sample material might be influenced by the induction of phase I and phase II enzymes present in the respective individual or wildlife species exposed.

It has been demonstrated that BCPS can induce phase I and phase II enzymes (e.g., CYP450 enzymes, UDPGT and GST) in the aforementioned toxicokinetic studies. Mathews *et* al. 1996 determined at 10 mg/kg/day and above doubled cytochrome P450 levels, but did not see large increases in two enzyme activities. Poon *et al.* 1996 observed a dose-dependent induction in CYP2B related enzyme activities and other metabolic enzymes. The excretion of BCPS increased dose-dependently after repeated dosing in Mathews et al 1996, and the retention of BCPS in tissues decreased dose dependently (in relation to administered dose) in Poon *et al*. 1996, consistent with a determinative role of metabolism in the excretion of BCPS. The data demonstrate that the metabolism and rate of excretion of BCPS is affected by the dose of BCPS. Thus the half-life of BCPS measured after a dose of 10 mg/kg may underestimate the half-life of BCPS at lower doses of BCPS. More data or information on the influence of BCPS on different

[9] https://echa.europa.eu/documents/10162/13632/information_requirements_r7c_en.pdf

CYP450 isoforms would be of interest to further characterise enzymatic metabolism attributable to BCPS among different species and to explain differences in found BCPS levels across species.

3.4.3 Field data

Biota / Biomonitoring

BCPS was monitored in different wildlife species over various trophic levels from fish in fresh and sea water, up to top predators (e.g., grey seals, fish-eating birds and eggs, mink, otters, buzzards). Monitoring data are summarised and sorted according to different taxonomic groups (fish, seals and birds, other organisms) and humans (ref. to Annex I). Data were mostly generated in the Baltic region (Latvia, Sweden, Poland and Estonia), but also in the Norwegian Arctic Sea, Canada, Faroe Islands and Iceland, as well as samples from German rivers. As the occurrence of BCPS focused on the Baltic region and Northern Europe, further and more recent data from biota (e.g., birds, fish) were collected, which includes data from North America, Austria, and the Black Sea. Monitoring data are summarised below and ordered chronologically. Information on the validation parameters of the monitoring studies e.g., LOD, LOQ, recovery, calibration range and blanks is given in the study descriptions below or in Annex I.

3.4.3.1 Biomonitoring – Fish

Marine and freshwater fish have been investigated for the presence of BCPS. Perch represents a good indicator species for local contamination, as it has a stationary behaviour. In general perch is a very lean fish. Herring is a food source for grey seals and guillemot and is ideally suited to compare the biota levels found. Younger herring (<4 years) were mostly selected as they are more stationary. The lipid content of herring was approximately 3% based on a yearly mean for > 20 years (Miller *et* al., 2014). Arctic char is a freshwater fish sampled in remote areas (oligotrophic Lake Vättern) with no local industry. Bream samples were analysed in Germany and recently various predator species (Zander, Wels catfish, Burbot) were analysed from the river Danube, Austria. In general, as BCPS tends to accumulate in fat, fish with higher fat contents might be preferred over lean fish for monitoring purposes.

Olsson and Bergmann, 1995

The first study analysing BCPS in fish muscle was performed by Olsson and Bergman (1995); herein BCPS has been identified in 2-year-old perch (*Perca fluviatilis*) as an environmental pollutant in the Latvian coastal area collected at Daugavgriva, Salacrgriva and Libelibre. Olsson *et* al. 1995 reported the analysis of BCPS in fish samples by using gel permeation chromatography (GPC) followed by HPLC equipped with a nucleosil NO_2 column for clean-up purposes. Extracts were collected and analysed by electron ionization gas chromatography mass spectrometry (EI-GC-MS). Validation parameters (LOD; LOQ; linearity, etc.) of the described analytical method are not disclosed within this paper. Mean recovery for BCPS (5 samples) is 92% (range: 89-95 % recovery). In all 30 fish samples BCPS was found, frequency of detection was 100%. Samples were taken in July and August 1994. The concentrations ranged between 40 – 100 ng/g lipid weight (l.w.) in the muscle. The sampling site Daugavgriva is influenced by industry (mean BCPS concentration in perch muscle = 72 ng/g l.w.; n=10), in contrast to the two other sites located in Salacrgriva and Libelibre (mean BCPS concentration in perch muscle = 76 ng/g l.w., n =10 and mean BCPS concentration in perch muscle= 56 ng/g l.w., n=10).

Olsson *et al.*, 1999

The aim of the study was to investigate the pollution in fish muscle from the Latvian coast. The same analytical method as described in Olsson *et* al. 1995 was used. To determine the location of pollution, perch served as indicator species as they are very stationary in their behaviour. The freshwater input into the Gulf of Riga is part of the eastern Baltic Proper, which comes mainly through the Daugava, Lielupe and Gauja rivers. Libelibre sampling location is a background area

with only sparse agricultural and industrial activities. BCPS concentration was in average 55 (in 1994, n=10) and 53 (in 1995, n=10) ng/g l.w. Daugavigriva and Lielupe contribute more than 70% of the total freshwater input to the Gulf. Daugavgriva is influenced by industry and concentration of BCPS was at average 71 ng/g l.w. in 1994 (n=10) and 82 ng/g l.w. in 1995 (n=10). Riga area is highly industrialised and is located upstream the Daugava River. Salacgriva (Kurmrags) is 60km north from Daugavgriva and lacks industrial pollution, average concentration was between 61 (in 1995, n=10) and 75 (in 1994, n=12) ng/g l.w.

The similar concentrations of BCPS at all study locations might indicate that it is mainly transported to and distributed in the area by air or via municipal WWTP, which is in contrast to what was obtained by Valters *et* al (1999). Lateral fish muscle was analysed for BCPS, frequency of detection was 100% and the concentration was in the range of 38 – 100 ng/g l.w. The BCPS concentrations in perch muscle were in the range of 50 – 75% of the concentration of the polychlorinated biphenyl (PCB) congeners CB-138 (2,2',3,4,4',5'-Hexachlorobiphenyl, CAS No 35065-28-2) and CB-153 (2,2',4,4',5,5'-Hexachlorobiphenyl, CAS No 35065-27-1).

Valters *et al.*, 1999

In 1997, BCPS was analysed in lateral muscle of perch (n= 23) at six different sampling sites in Latvia, the concentration ranged from min. 28 to max. 190 ng/g l.w. (ref. to Annex I). Valters et al. 1999 used a similar method as Olsson *et* al. 1995 for determination of BCPS (and other contaminants) in perch samples by using GPC-HPLC clean-up after addition of surrogate standards (CB-189 (2,3,3',4,4',5,5'-heptachlorobipheny, CAS No 208263-73-4) and DFDT (1,1,1-trichloro-2,2-bis(4-fluorophenyl)ethane) for recovery calculation. HPLC fractions were analysed by GC-ECD. Concentrations of BCPS found from 6 sampling sites were in the range of 32 – 160 ng/g l.w (based on geometric mean values). Mean recoveries were 76% (33 samples, CB-189 surrogate), 87% (31 samples, CB-189 surrogate) and 82% (27 samples, DFDT surrogate). Other validation parameters (i.e. LOD, LOQ, calibration range) were not disclosed. BCPS concentration increased from 53 (n=2) to 94 ng/g l.w. (n=4) and further to 160 ng/g l.w. (n=4) along the river Lielupe, finally entering the Gulf of Riga and indicating a local BCPS contamination source, but no specific source could be identified. In the river Daugava, at 3 sampling sites, similar BCPS concentrations (48 (n=5), 32 (n=5), and 44 (n=3) ng/g l.w.) were detected. Frequency of detection was 100%.

Arnér *et al.*, 2004

In 2003, BCPS was not determined in a quantitative way in any of the 28 aggregate Swedish perch samples analysed, as the LOQ of 2 µg/g l.w. was very high compared to the e.g., LOQ for BCPS of 0.2 ng/g l.w. from Norström *et al.* (2004).

Norström *et al.*, 2004

BCPS concentration in salmon muscle increased from 1971 to 1996 from 8.7 ng/g l.w. (n=10, one pooled sample) to an average concentration of 32 ng/g l.w. (2 pools analysed each with 4 fish, total n=8) in Gotland, Sweden, whereas the concentration of 4,4´- DDE decreased from 7100 to 800 ng/g l.w. in salmon in the same sample. Analysis and quantification of BCPS were performed by ECNI-GC-MS after homogenisation with n-hexane/acetone and extraction with n-hexane/MTBE (methyl tert-butyl ether). LOD (BCPS) = 0.2 ng based on background amount of BCPS in the blank solvent samples. LOQ (BCPS) was set to three times LOD = 0.6 ng. 14C-labelled BCPS gave recoveries of 99%. The recoveries and (SD) of surrogate standards are as follows: 94% (22%) for Trifon and 90% (28%) for CB-189. Frequency of detection in salmon was 100%. Technical DDT contained up to 0.03 – 0.6% BCPS as an impurity originating from the technical production process (IARC, 1991). As BCPS increased, the source of BCPS cannot be DDT, as the DDT metabolite 4,4´- DDE determined in the study decreased substantially. In addition to sea water also freshwater fish, Arctic char, was analysed for BCPS in Lake Vättern, Sweden. In 1972, 10 fish were sampled and BCPS could not be detected (LOD = 0.47 ng/g l.w.). In 1996, BCPS was detected at low concentration of 1.8 ng/g l.w. in fish muscle (n=5). Again,

the same decreasing trend for 4,4´- DDE (fish muscle) was observed. Far north, in samples from Arctic char BCPS was not detected in Abiskojaure in Sweden. In 1998, the concentration of BCPS in perch muscle was at the Northern Baltic coast (15.5 ng/g l.w., n=10) lower than at the Southern Baltic coast (45 ng/g l.w., n=10). In the Baltic Sea, Baltic herring was sampled in 1998 and a concentration of 30 ng/g l.w. (n=20) was analysed.

Norström *et al.*, 2010

Different matrices (air and deposition samples, surface water, effluent of WWTP, fish samples) were analysed to determine the source and transport pathway of BCPS to elucidate the elevated levels found in biota especially the Baltic Sea environment. BCPS was detected in all fish muscle samples (herring and perch, ref. to Figure 3, n= 11). In 2008, the concentration of BCPS in fish muscle was in the range of 20 – 69 ng/g l.w., the levels in perch and herring were similar. There were according to the author no trends in concentration and species, country, or sampling location.

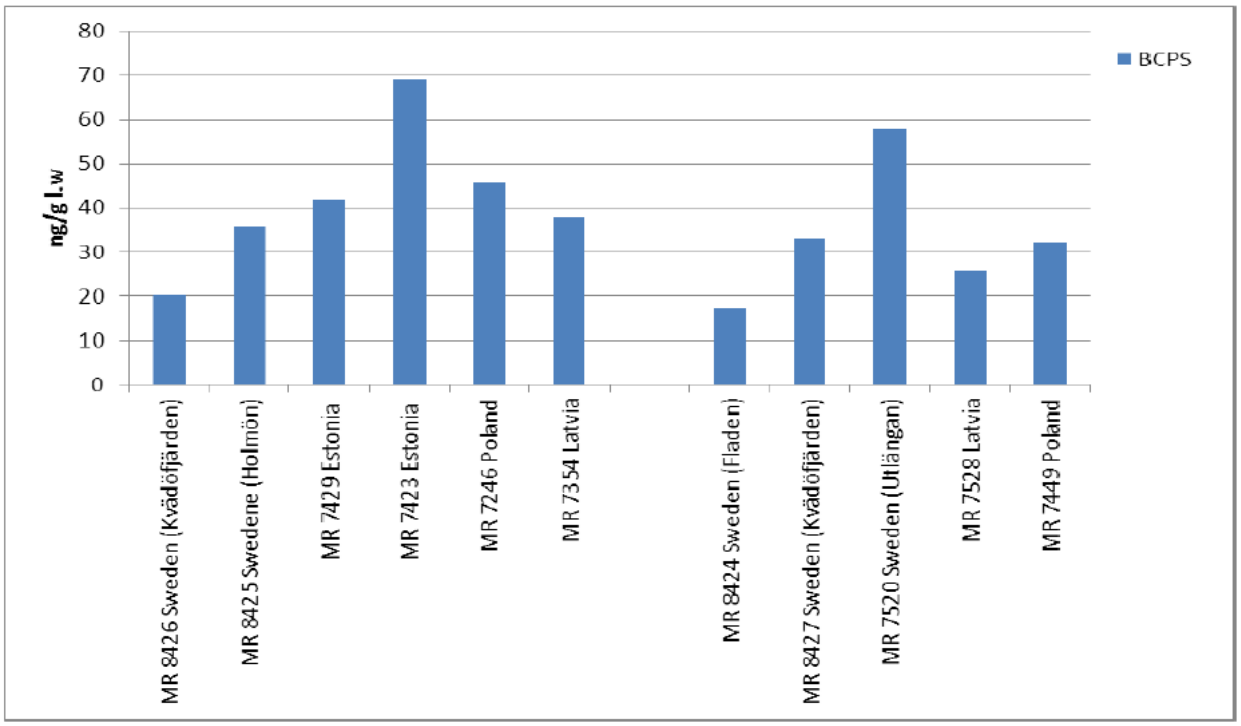


Figure 3: BCPS concentration in perch and herring muscle (ng/g l.w.) in the Baltic Sea and in the North Sea (Fladen), year 2008 (source, Norström et al., 2010)

Black Sea

BCPS was detected in five fish samples from the Black Sea, one from Ukraine and four from Georgia (Black Sea: project JBSS, 2017). The concentration levels in biota samples ranged from 0.9 to 2.2 ng/g wet weight. Fat content was not measured, but assuming a fat content of around 5%, this would yield a BCPS concentration of 18 – 44 ng/g l.w.

Hornek-Gausterer *et al.*, 2021

In summer 2019, healthy specimens of the following predatory freshwater fish species were collected at two Austrian locations at the river Danube (Aschach, Hainburg): *Sander lucioperca*, *Silurus glanis*, and *Lota lota*. The sampled fish range in body size from 0.04 – 1.2 kg with lipid concentrations ranging from 1.2 to 9.8%. Whole fish samples were analysed for BCPS and DDT (including metabolites). BCPS levels in predatory freshwater fish ranged from 1.3 to 9.3 ng/g fat (cf. Table 32, mean: 4.9 ng/g fat, n = 8), DDT (incl. metabolites) was investigated but not

detected in any fish sample (LOD of DDT = 0.003 mg/kg).

Table 32: Analytic results of BCPS levels in whole fresh-water fish samples (Austria, Hornek-Gausterer *et al.,* 2021)

Species	Weight [g]	Length [cm]	Trophic level	BCPS [ng/fat]	Lipid content [%]	LOQ [ng/fat]	LOD [ng/fat]	Location	Year
Zander (*Sander lucioperca)*	370.82	37	high	1.3	9.3	1.3	0.65	Aschach, Danube, Austria	2019
Wels catfish (*Silurus glanis)*	1202.8	56	high	6.4	2.7	4.8	2.4	Aschach, Danube, Austria	2019
Burbot (*Lota lota)*	339.93	35	high	4.2	3.4	4.4	2.2	Aschach, Danube, Austria	2019
Goby (*Neogobius melanostomus*)	39.8	15	low	2.7	3.5	2.1	1.1	Hainburg, Danube, Austria	2019
Zander (*Sander lucioperca)*	397.58	40	high	5.1	1.7	3.2	1.6	Hainburg, Danube, Austria	2019
Wels catfish (*Silurus glanis)*	1099.8	56	high	9.3	1.2	7.3	3.7	Hainburg, Danube, Austria	2019
Burbot (*Lota lota)*	1090.8	60	high	3.3	4	2.5	1.3	Hainburg, Danube, Austria	2019
Chondrostoma nasus in Cormorant	-	-	high	5.5	6.5	0.66	0.33	Lower Austria, Austria	2019

Trends – biomonitoring in fish

Monitoring data per fish species for the occurrence of BCPS are discussed below.

Perch

In Latvia, the level of BCPS (1994 – 2008) in perch was in the range of 32 – 160 ng/g l.w. (Figure 4). BCPS concentration in perch increased along the river Lielupe from 53 to 94 and further to 160 ng/g l.w., finally entering the Gulf of Riga, indicating either a local BCPS contamination source discharging BCPS into the water (Valters *et* al., 1999) or diffuse sources (e.g., multiple wastewater treatment plants) along the river. Interestingly, the BCPS concentration in perch did not change significantly in Daugava, Latvia between 1997 and 2008. Geometirc mean value of perch BCPS concentration in 1997 (location: Daugava) was 40.7 ng/g l.w. (Valters *et* al., 1999; Olsson *et* al., 1999), in 2008 the BCPS concentration in perch was 38 ng/g l.w (location: near Daugava).

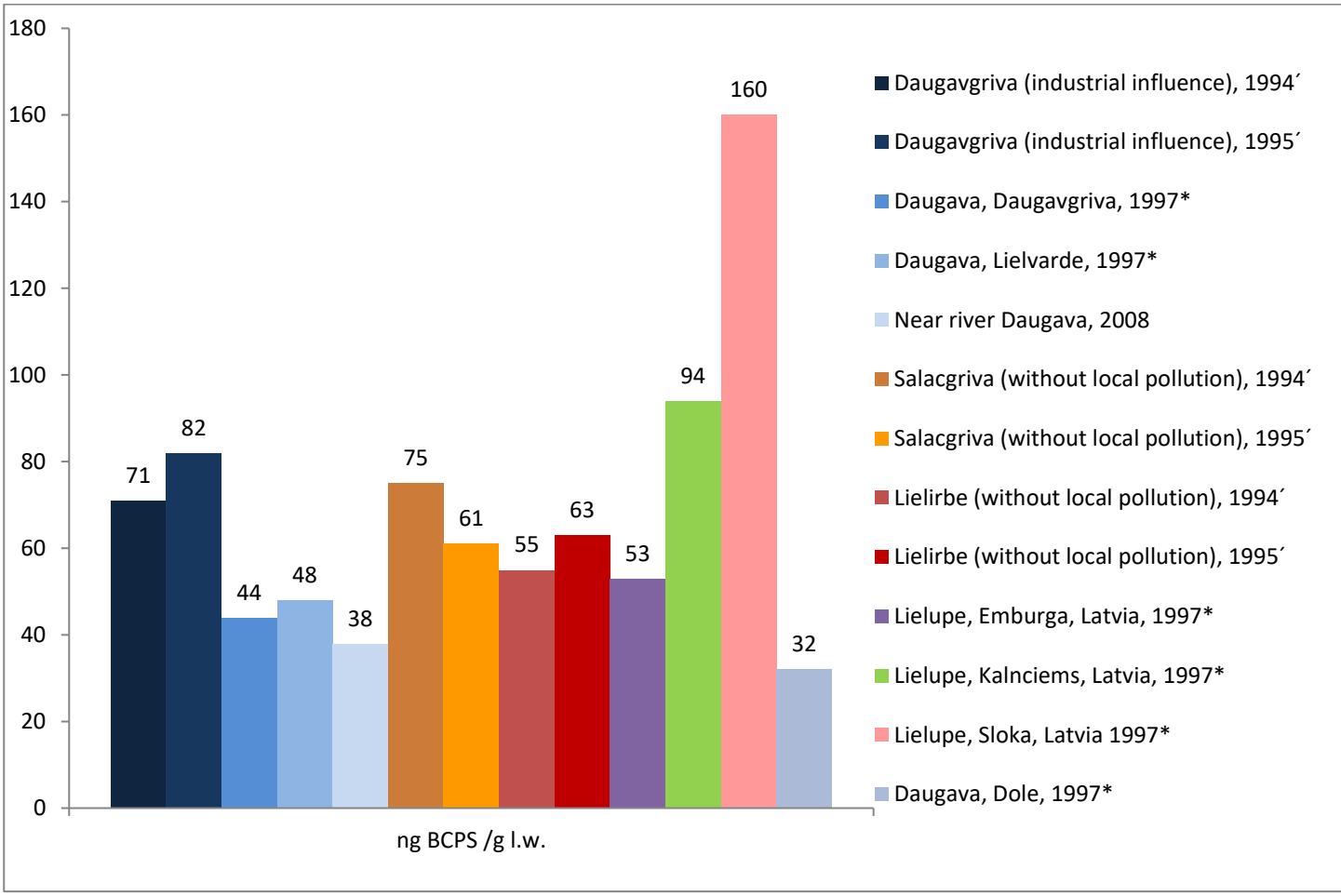


Figure 4: BCPS levels in Perch (Latvia) including published values from Olsson *et* al., 1999´; Valters *et* al., 1999* (geometric mean values) and Norström *et* al., 2010.

In Sweden, the BCPS concentration of all perch muscle samples from 1998 (Norström *et al*., 2004) was lower in the Northern Baltic coast (15 – 16 ng/g l.w., n=10) than in the Southern Baltic coast, (35 –37 ng/g/l.w., n=10). In 2008, perch samples from Estonia revealed BCPS concentrations between 42 - 69 ng/g l.w. and in Poland 46 ng/g l.w., which are similar to the concentrations found in Latvia (Norström *et al.,* 2010).

Herring

From 1998 and 2008, the concentrations of BCPS in herring were in the range between 17 – 58 ng/g l.w. Concentration seems to stay at a certain level of around 30 ng/g l.w. in herring obtained from Sweden, Poland and Lithuania (Norström *et* al., 2004 and 2010).

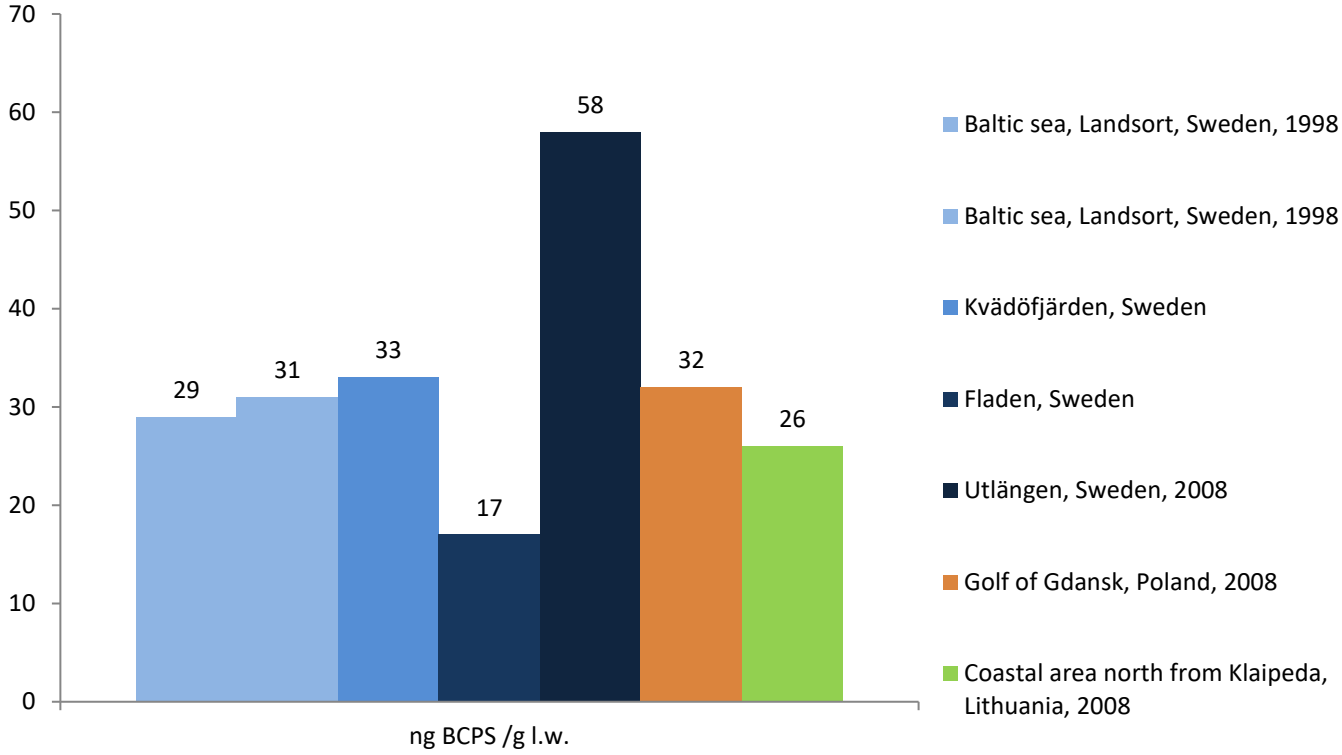


Figure 5: BCPS levels in herring including published values from Norström *et al.* 2004 and 2010.

Salmon

The concentrations of BCPS in salmon (muscle) from the Baltic Sea increased comparing samples from 1971 to 1996 (Gotland, Sweden) from 8.7 ng/g l.w. (n=10) to 32 ng/g l.w. ((n=8) Norström *et al.,* 2004, ref. to Figure 6). DDT contained BCPS as impurity, but has already been successfully phased out in the late seventies, however, the concentration of BCPS comparing both time points shows a 3.7-fold increase.

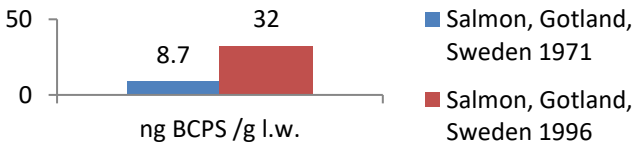


Figure 6: BCPS levels in salmon including published values from Norström *et* al., 2004

Artic char

BCPS levels in Arctic char from the oligotrophic freshwater lake Vättern, Sweden was much lower than compared to Baltic Sea salmon but, increased from not detected to 1.8 ng/g l.w from 1972 – 1996 (Norström *et* al., 2004). In 1999, in a very remote area of Sweden, Abiskojaure, BCPS could not be detected (Norström *et al*., 2004).

Bream

In Germany, bream (*Abramis brama*) sampled (sampling year: 1997) at 4 different locations in two German rivers (Elbe and Rhein) showed BCPS concentrations with up to 10-fold difference between the sampling sites (3.4 - 34 ng/g l.w) cited in Norström *et al.* (2004 and 2010).

Summary biomonitoring in fish

Analyses of BCPS in various fish species from different countries (Latvia, Lithuania, Poland, Estonia, Germany, Sweden, Austria, Georgia, and Ukraine) revealed that BCPS is detected in fresh and marine fish samples with a detection frequency of 100% (e.g. Norström *et* al., 2004; Norström *et* al., 2006; Norström *et* al., 2010; Olsson *et* al., 1999; and Valters *et* al., 1999; Hornek-Gausterer *et* al., 2021; Black Sea: project JBSS, 2017), except for one very remote region. In a Swedish report, BCPS in fish was not detected, but it seems plausible that the reason was the insensitive analytical method, as the LOD was very high (Arnér *et* al., 2004).

The highest fish BCPS values are found in the Baltic Sea, which is among the most polluted water bodies in the world. It is a semi-enclosed water body having limited water exchange to the North Sea. Increasing BCPS trends have been observed by Norström *et* al., 2004 in salmon (1971 to 1996) from the Baltic Sea and in Artic char (1972 to 1996) obtained from an oligotrophic lake in Sweden.

In Lativia, from 1997 to 2008, the BCPS level in perch was at one location (Daugava) within a range of 38 to 48 ng/g l.w. (Norström *et* al., 2010; Valters *et al.,* 1999).

A more or less same stable concentration over 10 years (1998 – 2008) was observed in herring, which was around 30 ng/g l.w. from different locations in Sweden, Poland and Lithuania (Norström *et al.,* 2004 and 2010).

BCPS was detected in five fish samples from the Black Sea, one from Ukraine and four from Georgia (Black Sea: project JBSS, 2017). The concentration levels in fish samples ranged from 0.9 to 2.2 ng/g wet weight. Fat content was not measured, but assuming a fat content of around 5% this would yield a BCPS concentration of 18 – 44 ng/g l.w.

Recent data from freshwater fish (Danube, Austria) show max. BCPS level of 9.3 ng/g fat (Table 1, Hornek-Gausterer *et* al., 2021).

Local industrial input sources or diffuse sources (e.g., multiple waste water treatment plants along a river) might be responsible for the different BCPS concentrations measured. Recent monitoring from 2019 shows, that DDT (incl. metabolites) in contrast to BCPS could not be detected in any Austrian freshwater fish samples (Hornek-Gausterer *et al.,* 2021).

3.4.3.2 Biomonitoring - Birds

In a variety of the investigated bird samples (eggs, breast muscles, liver, and plasma) BCPS was detected, indicating that BCPS is bioavailable to birds from different geographic locations (Sweden; California, USA; Iceland; Faroe Islands; Norway; Austria) including the Norwegian Arctic. BCPS was investigated and detected in different bird species (*Haliaeetus albicilla*, *Uria aalgae*, *Rynchops niger, Phalacrocorax carbo carbo, Larus hyperboreus*) by e.g., Olsson, 1995; Letcher *et al.*, 1995; Helander *et al.,* 2002; Verreault *et al*., 2005; Jörundsdóttir *et al*., 2006 and Jörundsdóttir *et al.,* 2008; Norström *et al.,* 2004; Norström PhD thesis, 2006; Millow *et al*., 2015; Hornek-Gausterer *et al.,* 2021).

Data are summarised below chronologically and concentrations of BCPS in birds and eggs are summarised in Annex I.

Letcher *et al.*, 1995

In one herring gull (*Larus argentatus*) egg from Canada (sampling year 1989), BCPS was identified.

Olsson and Bergman, 1995

In a study performed by Olsson and Bergman (1995) white-tail sea eagle (*Haliaeetus albicilla*) eggs at the Swedish Baltic coast (Söderköpnig, Sweden) were investigated for the occurrence of BCPS. In one unhatched egg BCPS was measured at a concentration of 500 ng/g lipid weight (l.w.) (sampling year: 1987).

Helander *et al.*, 2002

In a monitoring study (Helander *et* al., 2002) the reproduction success of white tail sea eagle (*Haliaeetus albicilla*) was monitored from 1964 – 1999 in three different sub-populations from the Baltic Sea, inland central Sweden and Lapland. The main issue was whether DDT and its metabolites and/or PCB and its congeners directly affect the reproduction success of this bird species.

The authors explained that the clean-up method used was not primarily designed for analysis of BCPS. Samples were extracted by MTBE after surrogate addition (for recovery determination). The purified extract was analysed by GC-ECD. Mean recoveries range from 75% (13 samples, CB-77 (3,3',4,4'-tetrachlorobiphenyl)) to 99% (11 samples, CB-53 (2,2',5,6'-tetrachlorobiphenyl)). Other validation parameters (i.e., LOD, LOQ, calibration range) were not disclosed. From all investigated substances within this study only BCPS increased over time from the 70s to the 80s.

In detail, in the years from 1971-76 BCPS ranged from n.d. to low concentrations of maximum of 16 ng/g. From 1987-1991 BCPS was detected in all eggs with geometric mean conc. of 170 (egg from eagles with no reproduction) and geometric mean concentration of 110 ng/g l.w. (eggs from eagles with good reproduction). The highest value was obtained for one egg with a BCPS concentration of up to 610 ng/g l.w. (time period: 1987 – 1991). No correlation between reproductivity within the three different sub-populations and the detected concentrations of BCPS was observed. A positive time trend of BCPS was detected. The BCPS concentrations were low compared to DDE and other congeners in this study. In this monitoring study, which was not designed to assess reproductive toxicity of BCPS, no signs of toxicity to reproduction were observed.

Norström *et al.*, 2004

In a screening study several biota samples from different species e.g., fish, mammals (grey seals) and guillemot bird species were analysed and screened for the occurrence and distribution of BCPS and other organochlorine contaminants in the Swedish Baltic coast.

Guillemots are a common name for several species of seabirds in the auk family. The highest concentrations in the different species were found in the guillemot samples from 1989 in the breast muscle with a range of 1600 (n=5) to 1900 (n=5) ng/g l.w. from St. Kalslö, Sweden. The data indicate a strong retention of BCPS in the Baltic fish-eating guillemot (Norström *et* al., 2004). The author concluded that temporal trends and more data must be gathered in order to better understand the potential impact of BCPS in birds.

Verreault *et al.*, 2005

Verreault *et* al. (2005) determined the occurrence of new organic organochlorine contaminants and their metabolites in the blood (plasma) and eggs of the Arctic bird glaucous gull (*Larus hyperboreus*). Details of the study are included in the section 3.3 Long-range transport potential.

Jörundsdóttir *et al.*, 2006 and Jörundsdóttir *et al.*, 2008

The temporal trend of BCPS was analysed in Baltic guillemot (*Uria aalgae*) eggs from 1971 - 2001, a comparison was made to 4,4´-DDE and PCB. Samples were analysed by ECNI-GC-MS after mixing with n-hexane/acetone and extraction with n-hexane/MTBE. The recovery and standard deviation (SD) were calculated for each surrogate standard (SS) after the entire analysis. Other validation parameters (i.e., LOD, LOQ, calibration range) were not disclosed (Jörundsdóttir *et al.,* 2006).

Guillemot feeds mostly on herring (*Clupea harengus*) and sprat (*Sparatus spratus*), the birds stay in the Baltic region all year long (Jörundsdóttir, 2009). Replacement eggs were sampled and analysed (every 5 years, n=5) from Stora Karlsö, an island in the Baltic Sea in Sweden. In the first publication of Jörundsdóttir, a temporal trend from 1971 – 2001 with a statistically significant BCPS decline of annually 1.6% was obtained (Jörundsdottir et al., 2006). In this publication, 4,4´-DDE showed a more pronounced decrease of 16% (1971 – 2001) compared to BCPS. The authors conclude that a cautious interpretation has to be made for BCPS, as the sampling cycle was 5 years. Interestingly, the decreasing trend could not be confirmed by a second monitoring study, as the results from 2003 (Jörundsdóttir *et al*., 2008) showed, that the BCPS concentrations in eggs were increasing to 1100 ng/g l.w. (n=10, Table 33).

In total, 45 eggs have been analysed from year 1971 – 2003 (Jörundsdottir *et al.*, 2006 and 2008). For time trends, the quality of the study increases with the number of sampling years and long time trends are crucial to determine development of trends of environmental pollutants. Guillemot eggs from the Baltic Sea are suitable to investigate environmental contaminants and have been used for monitoring since 1968 (Miller *et al.*, 2014). This piscivorous birds include features like: high trophic feeding level, the ability to accumulate substance to detectable concentrations, the migration patterns of these birds are known. Guillemot do not migrate far from Stora Karlsö, and their contaminant concentrations are locally acquired. Due to this reason eggs can be assumed to be a rather "stable" matrix, this is also shown as the lipid content of eggs is consistently high (yearly mean for > 40 years, appr. 12%, Miller *et al.*, 2014). Guillemot nest in few colonies with high densities, making the colonial population very homogenous, additionally the variation in food is low, as they mostly feed on sprat and herring. The age of egg laying bird has been shown to have no effect on levels of contaminants in eggs (Jörundsdottir et al., 2009). Based on this, Guillemot eggs serve as an ideal matrix for long-term monitoring, this is also reflected by the low variation between the pooled samples from 1971 – 2003.

Table 33: BCPS and 4,4´- DDE levels in guillemot eggs and breast muscle tissue (1971 – 2003)

Species	Matrix	Range BCPS ng/g l.w.	BCPS[10] ng/g l.w.	4,4´DDE ng/g l.w.	Location	Year	Reference
Guillemot	replacement egg[11] (n=5)	1100 - 2600	1400	950	Stora Karlsö, island in the Baltic Sea, Sweden	1971	Jörundsdóttir *et al*., 2006
Guillemot	replacement egg (n=5)	1100 - 1900	1500	560	Stora Karlsö, island in the Baltic Sea, Sweden	1976	Jörundsdóttir *et al.,* 2006
Guillemot	replacement egg (n=5)	810 – 1500	1200	87	Stora Karlsö, island in the Baltic Sea, Sweden	1981	Jörundsdóttir *et al.,* 2006
Guillemot	replacement egg (n=5)	900 – 1400	1100	79	Stora Karlsö, island in the Baltic Sea, Sweden	1986	Jörundsdóttir *et al.,* 2006
Guillemot	Breast muscle	--	*1600*[+]*; 1900*[+]	--	Stora Karlsö, island in the Baltic Sea, Sweden	1989	Norström *et al.,* 2004
Guillemot	replacement egg (n=5)	780 – 1200	900	36	Stora Karlsö, island in the Baltic Sea, Sweden	1991	Jörundsdóttir *et al.,* 2006
Guillemot	replacement egg (n=5)	770 – 980	890	14	Stora Karlsö, island in the Baltic Sea, Sweden	1996	Jörundsdóttir *et al*., 2006
Guillemot	replacement egg (n=5)	760 - 1400	1000	10	Stora Karlsö, island in the Baltic Sea, Sweden	2001	Jörundsdóttir *et al*., 2006
Guillemot	replacement egg (n=10)	850 - 1300	1100	--	Stora Karlsö, island in the Baltic Sea, Sweden	2003	Jörundsdóttir et *al*., 2008
Summary Guillemot	replacement egg (n=45)	760 - 2600 890 – 1100[12]	1118[13]	not determined	Stora Karlsö, island in the Baltic Sea, Sweden	1971 - 2003	Jörundsdóttir *et al.,* 2006 and 2008

+ pooled sample from 5 individuals

[10] Geometric mean

[11] The guillemot lays one egg but a lost egg can be replaced, in 14-16 days. This egg is called replacement egg (Hedgren *et* al., 1980). There are significantly higher amounts of organohalogen compounds in the replacement eggs, probably due to lower fat status of the maternal bird (Bignert *et al.,* 1995). The lipids in eggs is approximately 13% (Jörundsdóttir *et* al., 2009).

[12] Range of geometric mean values.

[13] Geometric mean calculated from all geometric BCPS egg concentrations, in total 45 eggs.

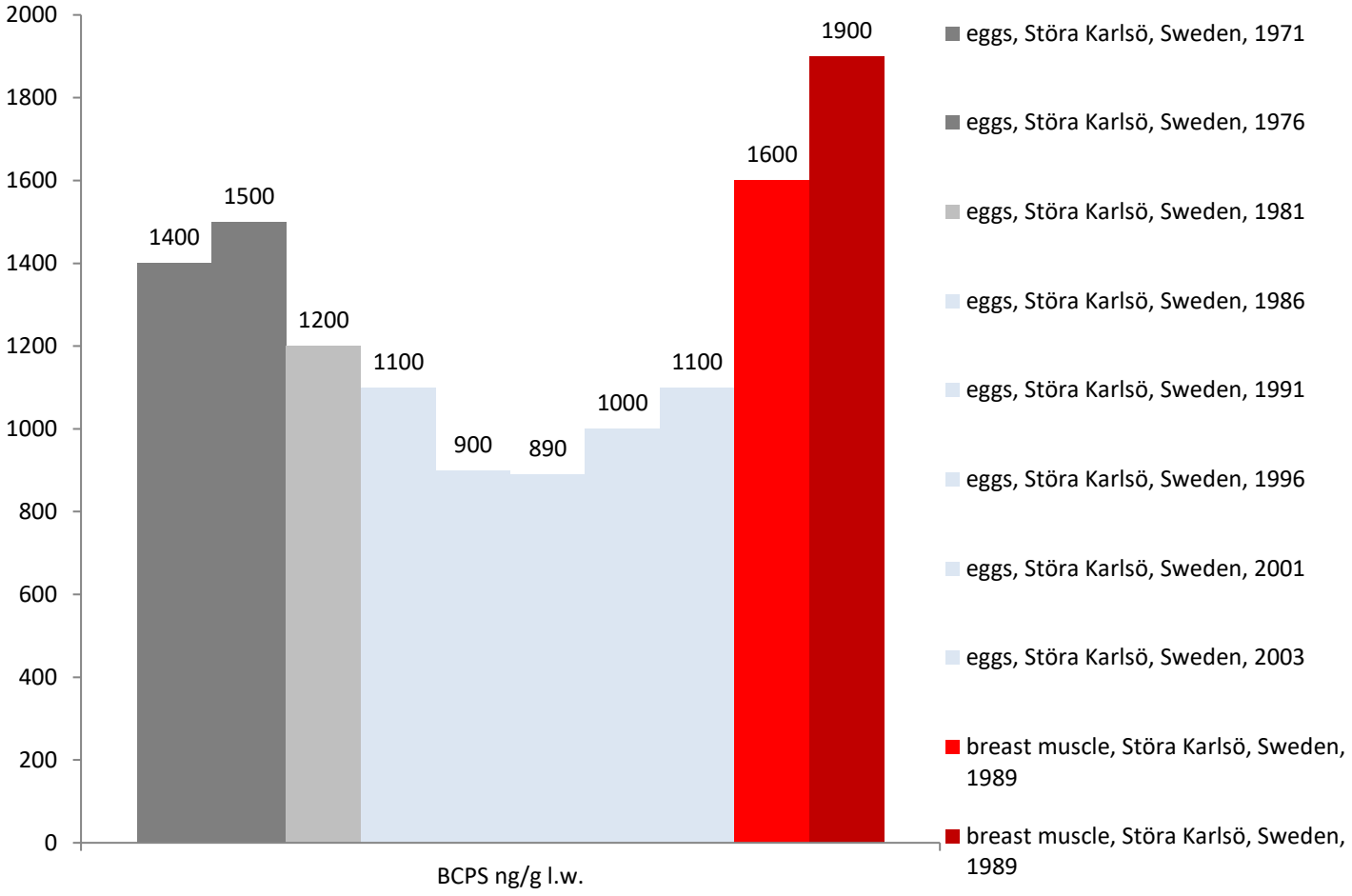


Figure 7: Levels of BCPS in guillemot eggs and breast muscle (1971 – 2003), sample location and dates are indicated in the legend (Source: Jörundsdóttir *et* al, 2006 and 2008; Norström *et* al., 2004)

Jörundsdóttir *et al.*, 2008

The study investigated organohalogen pollutants in biota. Eggs of guillemot (*Uria aalgae*) were used as relevant matrices. BCPS was found at very low levels (< 13 ng/g l.w.) in eggs from Iceland, Faroe Islands, Norway compared to the levels found in the Baltic region. BCPS concentration is around 150-fold lower in the North Atlantic compared to concentrations found in the Baltic region. In comparison, 4,4´-DDE is 15-fold higher in the Baltic than in the North Atlantic. The author speculated that there are no local sources of contamination in Iceland, Faroe Islands, Norway locations compared to the Baltic region. The BCPS contamination in the Baltic Sea will not reach the Faroe Islands or Iceland, both because of slow transition of the water body in the Baltic Sea and the main surface currents towards Iceland and the Faroe Island is the Modified North Atlantic Water current, originating in the Oceanic Source Region, west of the Middle Atlantic Ridge (Hansen and Østerhus 2000). The concentrations found in the North Atlantic are therefore probably transferred via long-range transport from sources in Europe or North America.

Millow *et al.*, 2015

A non-targeted analytical approach (NTA) was used to identify halogenated organic compounds in California Black skimmer (*Rynchops niger*) eggs. Black skimmer are piscivorous seabirds which live up to 20 years. Egg sampling took place from June to August 2011 from the Salt Works colony. Birds lay 1-4 eggs in a shallow nest on the ground. In 3 of 4 analysed eggs BCPS was detected, but not further quantified.

Hornek-Gausterer *et al.*, 2021

In total, eleven cormorants were investigated for the presence of BCPS (ref. to Table 34, Table 35), five individuals from 2001 – 2005 (breast muscle), and six individuals from 2019 (breast muscle and liver). The sampling location was Austria. Cormorants feed on any fish that they can feasibly catch and swallow. The diet of cormorants has been investigated in more detail e.g., in Lyach *et* al., 2018. The cormorants had a body mass of 2.04 – 3.3 kg. BCPS levels in cormorants´ breast muscle from 2019 were in the range of 4.3 to 40 ng/g fat (arithmetic mean: 16.3 ng/g fat, n=6) and 28 to 86 ng/g fat (arithmetic mean: 53.5 ng/g fat, n=6) in liver samples. The BCPS concentrations in liver were 1.2 – 17.9-fold higher (mean: 6.7) than in breast muscle tissue, except for one individual with a liver to breast muscle ratio of 0.9.

The arithmetic mean BCPS breast muscle concentration in sub-adult cormorants was 8.85 ng/g fat (n=5) and the arithmetic mean concentration in adults revealed BCPS breast muscle concentrations of 17.9 ng/g fat (n=6), indicating an increase in BCPS concentration in breast muscle with age (time period: 2001 – 2019). Calculating the time periods separately adult median BCPS levels were higher than in sub-adults. However, due to the low sample size and as the results are not statistically significant, no final statement can be made.

Based on the study of Hornek–Gausterer *et* al. (2021) the BCPS concentration was higher in fish-eating birds (breast muscle arithmetic mean: 16.3 ng/g fat, n=6, sampling 2019) than in fish (mean: 4.9 ng/g fat, n = 8, sampling 2019). This might indicate that BCPS biomagnifies. A biomagnification factor (BMF) is the ratio of the concentration in the predator divided by the concentration in the prey, in this case the field $BMF_{\text{cormorant breast muscle, whole fish}}$ values is 3.2, which is higher than 1 and can therefore be considered as an indication for very high bioaccumulation (ECHA, 2017). While fish and bird samples do not originate from the same location and the same time point, the calculated BMF values are plausible because one cormorant had ingested fish with a BCPS level of 5.5 ng/g fat, whereas the BCPS level in the cormorant breast muscle was 23 ng/g fat, suggesting a BMF of 4.2.

No information is available about the cormorants' individuals' migration route, length of stay at various stop-over sites or arrival date in Austria. Depending on the overall European weather and local wintering conditions, cormorants may stay in Austria or will move onward using all kind of open surface water bodies as wintering grounds along their migration route (e.g., van Eerden *et* al., 2011). Food consumption may have taken place anywhere along the migration route as well as in the vicinity of different breeding areas.

Further, although the sample size was rather small, the results obtained so far (mean values of BCPS in bird muscles) showed an increasing time trend from 8.9 (2001- 2005) to 16 ng/g fat (2019).

Table 34: Analytical results of BCPS levels in cormorants (*Phalacrocorax carbo sinensis*) breast muscle samples (2001 – 2005), Austria, Hornek-Gausterer *et al.*, 2021)

Species	Age / sex	Weight [kg]	Trophic level	BCPS [ng/fat]	Lipid content [%]	LOQ [ng/fat]	LOD [ng/fat]	Year
P. carbo siensis	Young male	2.48	high	8.5	3.5	2.9	1.3	2001
P. carbo siensis	Adult, female	2.04	high	19	4.4	2.3	1.2	2001
P. carbo siensis	Young, male	2.53	high	4.7	2.4	5.1	2.6	2003
P. carbo siensis	Young, male	3.23	high	2.8	2.2	4.7	2.2	2005
P. carbo siensis	Adult, male	2.32	high	9.5	2.7	17	7.4	2005

Table 35: Analytical results of BCPS levels in Cormorants (*Phalacrocorax carbo sinensis*) breast muscle and liver samples (2019, Austria, Hornek-Gausterer *et al.*, 2021)

Species	Age	Weight [kg]	Trophic level	Breast muscle BCPS [ng/fat]	Liver BCPS [ng/fat]	Liver / Breast muscle	Breast muscle Lipid content [%]	Liver Lipid content [%]	Breast muscle LOQ [ng/fat]	Breast muscle LOD [ng/fat]	Liver LOQ [ng/fat]	Liver LOD [ng/fat]	Year
P. carbo siensis	adult	3.3	high	40	37	0.9	3.8	4.1	3.4	1.7	2.3	1.1	2019
P. carbo siensis	subadult	2.4	high	23	28	1.2	4.3	4	5.6	2.8	2	1	2019
P. carbo siensis	subadult	2.5	high	4.3	39	9.1	3.7	4.1	2.5	1.3	2.2	1.1	2019
P. carbo siensis	adult	2.6	high	4.8	86	17.9	5.2	4.1	2.3	1.2	5.4	2.7	2019
P. carbo siensis	adult	2.4	high	16	56	3.5	3.1	3.2	6.4	3.2	3.5	1.6	2019
P. carbo siensis	subadult	2.3	high	9.8	75	7.6	2.6	2.6	4	2	5.5	2.6	2019

Summary biomonitoring in birds

Most of the investigated samples (eggs, breast muscles, liver, plasma) from birds (*Haliaeetus albicilla*, *Uria aalgae*, *Rynchops niger, Phalacrocorax carbo carbo, Larus hyperboreus*) detected BCPS, thus showing widespread bioavailability in birds from different regions (Sweden; California USA; Iceland; Faroe Islands; Norway; Austria) including the Norwegian Arctic (Helander *et* al., 2002; Verreault *et al.,* 2005; Jörundsdóttir *et al*., 2006; Jörundsdóttir *et al*., 2008; Jörundsdóttir 2009; Norström *et al*., 2004; Millow *et al.,* 2015; Hornek-Gausterer *et al.,* 2021).

In the time period 1971 – 1991, BCPS was detected from a non-detectable level up to highest values of 610 ng/g in the eggs of white tail sea eagle (Helander *et al*., 2002).

From all biota samples analysed so far, the BCPS levels detected were highest in guillemot (*Uria aalgae*) eggs from the island Störa Karlsö, Sweden (760 – 2600 ng/g l.w., mean: 1136, period: 1971 – 2003). BCPS was found at an at least constant level in Guillemot eggs from 1971 to 2003 (Jörundsdóttir *et* al., 2006 and Jörundsdóttir *et* al., 2008). Birds compared to other investigated biota showed the highest body burden of BCPS, possible related to species specific metabolic competence, however, more research would be needed to draw a definitive conclusion.

The concentrations of BCPS in herring between 1998 and 2008 were in the range between 17 – 58 ng/g l.w. (n=25), concentration stays in herring at a constant level of around 30 ng/g l.w. obtained from Sweden, Poland and Lithuania (Norström *et* al., 2004 and 2010). It is therefore reasonable to take the fish level of around 30 ng/g l.w. and to compare it with the concentrations found in guillemot breast muscle (1600 ng/g and 1900 ng/g l.w. (1989) from the Baltic region. The concentration of BCPS increases as the trophic level increases. Calculating a field BMF results in field BMF values of 53 to 63 for herring and Guillemot.

In a recent study from 2019 (Hornek-Gausterer *et al.,* 2021) eleven cormorants were investigated for the level of BCPS, five individuals from 2001 – 2005 (breast muscle), and six individuals from 2019 (breast muscle and liver). Levels found were in all cases above LOD. These data from breast muscle BCPS levels in cormorants (*Phalacrocorax carbo carbo*) in Austria show, that the concentration in 2019 is lower (4.3 – 40 ng/g fat, mean: 16 ng/g fat, n=6) compared to the breast muscle concentration from guillemot obtained in Störa Karlsö, Sweden (up to 1900 ng/g l.w.; Norström *et al.*, 2004), but underpin the results from guillemot eggs from Jörundsdóttir *et al.* (2006; 2008) in the sense, that, although the sample size of the cormorants was small, no decreasing trend in the BCPS level was obtained. The results showed an increasing trend in cormorant´s breast muscle from 8.9 (2001- 2005) to 16 ng/g fat (2019). Depending on the weather and local wintering conditions, cormorants may stay in Austria or will move onward using all kind of open surface water bodies as wintering grounds along their migration route (e.g., van Eerden *et* al., 2011). The individual´s migration route is unknown, and food could have been taken up along the way. The arithmetic mean BCPS concentration in sub-adult cormorants was 8.85 ng/g fat and the arithmetic mean concentration in adults revealed BCPS concentrations of 17.9 ng/g fat, indicating an increase in BCPS concentration in breast muscle with age and accumulation over lifetime. But due to the low sample size and as the results are not statistically significant, no final conclusion can be drawn (Hornek-Gausterer *et al.,* 2021). In 2019, the BCPS concentration was higher in fish-eating cormorants (breast muscle arithmetic mean: 16.3 ng/g fat, n=6) than in fish (mean: 4.9 ng/g fat, n = 8), which indicates that BCPS biomagnifies. In this case the field $BMF_{cormorant\ breast\ muscle,\ whole\ fish}$ value is 3.2, which is significantly higher than 1 and can therefore be considered as an indication for very high bioaccumulation (ECHA, 2017). Further when comparing the whole fish concentration with liver this would yield a field $BMF_{cormorant\ liver,\ whole\ fish}$ of 10.9. One cormorant had ingested fish, with a BCPS level of 5.5 ng/g fat, the BCPS level in the cormorant breast muscle was 23 ng/g fat, suggesting a BMF of 4.2.

3.4.3.3 Biomonitoring – Grey seals (*Haliochoerus grypus*)

Grey seals are a good indicator species to measure environmental pollutants due to their position in the food web and their long life. Grey seals are present mainly in the north and centre of the Swedish east coast. Liver, lung, and blubber from Swedish grey seals were investigated for the presence of BCPS (Figure 8, Olsson and Bergmann, 1995; Larsson *et al*., 2004; Norström *et al*., 2004).

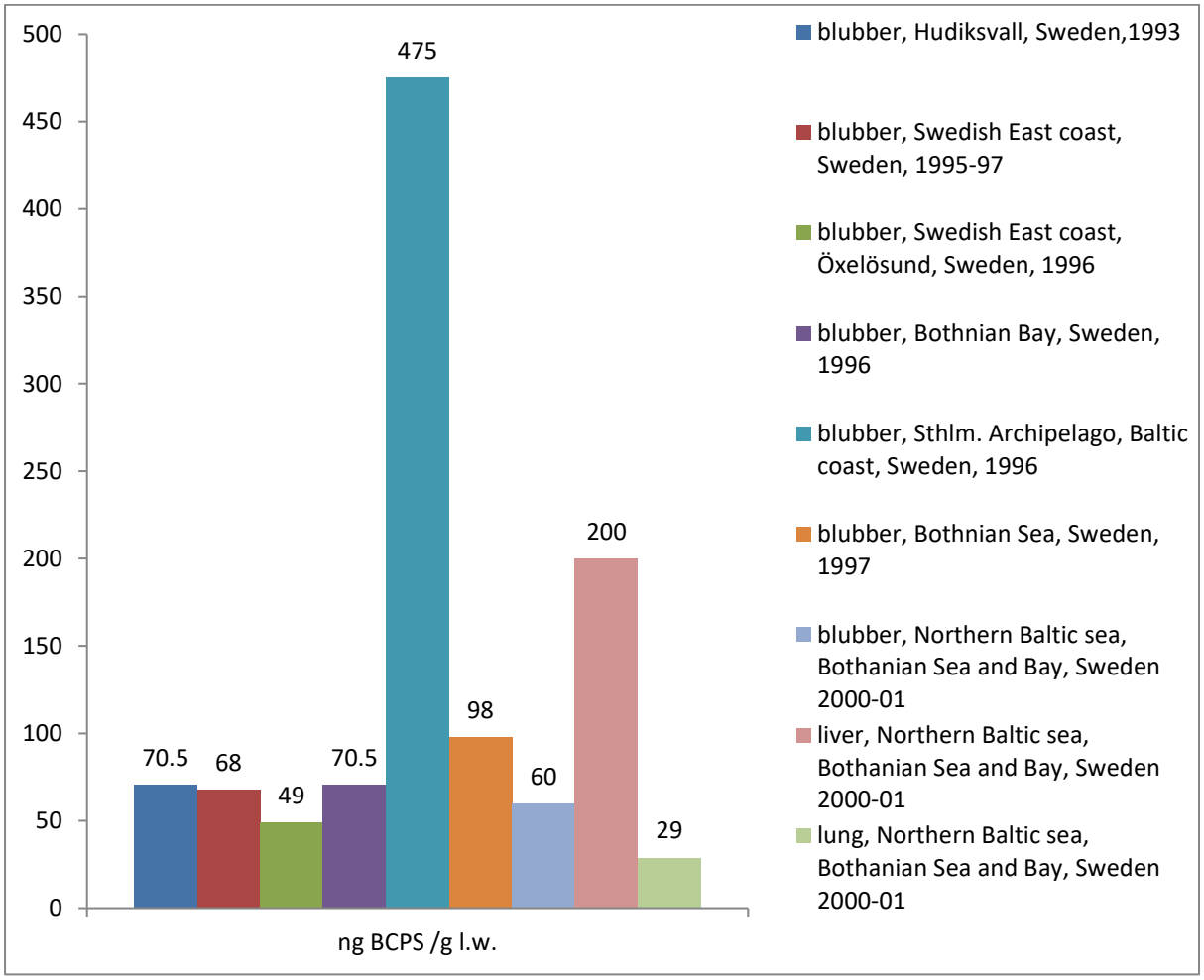


Figure 8: BCPS concentration in grey seals, blubber, liver and lung. Concentrations are mean/median values (n=10), except for the conc. of 70.5 ng BCPS/g l.w. (n=2); other values represent measured values of one individual seal, for details refer to Annex I.

Olsson and Bergmann, 1995

In the blubber of three individual grey seals BCPS was detected at levels between 53-88 ng/g (mean: 70.5; n=2) (sampling year: 1993, location: Hudiksvall Sweden).

Larsson *et al.,* 2004

In a study performed by Larsson *et* al. (2004) BCPS was determined in liver, lung and blubber (adipose tissue) of grey seals from the northern part of the Baltic Sea (Bothanian Sea and Bay). Ten healthy seals were accidently caught in fishing nets (2 males and 8 females) during 2000 and 2001. Age of the seals was between 6 to 16 years. Duplicate samples from each tissue were analysed by ECNI-GC-MS after homogenisation in n-hexane/acetone, extraction with n-hexane/MTBE and clean-up by GPC. LOQ (BCPS) = 3.5 ng/g l.w. which was calculated as five times the mean background amount (0.7 ng) in the

blank solvent samples. Detected BCPS levels were unaffected by age, size and gender. The highest concentrations of BCPS were detected in the liver with a maximum of 700 ng/g l.w. (median: 200 ng/g l.w.), whereas in the blubber (max. of 240 ng/g l.w., median: 60 ng/g l.w.) and in the lung (max. 98 ng/g l.w. and median of 29 ng/g l.w.) the concentrations were lower. The difference between the concentrations in the different tissues was significant. Averaged concentrations are presented in Annex I. BCPS showed a high selective retention to the liver (Larsson *et* al., 2004). The reason for the specific retention may be due to protein binding behaviour of BCPS and the presence of the sulfone group in the substance which is crucial for such binding (Larsson *et* al. 2004). Protein binding was also suggested by Larsen *et* al. 1991. The authors concluded that hepatotoxicity of BCPS is of concern in the light of the high accumulation in the liver in grey seals.

Norström *et al.*, 2004

In the blubber of grey seals (n=5) BCPS was detected in concentrations between 49 ng/g l.w. (Swedish East coast, Öxelösund, Sweden; sampling: 1996) to 98 ng/g l.w. (Bothnian Sea, Sweden; sampling: 1997). Only one individual had very high concentrations of 475 ng/g l.w, but this animal was considered as unhealthy as the lipid content was very low (only 32%) in contrast to healthy individuals (around 90% lipids), also the 4,4´-DDE concentration was very high in this individual. The highest concentrations of BCPS were detected in the oldest individual (10 years) containing 98 ng/g l.w. (Bothanian Sea, Sweden, 1997).

Summary – biomonitoring in grey seals

Grey seals are in general highly contaminated due to their food and their long life, but this could apply to many other species at top of the food chain as well. Grey seals are present mainly in the north and centre of the Swedish east coast and feed mostly on fish. Monitoring data indicate that BCPS concentration may increase with age, however in Larsson et al., BCPS levels were unaffected by age, size and gender. Additionally, the health status of seals seemed to affect the BCPS levels detected in the blubber of seals, as shown for an unhealthy individual where the blubber concentration was higher (480 ng/g l.w.) compared to healthy individuals (range: 49 – 98 ng/g l.w.; Norström *et* al., 2004), but it might be also that the health was affected because of the high contaminant concentrations. Details on the effects were not mentioned in the publication. Highest concentration occurred in liver (median: 200 ng/g l.w.; range 55 – 700 ng/g l.w.; n=10), followed by blubber (median: 60 ng/g l.w.; range: 41 – 240 ng/g l.w.; n=10). However, not all organs were investigated (e.g., brain) and sample size was small.

3.4.3.4 Biomonitoring - other organisms

Top predators and their prey from LIFE APEX project[14]

Under this project additional species in several countries (DE, UK, NL, S) were investigated for BCPS as depicted in Table 36. BCPS was detected in liver of top predators (otters) at levels from 1.1 – 7.2 ng/g wet weight (<LOD – 236 ng/g fat).

Table 36: BCPS concentration in various biota

Sample description	BCPS concentration (ng/g wet weight)	Country	Sampling year	water content (%)	lipid content (%)	BCPS (ng/g fat)
Bream muscle from Rhine Bimmen	2.8	Germany	2015	79.8	2.9	95.3
Eelpout muscle from Baltic Sea, Darßer Ort	< 0.9 (LOQ=0.9)	Germany	2015	80.6	1.2	<74 (LOQ)
Otter liver from North Wales	< 0.9 (LOQ=0.9)	United Kingdom	2017	69.6	1.7	<54 (LOQ)
Otter liver from Overjissel	5.2	Netherlands	2018	67.2	2.5	206
Otter liver from Groningen	1.1	Netherlands	2018	69.3	1.5	75
Otter liver from Harich, Friesland province	7.2	Netherlands	2018	71.4	3.7	194
Bream muscle pooled from Zuid - Holland	< 0.9 (LOQ=0.9)	Netherlands	2019	71.9	1.8	50.9 (<LOQ)
Buzzard liver pooled from Mecklenburg Vorpommern	< 0.9 (LOQ=0.9)	Germany	2015, 2016, 2018	72.1	3.4	<26.6 (LOQ)
Otter liver pooled from Västmanland/Örebro	< 0.9 (LOQ=0.9)	Sweden	2015, 2017	68.1	3.0	<29.9 (LOQ)
Otter liver from Plön	1.2	Germany	2017	66.6	0.5	236.1

In Germany, bream muscle (*Abramis brama*) sampled (sampling year: 1997) at 4 different locations in two German rivers (Elbe and Rhein) showed BCPS concentrations with up to 10-fold difference between the sampling sites (3.4 and 34 ng/g l.w) cited in Norström *et al.* (2004 and 2010). In 2015, 95.3 ng/g fat was measured in Bream muscle samples from the river Rhine. Comparing these values from 1997 and 2015 indicates a 2.8-fold increase. It is acknowledged that the sample size is low.

3.4.3.4 Biomonitoring – humans

Two studies (Ellerichmann *et al.,* 1998; Plaßmann *et al*., 2016) analysing BCPS in human

[14] https://lifeapex.eu/

matrices (liver, blood) are available and summarised in

Table **37**.

BCPS was detected in human liver samples (Ellerichmann *et al.,* 1998), in which also two types of PCBs (3-132, 3-149) and MeSO2-DEE were found. The samples (n=6) were obtained from a forensic institute. The individuals passed away because of accidents or heart-failures.

In the post-mortem analysis a quantification of the BCPS content has not been carried out, however, data indicate that the BCPS peak was about five times higher compared to $MeSO_2$-PCBs. BCPS concentration is estimated to be between 2-40 ng/g lipid compared with measured PCB content. Authors noted that both laboratories involved encountered considerable background level of BCPS in previous investigations. Thus, special caution has been applied in the study to verify the content of BCPS by using authentic standard compound and by "blank measurements".

In a non-target screening analysis (Plaßmann *et* al., 2016) BCPS was not found in human blood samples (n=8, lowest detectable concentration 2 ng/mL, which is in concordance with a rat toxicokinetic study of Mathews *et al.* (1996) demonstrating that BCPS levels in blood are low and that the substance is distributed into tissues.

Table 37: Human biomonitoring data

Method	Results	Remark	Reference
Six human post-mortem liver and lung samples (3 males, 3 females), the samples were obtained from a forensic medicine institute after the persons passed away (accidents, heart failure); the samples were stored at -70°C for the first week, and at –20°C until sample preparation. Analysis of MeSO2-PCBs, 3-MeSO2-DDE and BCPS GC/MS	BCPS was found in all liver samples, not in lung samples Characterisation of liver samples: Age of male/female (34-92yrs), liver weight (between 1260g and 3005g) and lipid weight (between 71g and 823 g)	Authors noted that both laboratories involved encountered considerable background level of BCPS in previous studies. Thus, special caution has been applied in the present investigation to verify the content of BCPS (blank, standard compound).	Ellerichmann *et al*., 1998

Development of screening methods in biological samples (human blood and urine) Analysis of human blood and urine samples (n=8) GC/MS	BCPS has not been identified in human blood. Several substances could be (tentatively) identified, among these were UV-filters like benzophenone-3 and several benzophenone metabolites, organophosphate flame retardants like triethylphosphate, 4-hydroxy-chlorothalonil and a bromo-quinolinole.	Screening study in which BCPS has been included in the screening list of contaminants in human blood (not in urine). BCPS is rapidly distributed from blood into lipid rich tissues. Blood is not the most appropriate surrogate to determine the presence of BCPS in humans.	Plaßmann et *al.,* 2016

It is stated in the PhD thesis of Norström (Norström, 2006), that in the study of Hovander et al. (Hovander *et* al., 2006) BCPS was detected as significant contaminant in participants' blood in Slovakia. The data are not published or scientifically peer-reviewed and thus the validity of the information could not be verified.

To summarise, there is evidence that BCPS is detected also in humans. The sampling size of the published study where BCPS is found post mortem in the liver is low (n=6).

3.4.3.5 Field data and biomagnification (field biomagnification factor, BMF)

According to the ECHA Guidance (ECHA, 2017a) field biomagnification refers to accumulation via the food chain. It may be defined as an increase in the (fat-adjusted) internal concentration of a substance in organisms at succeeding trophic levels in a food chain. The biomagnification potential can be expressed as either a trophic magnification factor (TMF) or a biomagnification factor (BMF), which is the ratio of the concentration in the predator and the concentration in the prey. According to ECHA (2017) a BMF value significantly higher than 1 can be considered as an indication for very high bioaccumulation. Further it is mentioned that to be able to compare BMF values in a direct and objective manner, they should, as far as possible, be lipid normalised for the assessment of substances that partition into lipids in order to account for differences in lipid content between prey and predator.

Concentrations in prey and predators are based on lipid weight and can be used directly from the original studies (ref. to Annex I), BMF values are summarised in Table 38.

Table 38: Calculated field biomagnification factors

Organism / matrices	**BCPS concentration**	**Year**	**Country**	**Field BMF**	**References of concentration in biota**
Baltic herring lateral muscle; Guillemots breast muscle	~ 30 ng/g l.w. (n=25) 1600 ng/g l.w. (n=5) 1900 ng/g l.w. (n=5)	1998-2008 1989	S (Landsort), PL, Lithuania S (St Karlsö)	Fish, bird 53 - 63	Norström *et al*., 2004 and 2010

Baltic herring lateral muscle; Guillemot eggs (surrogate for muscle)	~ 30 ng/g l.w. (n=25) 1118 ng/g l.w. (n=45) geometric mean 760 – 2600 ng/g l.w. (n=45) min – max	1998 - 2008 1971 - 2003	S, PL, Lithuania S (St Karlsö)	Fish, bird 37 25 - 86	Norström *et al.*, 2004; Jörunddsdottir *et al*., 2006 and 2008
freshwater fish, whole fish; Cormorants breast muscle Cormorant liver	mean*: 4.9 ng/g fat (n=8) (individual: 5.5 ng/g fat) mean*: 16.3 ng/g fat (n=6) (individual: 23 ng/g fat) mean*: 53.5 ng/g fat (n=6)	2019 2019 2019	AT Danube, 2 locations) AT (Lower Austria)	Fish, bird 3.3 – 4.2 10.9	Hornek-Gausterer *et al.,* 2021
Baltic herring lateral muscle Grey Seals liver, blubber	~ 30 ng/g l.w. (n=25) liver**: 200 ng/g l.w.; (n=10) blubber**: 60 ng/g l.w. (n=10) blubber: 49 – 98 ng/g l.w. (n=3)	1998-2008 2000-2001 1997	S, PL, Lithuania S S S	Fish, seals 6.7 2 1.6 – 3.2	Norström *et al*., 2004 and 2010; Larrson *et al*., 2004 Norström *et al*., 2004

*artithmetic, **median

Field BMF values (fish, bird)

Fish, guillemots: The concentrations of BCPS in herring between 1998 and 2008 were in the range between 17 – 58 ng/g l.w., concentration seems to stay at a constant level of around 30 ng/g l.w. in herring obtained from Sweden, Poland and Lithuania (Norström *et* al., 2004 and 2010). The concentration in herring muscle in 1998 was between 29-31 ng/g l.w. (Norström *et* al., 2004, Sweden, n=20). There was no obvious trend between country or sampling location (Norström *et* al., 2010). Therefore, it seems reasonable to take the fish muscle BCPS level of around 30 ng/g l.w. and to compare it with the BCPS concentrations found in guillemot breast muscle of 1600 ng/g l.w. (n=5) and 1900 ng/g l.w. (n=5; 1989) from the Baltic region (Norström *et* al., 2004). When calculating field BMF values (ref. to Table 38), the concentration in the predator is divided by the concentration in the prey, which results in field $BMF_{guillemot\ breast\ muscle,\ herring\ muscle}$ of 53 to 63, showing biomagnification of BCPS over food chains. It needs to be noted, that location and time of sampling varied. However, based on the consistent measured levels in fish from the Baltic Sea over several years, it is reasonable to conclude that BCPS biomagnifies among food chains. Further support for biomagnification comes from avian eggs (Table 38), which are used as matrix to investigate contaminants, as its composition directly

reflects that of maternal tissues (e.g., Drouillard and Norstrom, 2001). As mentioned within the Drouillard and Norstrom (2001) publication egg-to-maternal tissue concentration is often less than one (typically in the order of 0.3 – 0.7), but depend on fat reserves of the female, clutch size and physico-chemical factors of the substances. Based on the analysed concentration in eggs, the BCPS concentration in female's tissue such as muscle would have been very likely in the same order or even higher. In total, 45 eggs have been analysed between 1971 – 2003, showing a geometric mean BCPS concentration of 1118 ng/g l.w. using the values from Jörundsdóttir *et* al., 2006 and 2008. Herring was taken between 1998 – 2008, showing a concentration of around 30 ng/g l.w. (Norström *et* al., 2004 and 2010), this would yield a field $BMF_{guillemot\ eggs,\ herring\ muscle}$ of 37.

Fish, cormorants: The BCPS concentration was higher in fish-eating cormorants (breast muscle arithmetic mean: 16.3 ng/g fat, n=6) than in fish (mean whole fish: 4.9 ng/g fat, n = 8) in samples dated in 2019, which indicates that BCPS biomagnifies. In this case the field $BMF_{cormorant\ breast\ muscle,\ whole\ fish}$ value is 3.2, which is significantly higher than 1 and can therefore be considered as an indication for very high bioaccumulation (ECHA, 2017). Further when comparing the whole fish concentration with liver this would yield a field $BMF_{cormorant\ liver,\ whole\ fish}$ of 10.9. One cormorant had ingested fish, with a BCPS level of 5.5 ng/g fat, the BCPS level in the cormorant breast muscle was 23 ng/g fat, suggesting a BMF of 4.2.

Field BMF values (herring, seals)

Fish, grey seals: The concentrations of BCPS in herring between 1998 and 2008 were in the range between 17 – 58 ng/g l.w., concentration stays in herring at a certain level of around 30 ng/g l.w. obtained from Sweden, Poland and Lithuania (Norström *et* al., 2004 and 2010). It is therefore reasonable to take the fish level of around 30 ng/g l.w. and to compare it with the concentrations found in liver and blubber from grey seals (liver: 200 ng/g and blubber: 60 ng/g) from the Baltic region. The field BMF values results in $BMF_{herring\ muscle,\ seals\ liver}$ values of 6.7 and a field $BMF_{herring\ muscle,\ seals\ blubber}$ of 2. However, location and time of sampling varied but based on the consistent measured levels in fish from the Baltic Sea over several years BCPS biomagnifies.

Discussion on uncertainties of BMF values

Ideally, field BMFs should be based on whole-body concentrations measured in all organisms in the food web or to compare the same tissue (organ) in prey and predator.

BMF values based on same tissue

BCPS concentration from guillemot breast muscle and Baltic herring lateral muscle were used to calculate the field BMF value of 53-56. From the same location not only breast muscle, but also 45 guillemot eggs have been analysed between 1971 and 2003 (Jörundsdóttir et al., 2006 and 2008, Table 38). BCPS concentration in eggs ranged from 760 – 2600 ng/g l.w., showing a geometric mean BCPS concentration of 1118 ng/g l.w. The chemical composition of eggs directly reflects that of maternal tissues (e.g., Drouillard and Norstrom, 2001). As mentioned within the Drouillard and Norstrom, 2001 publication egg-to-maternal tissue concentration is often less than one (typically in the order of 0.3 – 0.7), but depends on fat reserves of the female, clutch size and physico-chemical factors of the substances. Based on the analysed concentration in eggs, the BCPS concentration in female's tissue such as muscle would have been very likely in the same order or even higher. So, despite the limited number of breast muscle samples from guillemot (n=5 for each value), concentrations in 45 eggs from the same location substantiate the conclusion that the concentration of BCPS increases as the trophic level increases. Further if eggs are used as "surrogate" for female tissue concentration and compared to Baltic herring this would yield a $BMF_{guillemot\ eggs,\ herring}$ of 37. Both field BMF values are >1.

BMF values using different tissues

For small organisms at lower trophic levels whole-body concentrations are feasible, but not for large organisms at higher trophic levels like birds and seals. So, for large biota typically specific tissues, blood or organs are used to measure contaminants. In the study from Hornek-Gausterer *et* al. (2021) whole fish concentrations were determined by homogenising the whole fish before BCPS analysis. Fish-eating birds like cormorants, but also seals feed on whole fish, and not like polar bears, which show preference for certain tissues like blubber (Franklin, 2016). For cormorants and seals whole-body concentrations are not available, but breast muscle and liver concentrations are available for cormorants and liver, blubber and lung are available for seals.

Extrapolations of measured BCPS concentration in tissues to whole-body concentrations introduce uncertainties and were avoided. Jürgens *et* al. (2013) discussed the differences in contaminant content in whole fish versus tissues and pointed out that hydrophobic substances tended to be higher in liver than in the rest of fish, but the differences disappeared when results were lipid normalised, this might be true for other organisms than fish as well.

Franklin (2016) notes that BMF values for liver are not a good measure for the whole body BMF, as the BMF might be higher or lower. For PFAS the author noted that liver-based BMFs are systematically lower than values on muscle or whole-body concentrations, as liver often represents less than 50% of the total body burdens (Franklin, 2016). BCPS behaves differently to PFAS mentioned. For BCPS it is reasonable to assume a more hydrophobic mode for bioaccumulation. In this case, taking whole fish and cormorant breast muscle or liver BCPS concentrations, the calculated BMF value results are 3.3 and 10.9 (Table 38), respectively. Using seals liver and herring, the calculated BMF value is 6.7.

In grey seals, the highest concentration was found in liver (200 ng/g l.w.), followed by blubber (60 ng/g l.w.) and lung (29 ng/g l.w.) (Larsson *et al*., 2004). The BMF values using Baltic herring and grey seals liver and blubber are higher for liver (6.7) than in blubber (1.6 – 3.2).

BMF values using migratory birds

Migratory birds can take up contaminants from different locations. Cormorants in Austria may stay or move onwards using all kinds of open surface water bodies as wintering grounds along their migration route. To get knowledge on their individual flay-way-pattern, species can be ring recovered or get a transmitter. Both measures are time-consuming and also resource-intensive and are not regularly performed.

In the study of Hornek-Gausterer et al. (2021) four birds out of the total sample size analyzed have been ringed as nestlings in their breeding colonies (1x Denmark, 2x Finland, 1x Sweden). Cormorants investigated have been shot in midwinter (January 2019) in Lower Austria, but there is no further information available about the individuals' migration routes, length of stay on various stop-over sites or arrival date in Austria.

However, some build roosting colonies and are stationary in Austria (Steffens, 2011, and at Kormoran | Nationalpark Donau-Auen (donauauen.at)). Hence, food consumption - the relevant factor for a potential BCPS accumulation in birds - could have taken place anywhere along the migration route as well as in the vicinity of different breeding areas, also in Austria. To get a better picture of the contaminant levels in food, an overview of the various fish species along the migration route or surrounding the breeding colonies, would be beneficial. In the study of Hornek-Gausterer et al. (2021), various fish species from two locations (Danube) were taken, one location was in proximity of the assumed breeding colonies (Steffens, 2011, and at Kormoran | Nationalpark Donau-Auen

(donauauen.at)). However, it is not possible for ethical reasons to sample a large number of top predators and their prey.

3.4.3.6 BCPS in biota – due to former usage of DDT

The registrant(s) of BCPS assume (personal communication, 2018) that the contamination of the environment with BCPS mainly results from wide dispersive use of agricultural products, which were used in the past.

In these products BCPS has either been used intentionally as an insecticide on its own (Tarasenko, 1969) or has occurred as an impurity of such products. There is information that technical DDT contained up to 0.03 – 0.6% BCPS as an impurity originating from the technical production process (IARC, 1991). It is stated that BCPS was an impurity in 4-chlorobenzene sulphonamides insecticides. DDT was partly banned for agricultural uses in December 1978 via Directive 79/117/EEC[15] with exemptions for several minor uses (tree-nurseries, sugar beets, etc.) in EU Member States. This Directive confirmed and harmonised several initiatives already taken by Member States since 1972. The total ban for agricultural uses of DDT followed in March 1983 by Directive 83/131/EEC[16].

In the past, especially in the Baltic region, very high BCPS and DDT levels were found in birds' eggs. In studies conducted by Jörundsdottir *et* al., 2006 and 2008, 4,4´DDE together with BCPS was measured in birds' eggs from 1971 – 2003. Trend analysis showed that, 4,4,-DDT decreased from 950 ng/g l.w. (1971) to 87 ng/g l.w. (1981) and further to 10 ng/g l.w. (2001).

In contrast to this observation, from 1996 to 2003, BCPS increased from a high level of 890 ng/g l.w. in 1996 to 1000 ng/g l.w. in 2001 and to 1100 ng/g l.w. in 2003. This demonstrates that DDT has been successfully phased out in the late seventies in the Baltic region, as shown by decreasing trends in the marine food web.

While pesticide use might contribute to the body burden observed in bird species and eggs, the past BCPS levels in the Baltic region and the differences in the trends of BCPS and the DDT-metabolite (4,4-DDE) indicate, that the use as pesticide cannot be claimed as a major contamination source, as BCPS in contrast to the DDT metabolite remained at least constant over 30 years, even increased during the period of 1996 -2003 (Jörundsdóttir *et al*., 2006 and 2008).

These findings are confirmed by recent monitoring data from 2019 in Austrian fresh water, which showed that DDT (incl. its metabolites) could not be detected in Austrian freshwater fish samples, but BCPS levels were determined with maximum levels of 9.3 ng/g fat BCPS in all investigated specimens (Table 1, Hornek-Gausterer *et al*., 2021).

The arguments presented above, question the claims by the registrant(s) that the BCPS levels found in the environment might mainly originate from historical use of agricultural products containing BCPS. The measured levels of BCPS in biota could also reflect likely increases of the production of BCPS since 1971.

BCPS (DT_{50}, re-caclulated to 12°C: 2.3 -7.5 years in sediment, Unpublished study report, 2014) is less stable than DDT (half-life: 2-15 years in soil, multiple studies, US EPA 2000[17]) and 4,4´DDE, which is more persistent than DDT (ATSDR, 2022[18]). While DDT and its

[15] Council Directive 79/117/EEC of 21 December 1978 prohibiting the placing on the market and use of plant protection products containing certain active substances; repealed
[16] Commission Directive 83/131/EEC of 14 March 1983 amending the Annex to Council Directive 79/117/EEC prohibiting the placing on the market and use of plant protection products containing certain active substances; repealed
[17] http://npic.orst.edu/factsheets/archive/ddttech.pdf
[18] https://www.atsdr.cdc.gov/toxprofiles/tp35-c5.pdf

metabolites´ levels sharply decreased since phase out of DDT in Europe, no such trend was evident for BCPS in biota and WWTP (cf. chapter 3.2.4 field data). Therefore, it seems very unlikely that "historic" BCPS is the only source of the observed detections.

3.4.3.7 Benchmark approach: known POPs and BCPS

To support the identification of BCPS as vB, a benchmark approach was used to compare concentrations of known structurally unrelated persistent organic chemicals (POPs) with BCPS in biota. POPs in the benchmark approach, which are proven to fulfil the vB criteria were identified by the OECD tool[19] to model the long-range transport potential. Chemicals behaving similar to BCPS (e.g., α-HCH among others) were used as reference chemicals. The concentrations in biota were extracted for these reference chemicals from publications and respective POP risk profiles available at the Stockholm Convention Website[20]. Concentrations of known POPs were compared to concentrations of BCPS in respective biota.

Table 39: Benchmark approach known POPS and BCPS

Organism (tissue) (No.ind. n)	Reference & Location (sampling years)	POPs Substance Average (range)	Organism (tissue) (No.ind. n)	Reference & Location (sampling years)	BCPS Average (range)
Marine mammals: Seals					
Grey Seal (maternal blubber) (n=10)	Sørmo et al. 2003. Gulf of St. Lawrence, Canada (1995)	α-HCH: 39 (24-73) ng/g lw	Grey Seal (blubber) (n=8)	Norström *et al.*, 2004 Sweden (1995-1997)	71 (49-98) ng/g lw 475 ng/g lw (unhealthy individual)
Grey Seal (pub blubber) (n=10)	Sørmo et al. 2003. Gulf of St. Lawrence, Canada (1995)	α-HCH: 33 (12-58) ng/g lw	Grey Seal (blubber) (n=10)	Larsson *et al.*, 2004 Sweden (2000-2001)	(41-240) ng/g lw
Elephants Seals (blubber)[21] Adult males Adult females Juveniles Pups	Miranda-Filho et al. 2007 Elephant Island, Antarctica (1997-2000)	Lindane (γ-HCH): 1.04±0.39 ng/g lw 0.65±0.07 ng/g lw 0.34±0.05 ng/g lw 0.25±0.02 ng/g lw			

[19] http://www.oecd.org/document/24/0,3343,en_2649_34379_45373336_1_1_1_1,00.html
[20] Stockholm Convention - Home page (pops.int)
[21] In total 19 adult males (m), 22 adult females (f), 53 juveniles (j) and 41 pub (p) elephant seals were analysed. Stated mean values are based on detected concentrations only. Lindane (γ-HCH) was detected 4 (m), 17 (f), 17 (j), 36 (p) grey seals. α-HCH was detected 10 (m), 19 (f), 22 (j), 37 (p) grey seals.

		α-HCH: 0.51±0.04 ng/g lw 0.47±0.05 ng/g lw 0.43±0.03 ng/g lw 0.28±0.02 ng/g lw			
Bearded Seal (blubber)	POPs Risk Profile PeCB citing ICCA/WCC, 2007 citing Muir et al., 2003 White Sea in Northwestern Russia (1992-1988)	PeCB: 0.9 ng/g lw			
Harp Seal (blubber)	White Sea in Northwestern Russia (1992-1988)	PeCB: 12.0 ng/g lw			

Organism (tissue) (No.ind. n)	Reference & Location (sampling years)	POPs Substance Average (range)	Organism (tissue) (No.ind. n)	Reference & Location (sampling years)	**BCPS** Average (range)
Bird					
Guillemot/Common murre *Uria aalge* (egg) (n=10 per location)	Jörunddsdottir et al. 2009b Vestmannaeyjar, Iceland (2002)	99-BDE: 11 (5-24) ng/g lw	Guillemot/Common murre *Uria aalge* (egg) (n=10 per location)	Jörunddsdottir *et al.*, 2009b Vestmannaeyjar, Iceland (2002)	6.4 (5.1-8.8) ng/g lw
	Jörunddsdottir et al. 2009b Sandøy, Faroe Islands (2003)	99-BDE: 7.8 (3.2-20) ng/g lw		Jörunddsdottir *et al.*, 2009b Sandøy, Faroe Islands (2003)	6.7 (4.5-16) ng/g lw
	Jörunddsdottir et al. 2009b Sklinna, Norway (2005)	99-BDE: 2.1 (0.83-6.5) ng/g lw		Jörunddsdottir *et al.*, 2009b Sklinna, Norway (2005)	10 (n.d.-18) ng/g lw
	Jörunddsdottir et al. 2009b Hjelmsøya, Norway (2005)	99-BDE: 1.7 (0.64-4.7) ng/g lw		Jörunddsdottir *et al.*, 2009b Hjelmsøya, Norway (2005)	10 (6.3-17) ng/g lw
	Jörunddsdottir et al. 2009b Bjørnøya, Norway (2005)	99-BDE: 1.7 (0.69-3.4) ng/g lw		Jörunddsdottir *et al.*, 2009b Bjørnøya, Norway (2005)	6.2 (3.3-10) ng/g lw

	Jörunddsdottir et al. 2009b Stora Karlsö, Sweden (2003)	99-BDE: 23 (17-42) ng/g lw		Jörunddsdottir *et al.*, 2009b Stora Karlsö, Sweden (2003)	1000 (850-1300) ng/g lw
Guillemot/Common murre *Uria aalge* 30 sampling events à usually 10 eggs (n=299)	Sellström et al. 2003 Baltic Sea (1969-2001)	99-BDE: 71 (2-320) ng/g lw	Guillemot/Common murre *Uria aalge* (replacement egg) 5 eggs per sampling year (n=40)	Jörunddsdottir *et al.*, 2006 Stora Karlsö, Sweden (1971, 1976, 1981, 1986, 1991, 1996, 2001)	1140 (760-2600) ng/g lw)
Guillemot/Common murre *Uria aalge*	POPs Risk Profile Endosulfane citing Roseneau et al. 2008[22] Alaska	Lindane (γ-HCH): 1,46 ng/g lw (0.19 ng/g ww))			
Adelie penguin (egg) (n=6)	Corsolini et al. 2006 Antarctica (1995/6)	Lindane (γ-HCH): 5.70 ng/g lw (0.54±0.2 ng/g ww)			
		α-HCH: 0.53 ng/g lw (0.05±0.01 ng/g ww)			
		PeCB: 7.17 ng/g lw (0.68±0.6 ng/g ww)			
		99-BDE: 0.32 ng/g lw (0.03±0.02 ng/g ww)			

Organism (tissue) (No.ind. n)	Reference & Location (sampling years)	POPs Substance Average (range)	Organism (tissue) (No.ind. n)	Reference & Location (sampling years)	**BCPS** Average (range)
Fish					
Perch (usually 10 perch per location; n=62)	Olsson et al. 1999. Daugavgriva, Latvia (1994)	Lindane (γ-HCH): 21 (16-56) ng/g lw	Perch (usually 10 perch per location; n=62)	Olsson *et al.*, 1999. Daugavgriva, Latvia (1994)	71 (56-88) ng/g lw
		α-HCH: 15 (11-27) ng/g lw			
	Olsson et al.	Lindane (γ-		Olsson *et al.*,	82 (69-98)

[22] The detected concentration was reported in ng/g ww only, therefore lipid normalisation was carried out. Lipid content data of the common guillemot was collected from Helgason et al. 2008, Power et al. 2021, Sellström et al. 2003, Jörundsdottir et all. 2006 and Miller et al. 2014. The average lipid content was 13 %, calculated to 1g the derived conversion factor is 100/13 = 7.69. For Adelie penguin, a lipid content value was even reported in the Corsoline et al. (2006) study with 9.47 %, so a conversion factor of 10.55 was derived.

	1999. Daugavgriva, Latvia (1995)	HCH): 10 (8.2-14) ng/g lw		1999. Daugavgriva, Latvia (1995)	ng/g lw
		α-HCH: 11 (7.4-16) ng/g lw			
	Olsson et al. 1999. Kurmrags, Latvia (1994)	Lindane (γ-HCH): 22 (14-45) ng/g lw		Olsson *et al.*, 1999. Kurmrags, Latvia (1994)	75 (52-100) ng/g lw
		α-HCH: 21 (12-60) ng/g lw			
	Olsson et al. 1999. Kurmrags, Latvia (1995)	Lindane (γ-HCH): 14 (7.6-19) ng/g lw		Olsson *et al.*, 1999. Kurmrags, Latvia (1995)	61 (38-71) ng/g lw
		α-HCH: 12 (5.6-19) ng/g lw			
	Olsson et al. 1999. Lielirbe, Latvia (1994)	Lindane (γ-HCH): 27 (15-63) ng/g lw		Olsson *et al.*, 1999. Lielirbe, Latvia (1994)	55 (40-78) ng/g lw
		α-HCH: 51 (14-126) ng/g lw			
	Olsson et al. 1999. Lielirbe, Latvia (1995)	Lindane (γ-HCH): 7.1 (5.4-12) ng/g lw		Olsson *et al.*, 1999. Lielirbe, Latvia (1995)	63 (46-72) ng/g lw
		α-HCH: 6.9 (4.7-13) ng/g lw			
			Perch (n=46)	Valters *et al.*, 1999 Latvia (1997)	72 (28-190) ng/g lw
			Perch (n=20)	Norström *et al.*, 2004 Sweden (1998)	25.8 ng/g lw
			Perch (n=5)	Norström *et al.*, 2010 Sweden, Estonia, Poland (2008)	43 (20-69) ng/g lw

Summary and conclusion of the benchmark approach: known POPs and BCPS

The available data for BCPS in marine mammals is limited to grey seals in blubber tissue sampled in Sweden between 1995 and 2001. The concentrations range from a minimum of 41 to 240 ng/g lw. In comparison, concentrations for α-HCH in grey seals (maternal and pub blubber) sampled in Canada in 1995 range from 12 to 73 ng/g lw. For an unhealthy individual a maximum BCPS concentration of 475 ng/g lw was detected. Additionally, data from elephant seals, bearded seals and harp seals in blubber tissue is available for γ-HCH, α-HCH and PeCB, which is lower than the above stated detected concentrations for BCPS, as the highest concentration is 12 ng/g lw for PeCB in harp seal.

A study from 2009 analysed simultaneously BCPS and 99-BDE in eggs of guillemot (*Uria aalge*) (Jörunddsdottir et al., 2009b). Direct comparison of the results demonstrates similar concentrations with BCPS slightly exceeding 99-BDE most of the time. The location

Stora Karlsö in Sweden is particular prominent, as the concentration of BCPS in eggs was by far the highest, ranging from 850 to 1300 ng/g lw. An earlier study detected similar high concentrations for BCPS at the same location (Jörunddsdottir et al., 2006). Detected concentrations for γ-HCH, α-HCH, PeCB and 99-BDE in guillemot eggs and/or adelie penguin eggs are mostly below the ones from BCPS in guillemot eggs.

The study by Olsson *et al.* (1999) allows direct comparison of detected concentrations of BCPS with γ-HCH and α-HCH in perch fish tissue. It can be observed that mean concentrations of BCPS (55-82 ng/g lw) exceed the ones from γ-HCH (7.1 – 27 ng/g lw) and α-HCH (6.9 – 51 ng/g lw) in all sampling locations.

The results show that the BCPS levels lie within the range of known POPs or are even higher.

3.4.4 Summary and discussion of bioaccumulation

Based on all lines of evidence and taking into consideration the uncertainties of the monitoring data, sample size and limited data for other air-breathing organisms, it is concluded that BCPS is very bioaccumulative, and thus qualifies as vB.

Aquatic bioaccumulation

- The screening criterion for bioaccumulation for aquatic organisms based on measured log Kow of 3.9 (OECD TG 107) is not fulfilled. Additionally, the predicted BCF values indicate a low to moderate bioaccumulation potential of BCPS in fish.

  An experimentally derived BCFss value of 82 (NITE, 2001) is considered to be reliable with restriction.

Biomagnification

- Field BMF values significantly higher than 1 have been found for BCPS thus indicating a very high bioaccumulation potential. In total, three food chains in the Baltic region and in Austria (fish - guillemot, fish - cormorants, fish - grey seals) were identified with BMFs >1.

- Field BMF values (fish, bird)

Fish, guillemots: The concentrations of BCPS in herring between 1998 and 2008 were in the range between 17 – 58 ng/g l.w., concentration seems to stay at a constant level of around 30 ng/g l.w. in herring obtained from Sweden, Poland and Lithuania (Norström *et* al., 2004 and 2010). The concentration in herring muscle in 1998 was between 29-31 ng/g l.w. (Norström *et* al., 2004, Sweden, n=20). There was no obvious trend between country or sampling location (Norström *et* al., 2010). Therefore, it seems reasonable to take the fish muscle BCPS level of around 30 ng/g l.w. and to compare it with the BCPS concentrations found in guillemot breast muscle of 1600 ng/g l.w. (n=5) and 1900 ng/g l.w. (in 1989) from the Baltic region (Norström et al., 2004). Calculated field **$BMF_{guillemot\ breast\ muscle,\ herring\ muscle}$ of 53 to 63**, indicate biomagnification of BCPS over food chains. It needs to be noted, that location and time of sampling varied. However, based on the consistent measured levels in fish from the Baltic Sea over several years, it is reasonable to conclude that BCPS biomagnifies over food chains. Further support for biomagnification comes from avian eggs (Table 38), which are used as matrix to investigate contaminants, as its composition directly reflects that of maternal tissues (e.g., Drouillard and Norstrom, 2001). As mentioned within the Drouillard and Norstrom (2001) publication egg-to-maternal tissue concentration is often less than one (typically in the order of 0.3 – 0.7), but depends on fat reserves of the female, clutch size and physico-chemical factors of the

substances. Based on the analysed concentration in eggs, the BCPS concentration in female's tissue such as muscle would have been very likely in the same order or even higher. In total, 45 eggs have been analysed between 1971 – 2003, showing a geometric mean BCPS concentration of 1118 ng/g l.w. using the values from Jörundsdóttir *et al*. (2006 and 2008). Herring was taken between 1998 – 2008, showing a concentration of around 30 ng/g l.w. (Norström *et al*., 2004 and 2010), this would yield a field **$BMF_{guillemot\ eggs,\ herring\ muscle}$** of **37**.

Fish, cormorants: The BCPS concentration was higher in fish-eating cormorants (breast muscle arithmetic mean: 16.3 ng/g fat, n=6, sample date: 2019) than in fish (mean whole fish: 4.9 ng/g fat, n = 8, sample date: 2019), which indicates that BCPS biomagnifies. In this case the field **$BMF_{cormorant\ breast\ muscle,\ whole\ fish}$ value** is **3.2**, which is significantly higher than 1 and can therefore be considered as an indication for very high bioaccumulation (ECHA, 2017). Further when comparing the whole fish concentration with liver concentration this would yield a field **$BMF_{cormorant\ liver,\ whole\ fish}$** of **10.9**. One cormorant had ingested fish, with a BCPS level of 5.5 ng/g fat, the BCPS level in the cormorant breast muscle was 23 ng/g fat, suggesting a BMF of 4.2.

- Field BMF values (herring, seals)

Fish, grey seals: The concentrations of BCPS in herring muscle between 1998 and 2008 were in the range between 17 – 58 ng/g l.w., concentration stays in herring at a certain level of around 30 ng/g l.w. obtained from Sweden, Poland and Lithuania (Norström *et* al., 2004 and 2010). It is therefore reasonable to take the fish level of around 30 ng/g l.w. and to compare it with the concentrations found in liver (concentration: 200 ng/g l.w; sample date: 2000-2001) and blubber (concentration: 60 ng/g l.w.; sample date: 1997) from grey seals from the Baltic region. A field BMF values results in **$BMF_{herring\ muscle,\ seals\ liver}$ values of 6.7** and a field **$BMF_{herring\ muscle,\ seals\ blubber}$** of **2**. However, location and time of sampling varied but based on the consistent measured levels in fish form the Baltic Sea over several years, BCPS biomagnifies in seals.

Field data

Several field studies measuring the concentration of BCPS are available from 1971 – 2019 (ref. Annex I). There is evidence, that BCPS was taken up and detected above Limit of Detection (LOD) in different wildlife species (marine and freshwater fish, grey seals, birds, mink, otters) throughout aquatic food chains, including top predatory fish, as well as grey seals *Halichoerus grypus* and fish-eating birds (like e.g., white tailed-sea eagle, guillemot, cormorants). Data were mostly generated for the Baltic region, but also include remote areas (Arctic) and data from North America, Austria, Black Sea and Danube delta.

- Highest BCPS levels constant over 30 years were detected in fish-eating bird eggs (high trophic level)

From all biota samples analysed so far, the BCPS levels detected were highest in guillemot eggs from the island Störa Karlsö, Sweden (760 - 2600 ng/g l.w., geometric mean: 1118 ng/g l.w., period: 1971 - 2003). BCPS was found in an at least constant level in eggs of the fish-feeding bird guillemot from 1971 to 2003 (Jörundsdóttir *et* al., 2006 and 2008).

- High BCPS levels in seals

The highest BCPS value (=480 ng/g l.w.) was found in grey seal blubber in an unhealthy 11-year old individual (Norström et al., 2004). Larsen *et* al., 2004 investigated lung, liver and blubber from grey seals from Sweden. The target organ of BCPS is the liver, exhibiting the highest concentrations (median = 200 ng/g l.w.; range 55 – 700 ng/g l.w., n=10). The concentration in the blubber was lower than in liver, which was in the range of 41 – 240 ng/g l.w (median 60 ng/g l.w., n=10).

- Recent data (Hornek-Gausterer *et* al., 2021)

In predatory fish species (2019, Austria, Danube) and cormorant samples (2019, Austria, samples from liver and breast muscle) BCPS was detected with 100% detection frequency. Levels in freshwater fish ranged between 1.3 and 9.3 ng/g fat. BCPS levels in cormorants breast muscle were in the range of 4.3 to 40 ng/g fat (arithmetic mean: 16.3 ng/g fat, n=6) and 28 to 86 ng/g fat (arithmetic mean: 53.5 ng/g fat, n=6) in the liver samples. But comparing the BCPS concentrations of cormorants' breast muscle from 2019 (mean: 16 ng/g fat, n=6) to the concentrations from 2001 – 2005 (mean: 8.9 ng/g fat, n=5), indicates that BCPS level is increasing, despite the small sample size and unknown food intake during the migration route of the individuals. Further, the arithmetic mean BCPS concentration in sub-adult cormorants was 8.85 ng/g fat (median: 6.6 ng/g fast) and the arithmetic mean concentration in adults revealed a BCPS concentrations of 17.9 ng/g fat (median: 16 ng/g fat), indicating an increase in BCPS concentration in breast muscle with age. But due to the low sample size and as the results are not statistically significant, no final statement can be made.

Bioaccumulation in air-breathing organisms

- BCPS is taken up by organisms and humans and detected in various wildlife species.

- Screening criteria for bioaccumulation in air-breathing organisms are fulfilled.

  Screening criteria[23] for air-breathing organisms have been established based on log K_{OW} > 2 and log K_{OA} > 5. The measured log K_{OW} of 3.9 (OECD TG 107) and the estimated log K_{OA} value of 9.2 (KOAWIN v.1.10) indicating, despite the low to moderate bioaccumulation potential in fish, a bioaccumulation potential for BCPS in air-breathing terrestrial and marine wildlife, as well as humans. Kelly *et* al. (2004) mentioned BCPS as an example for a hydrophilic compound to exhibit such bioaccumulation potential.

- BCPS exhibits a very long half-life in rats, which exceeds the recently established threshold values, and has a high affinity to adipose tissue.

  A very long terminal half-life of 12 days was observed in adipose tissue in rats after single i.v. application (ref. to 4.1 Toxicokinetics). BCPS is mainly distributed to adipose tissue and the affinity to adipose tissue is high. Accelerated clearance was observed after repeated dosing and a steady state was observed after 2-3 weeks. This observation can be attributed to liver enzyme induction and enhanced clearance. Liver metabolism might vary between species, e.g., it is known that the half-lives for polychlorinated biphenyls are much shorter in rats than in humans mostly due to a higher metabolism rate in rats.

- BCPS detected in human liver.

  BCPS has been detected in human liver samples (Ellerichmann *et* al., 1998) while liver is a target organ of BCPS toxicity in rats and mice.

- In a benchmark approach, the concentrations of known structurally unrelated POP substances (with known vB properties) were compared with BCPS in species at the top of the food chain. The results for BCPS lie within the range of known POPs.

To conclude, while screening information and a measured, very limited BCF value indicate a low to moderate bioaccumulation potential for fish, there is sufficient evidence that BCPS

[23] https://echa.europa.eu/documents/10162/13632/information_requirements_r7c_en.pdf

bioaccumulates in air-breathing organisms. Rat toxicokinetic data demonstrate that BCPS is rapidly distributed out of the blood into tissues, with adipose tissue as major storage site and the elimination is slow. Based on the derived terminal half-life in adipose tissue a BMF higher than 1 is anticipated for air-breathing mammals.

Monitoring data further supports findings from toxicokinetic data by the fact that the substance has been found in above Limit of Quantitation (LOQ) and partly very high concentrations in predatory organisms at the top of food-chains (e.g., fish-eating birds) and also in human liver samples. Further, but lower line of evidence comes from field BMF values in three food-webs (fish – guillemot, fish – cormorants, fish – seals), which show BMF values significantly higher than 1 and BCPS concentrations in biota, which are in the range of known POPs (see Table 39).

4. Human health hazard assessment

Information relevant for the bioaccumulation is summarised in the following chapters (4.1. Toxicokinetics, 4.2. Repeated dose toxicity).

4.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

4.1.1 Non-human information

QSAR predictions

During the Consultation the registrants provided in-silico/QSAR predictions for estimating the bioaccumulation potential of the substance and recommended to consider them in the WoE-approach (Arnot *et al.,* 2022). Considering the applied methods, the derived values are reproducible. The use of these QSAR-models and the derived predictions have been considered for the WoE.

The registrants used IFS-QSAR and QSARINS to predict total elimination half-life (HL_T) and biotransformation half-lives (HL_B) in human (mammals). The half-life (HL) was predicted to be in the range of about 20 to 110 h (geomean = 60h) based on 6 human HL predictions. The geomean of the HL_B-QSAR predictions that are within the applicability domain was 2.8 d (68 h) for a 70 kg adult human.

Furthermore, the registrants applied IFS-QSAR, QSARINS, BCFBAF, and OPERA to predict HL_T and HL_B in fish. The *in vivo* and *in silico* HL_B estimates in fish range from 4.6 to 250h. The geometric mean of the five predictions was 56 h (2.3 d) for fish.

Fish: It is concluded that, while there is some variability in the *in vivo* and *in silico* estimates, they build a strong weight of evidence that BCPS is subject to relatively fast rates of biotransformation in fish.

Human (mammals): While most of the predictions are within the applicability domain as defined by the models, the QSAR-predictions are considered to be more uncertain than experimental data, as there is a lack of similar substances (having the sulphone fragment bound to two aromatic rings) with experimental data in the training sets which could support the reliability of the derived predictions. Therefore, available experimental data are considered to have higher weight in a weight of evidence approach due to uncertainty in the HL QSAR predictions.

Birds: Regarding bioaccumulation in birds, the registrants conducted a literature review to determine, if there are any TK data available for birds. The registrants confirm that there are no *in vitro* or *in vivo* TK measurements and no specific QSARs for predicting HL_T and HL_B for birds. Any QSAR-predictions on the bioaccumulation potential of the substance in birds are based on mammal data. Referring to Jörundsdóttir et al. (2006) it is considered to be likely that there is a different metabolism between birds and mammals. Jörundsdóttir et al. (2006) indicated that birds are less capable of metabolizing para-halogen substituted phenyl rings. Therefore, monitoring data are considered to be more reliable than any modeled data in the weight of evidence approach. Based on the available monitoring data, birds seem to be the most sensitive group of animals.

The QSAR predictions are valuable to support a screening-level chemical assessment, but should be given - based on the reasons listed above - a lower weight than experimental data in a weight of evidence approach.

The applied QSAR predictions for half-lives in humans, birds and fish are considered more uncertain for the B assessment than experimental or monitoring data and they are given a low weight.

In vivo studies – rodents

The toxicokinetic behaviour of BCPS was studied in rats after single (intravenous and oral application) and after repeated (oral) administration of radiolabelled BCPS. In the 7 day repeated dose toxicity study with different doses (oral administration) also hepatic enzyme induction has been determined (Mathews *et al.*, 1996). In a further repeated dose study (Poon *et al.*, 1999) the distribution of unlabelled BCPS, as well as hepatic enzyme induction and the toxicological effects of BCPS (see also chapter 4.2. repeated dose toxicity) were investigated in rats.

There are no experimental data available on BCPS toxicokinetics following dermal or inhalation exposure.

Table 40: Overview of experimental studies on absorption, metabolism, distribution and elimination

Method	Results	Reference / remarks
Test species: rat (Fischer 344) male Number of animals: 4/group Test material: [^{14}C]BCPS (Purity: 96%) Vehicle: Emulphor EL-620 **Single dose experiments:**		Mathews *et al.* (1996) Klimisch 2 similar to OECD Guideline 417 (Toxicokinetics)
Study A: intravenous application (i.v.), 10 mg/kg bw [^{14}C] BCPS, observation period 21 days post treatment (various sampling times to determine terminal elimination half-life and distribution pattern over time) (measurement of disposition of radioactivity)	Study A: BCPS is rapidly distributed out of blood mainly into adipose tissues; Disposition of radioactivity 72 h post application of 10 mg/kg in adipose tissue (40.9%) > skin (16.1%) > muscle (11.9%) > liver (1.69%) > blood (0.35%) > kidney (0.16%). After 24 hrs the tissue/blood ratio for BCPS in adipose tissue reached 90, this ratio was maintained for at least 21 days post dosing. The ratio between lean tissues/blood was around 3-7. A terminal adipose tissue half-life of BCPS was determined to be 12 days.	No rationale for vehicle used, no statistical analysis provided. Tissue data are provided in Table N1 of NTP, 2001. The half-life of BCPS in adipose tissue between days 3-21 was determined as ~10 days.
Study B: oral gavage, different doses: 0, 10, 100, 1000 mg/kg bw [^{14}C] BCPS, sampling time: 3d (72 hour) post treatment (measurement of disposition of radioactivity)	Study B: Effect of dose 0, 10, 100 and 1000 mg/kg bw [^{14}C] BCPS by single gavage application on tissue distribution and excretion was studied. The data demonstrate that the distribution is irrespective of dose, with a trend towards lower	

	percentages of the total dose found in adipose tissue, liver, skin and muscle as the dose increased (see **Table 41**). Nearly complete absorption (10 mg/kg bw: 85.5%, 100 mg/kg bw: 71.9%, 1000 mg/kg bw: 71.0%) The total excretion (urine, faeces) after 72 hrs was 20.0 to 28.9 % of total dose applied. **Comparison of i.v. and oral study (dose 10 mg/kg bw [^{14}C] BCPS):** Oral dose of 10 mg/kg bw was nearly completely absorbed and distributed in a manner similar to that seen with iv injection. Tissue/blood ratios not affected by route of administration.	
Repeated dose experiments: Study C: 1, 10, 100 mg/kg bw/d [^{14}C] BCPS, 7-day repeat dosing experiment, Sampling time: 3 d (72 hours) after final repeat dosing; oral gavage, (measurement of disposition of radioactivity)	Study C: The tissue distribution after a repeated dose regime of 7 days is similar in various tissues to the single dose experiments, with adipose tissue again the major storage site. Repeated administration resulted in a dose-dependent increase in percentage of dose eliminated in urine and faeces (with appr. 50% of the two highest doses excreted vs. 30% in the lower dose group). Repeated dose resulted in concomitant dose-dependent decrease in percentage of dose retained in tissue. After a daily dose of 1 mg/kg BCPS for 7 days, 41% of the administered dose was found in the adipose tissue, whereas after a daily dose of 100 mg/kg BCPS for 7 days, only 19.7 % of the administered dose was found in adipose tissue.	
Study D: 2, 3 and 5 weeks repeat dosing with 5 d/wk; oral gavage, 10 mg/kg bw/d [^{14}C] BCPS	Study D: The radiochemical content in adipose and blood peaked at 3 weeks and adipose concentration declined by 5 weeks. BCPS concentration in tissue after 2	

(measurement of disposition of radioactivity) Determination of metabolites in the urine and faeces (Study A, B, C) 0-72 hrs after last application Enzyme induction was determined in Study C	weeks was 28.4 mg/kg bw (corresponding to 28.4 % of total dose applied), after 3 weeks 34.2 mg/kg bw (corresponding to 22.8% of total dose applies) and after 5 weeks 25.3 mg/kg bw (corresponding to 10.1% of total dose applied). In the period between 3 and 5 weeks, the eliminated part is roughly equal to the administered part (99% and 106%) indicating that the steady-state has been reached. (raw data not shown in the publication). The main metabolites were mono-hydroxy-BCPS (hydroxyl-moiety in the *meta* position to the sulfone) and its respective glucuronide. Further minor metabolites (up to 5 components) were found, which were not further characterised. The mono-hydroxy-BCPS and glucuronide metabolites probably arise from hepatic metabolism of BCPS. Unmetabolised BCPS was found in faeces and predominantly only after application of single dose of 1000 mg/kg bw/day (16.6%). CYP450 and EROD activity (CYP 1A1/2) was two-fold increased in the 10 mg BCPS /kg bw/d group (1,75 ± 0.26 nmol/mg and 2.45 ± 0.23 nmol/mg/min) vs vehicle control (0.96 ± 0.07 nmol/mg and 1.47 ± 0.25 nmol/mg/min) or 1 mg/kg bw/day group (0.96±0.10 nmol/mg and 1.47 ± 0.25 nmol/mg/min); in the 100 mg/kg bw/day group modest CYP450 increase, no EROD increase; Benzphetamine N-demethylase activity (associated with CYP2B forms) was unaffected by administration of BCPS.	
Test species: rat (Sprague Dawley), male Number of animals: 6	Distribution: percentage of total dose in adipose >> liver > kidneys >lung >spleen >	Poon *et al.* (1999) Klimisch 2

animals/group, 10 groups Test material: unlabelled BCPS Purity: >99% Vehicle: corn oil Exposure duration: 28 days Application route: oral feed study Detection of BCPS: Gaschromatography/Electron Capture Detection (GC/ECD) Dose levels: 10, 100, or 1000 ppm in diet corresponding to 0.8±0.1, 8.1±1.3, and 75.6±8.4 mg/kg bw/d time course setting, administration of 75.6 mg/kg/d BCPS diet, animals were sacrificed at the end of week 1, 2, 3 and 4 and adipose tissue, liver, and kidneys were analysed for BCPS residues	brain remaining constant; in kidneys levels increased until end of study; retained substance in tissue increased with dose Increase of BROD (benzoylresorufin O-dealkylase) and PROD (pentoxyresorufin O-dealkylase) (CYP2B enzymes) and induction of GST (Glutathione S-transferase) and UDPGT (Uridine 5'-diphospho-glucuronosyltransferase) in a dose dependent manner, EROD (Ethoxyresorufin-O-deethylase) no effect, MROD (Methoxyresorufin O-demethylase) (CYP1A enzymes) even decreased (see text). Most pronounced toxic effect: liver (hepatomegaly), urinary ascorbic acid increase (metabolite of the glucuronic acid pathway), hypercholesterolemia, increased hepatic TBARS (thiobarbituric acid reactive substances)	Experimental study, non GLP, not guideline conform, presentation of methods and data sufficient

The toxicokinetic studies indicate that BCPS is nearly completely absorbed. BCPS is rapidly distributed to tissues, especially to adipose tissue (concentration in adipose tissue >> skin > liver > blood >kidney > brain, spleen, lung) (Mathews *et al*., 1996, Poon *et al*., 1999).

Increasing dose in adipose tissue of BCPS was observed up to 24 hours, followed by a low elimination rate, a terminal half-life of 12 days was determined in adipose tissue (single i.v. application, 10 mg/kg bw). The tissue measurements are tabulated in Table N1 of NTP, 2001, and a half-life of ~10 days can be calculated from adipose tissue concentrations from day 3-21. The BCPS equivalents in tissues were primarily parent unmetabolised compound.

Single dose oral gavage experiment (Study B) with different doses (10 mg/kg bw, 100 mg/kg bw, 1000 mg/kg bw) demonstrates that there is not a statistically significant difference in the % of total dose in tissue as a function of the administered dose and again adipose tissue is the major storage site. A trend towards lower percentages of the total dose found in adipose tissue, liver, skin and muscle, as the dose increased, was observed.

Table 41:Disposition of radioactivity 72 hrs after oral administration of [^{14}C] BCPS (from Mathews et al., 1996)

Tissues	% Dose in total tissue		
	10 mg/kg bw	100 mg/kg bw	1000 mg/kg bw
Adipose	48.9±3.1	42.5±2.2	37.0±6.9

Blood	0.310±0.036	0.405±0.145	0.275±0.044
Kidney	0.155±0.013	0.140±0.017	0.160±0.019
Liver	1.79±0.18	2.00±0.25	1.14±0.07
Muscle	11.7±3.7	5.92±1.18	5.57±0.95
Skin	17.7±0.9	9.74±2.48	6.93±1.57
Small intestine	2.54±0.33	5.29±1.07	6.91±0.44
Caecum	1.57±0.40	3.86±1.53	10.8±3.5
Large intestine	0.994±0.08	2.01±0.56	2.25±1.54
Total in tissue	85.5±7.0	71.9±3.2	71.0±5.5

Cumulative % dose excreted			
Urine			
0-24 hr	2.6±0.2	2.2±0.3	0.7±0.1
24-48 hr	4.1±0.2	4.0±1.1	3.6±3.9
48-72 hr	5.2±0.2	8.1±3.0	10.2±5.5
Faeces			
0-24 hr	1.9±1.1	1.4±0.7	2.6±1.4
24-48 hr	8.4±2.4	8.1±0.8	10.2±1.5
48-72 hr	14.7±2.6	19.3±0.9	18.7±3.8
Total	20.0±2.5	27.4±2.8	28.9±4.1

An increase in metabolism has been observed in relation to dose and time (Mathews *et al*., 1996). The metabolite profile indicates a hepatic first pass metabolism depending on the dose applied. Conversion to metabolites (aglycone and glucuronide metabolites) was doubled as the dose level in the 7 day repeated dose study increased from 1, 10 and 100 mg/kg bw. This might be explained by CYP P450 induction (Study C). Parameters associated with cytochrome P450 and CYP1A activity were at a dose level of 10 mg/kg bw/day group (applied for 7 days) 2 fold higher compared to the control or 1 mg/kg bw/day group.

Furthermore, a peak in tissue concentration was observed by week 3 in the repeated dose study (10 mg/kg bw over a time-period of 5 weeks, vehicle: Emulphor), followed by a decrease in tissue concentration after 5 weeks (Study D), but according to single dose experiments a steady state is expected at 6-7 weeks according to the authors, providing further indication for accelerated metabolism.

BCPS concentration in total tissue after 2 weeks was 28.4 mg/kg bw (corresponding to 28.4% of total dose applied), after 3 weeks 34.2 mg/kg bw (corresponding to 22.8% of total dose applies) and 25.3 mg/kg bw after 5 weeks (corresponding to 10.1% of total dose applied). The BCPS concentration in adipose tissue and skin declined from week 3 to week 5 by 26% and 30%, respectively. In blood, kidney and liver the BCPS concentrations peaked at week 3 and remained unchanged until week 5 (details see table below).

Table 42: Disposition of radioactivity after repeated oral dose of 10 mg/kg bw [14C]BCPS (from Mathews et al., 1996)

Sampling time/tissues	Tissue distribution	
	µg-eq BCPS/g tissue	% of total dose in tissue
2 weeks		
Adipose	265±19	19.6±1.4
Blood	2.3±0.2	0.125±0.010
Kidney	7.1±1.2	0.0556±0.0074
Liver	20±2	0.939±0.117
Skin	24±8	4.23±1.42
Total in tissue		28.3±3.3
3 weeks		
Adipose	312±20	15.3±1.01
Blood	3.4±0.3	0.125±0.014
Kidney	8.9±1.7	0.0456±0.0088
Liver	21±5	0.685±0.167
Skin	33±8	3.90±0.91
Total in tissue		22.8±2.0
5 weeks		
Adipose	231±33	6.72±0.98
Blood	3.9±0.4	0.0837±0.0084
Kidney	9.4±1.4	0.0276±0.0036
Liver	24±4	0.483±0.061
Skin	23±4	1.61±0.31
Total in tissue		10.1±1.5

In a further rat study of Poon *et al*. (1999) in which BCPS (75.6±8.4 mg/kg bw/d, diet, vehicle: corn oil) was applied to Sprague Dawley rats no decrease of BCPS content was found in tissues between week 1 and 4, even an increase in kidneys was observed at week 4.

A timeplot comparing the BCPS content in selected tissues (adipose, liver, kidney) at different sampling times after repeated dosing as described in the studies of Mathews *et al.* (1996) and Poon *et al.* (1999) is depicted in the graph below.

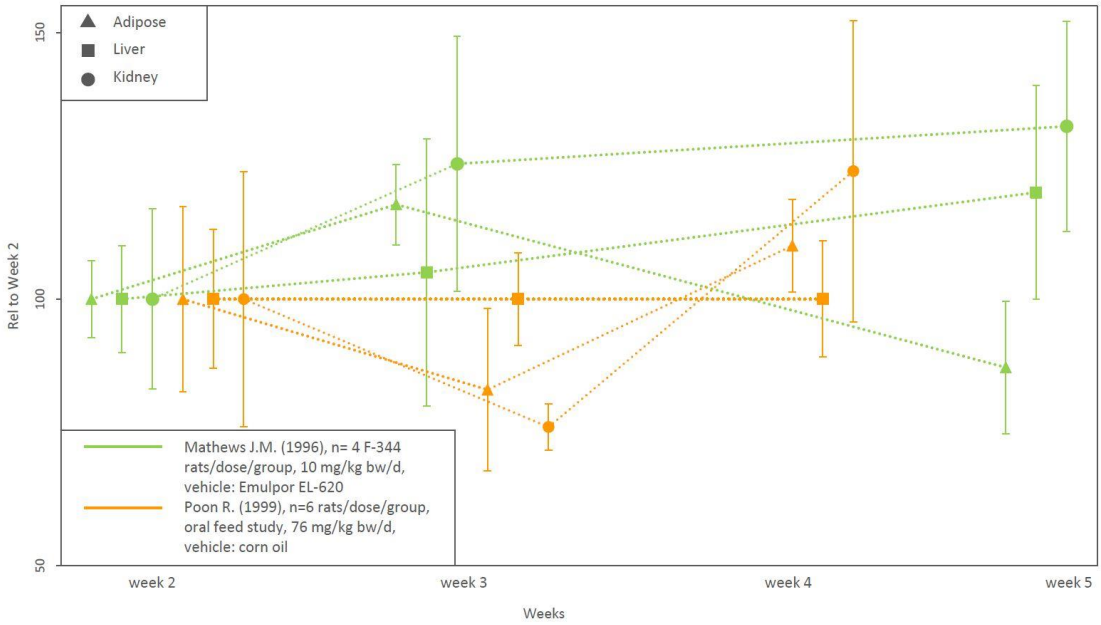


Figure 9: BCPS content in selected tissues - timeplot

The studies (Mathews *et al.,* 1996, Poon *et al*., 1999) also demonstrate that BCPS has the capability to induce hepatic enzymes such as CYP450 enzymes, UDPGT and GST. Liver enzyme induction is also dose dependent. For example, in the study of Mathews *et al.* (1996) parameters associated with CYP1A activity were at a dose level of 10 mg/kg bw/day group (applied for 7 days) 2 fold higher compared to the control or 1 mg/kg bw/day group. Comparing the available information, a clear pattern of enzyme induction (e.g,. which kind of CYP450 are induced) cannot be deduced (Poon *et al*., 1999, Mathews *et al.,* 1996). Differences between enzyme induction patterns in the aforementioned studies might be explained by various factors, e.g., different rat strains, exposure duration, vehicle and/or BCPS application.

The excretion of BCPS is rather slow and predominantly via faeces. The excretion of BCPS is dependent on metabolism to more polar compounds (mono-hydroxy-BCPS and its glucuronide), and relatively little parent compound was excreted before metabolism.

Besides experimental toxicokinetic data also a PBPK model has been established (Parham *et al.*, 2002) based on the data of Mathews *et al.* (1996) and from chronic feed studies in male and female rats and male and female B6C3F1 mice (NTP, 2001). The model confirms that BCPS follows non-linear kinetics. Although the model reproduced the data fairly well, the model predictions were generally better for low doses than for high doses, and there were some uncertainties in respect to species- and sex-specific toxicokinetics. Further parameters were estimated by fitting to experimental data: e.g., tissue/blood partition coefficients for BCPS and metabolites, metabolic rate constant, urinary/biliary excretion rate constant for BCPS and metabolites, maximum rate of absorption from gut. The authors also summarise that enzyme induction must be taken into account to accurately describe the BCPS kinetics, but for such enzyme induction an exact model cannot yet be established.

In summary, the experimental toxicokinetic data in rats indicate that BCPS is absorbed rapidly and distributed to mainly adipose tissue, where a slow elimination is followed. A terminal elimination half-life of 12 days in adipose tissue after single dose application provides evidence that BCPS accumulates in air-breathing organisms.

4.1.2 Human information (including bioaccumulation in humans)

No human data on half-life is available.

Allometric scalling may be applied, taking into account the terminal half-life of BCPS of 12 days in adipose tissue, a weight of 70 kg for humans and 0.25 kg for rats and b as fixed exponent of 0.25 (Caldwell et al., 2004) using the following equation:

$$t_{1/2\,\text{human}} = t_{1/2\,\text{rat}} \left(\frac{W_{\text{human}}}{W_{\text{rat}}}\right)^{b}$$

a human half-life of 50 days can be deduced.

Human biomonitoring studies:

There is evidence that BCPS is present in human liver samples (see

Table **37**).

4.1.3 Conclusion on toxicokinetics (and bioaccumulation in humans)

Animal data indicate a rapid distribution of unmetabolised BCPS mainly into adipose tissue, where a half-life of 12 days was observed in adipose tissue after single application. The elimination half-life of 12 days might be due to BCPS's high affinity to adipose tissues.

According to recent discussion paper (Expert Working Group, 2022) a field BMF of 1 can be translated into a whole-body, terminal elimination half-life of about 4 days in rats and 50 days in humans. If the terminal elimination half-lives are assessed to be longer than these, this is an indication that the substance has vB properties.

No whole body terminal half-lives are presented in the rat study (Mathews *et al*., 1996). BCPS is quickly distributed into adipose tissue and the terminal whole body half-life is driven by the slow elimination of BCPS from the adipose tissue. Therefore, it can be assumed that the terminal whole body half-life is in the same order of magnitude as the half-life in adipose tissue (about 12 days in rats), which indicates that the substance is a vB substance.

Accelerated clearance was observed in rats after repeated dosing explained by liver enzyme induction by BCPS in the experiments of Mathews *et al.* (1996). The steady state after repeated dosing was reached according to the study authors after 2-3 weeks. BCPS adipose and skin tissue concentration reached a peak at week 3 and declined at week 5 by 26% and 30%, respectively. Blood, liver, kidney concentrations were the highest at week 3 and remained constant until week 5. The total tissue concentration of BCPS peaked at week 3, and declined (by 26%) at week 5. In a further repeated dose study BCPS remained unchanged between week 1 and 4 (Poon *et al.*, 1999), whereas a slight increase in concentration in the kidney was observed.

There are some limitations on the provided data set for example no information concerning repeated low dose application (more than seven days) is available, which would be of interest since liver enzyme induction is dependent also on the applied dose. The level to which BCPS might have the property to accumulate is dependent on factors like the BCPS exposure pattern (e.g., concentration) and on induction of liver enzymes in individuals or wildlife species, which have the capacity to metabolise BCPS. Hereby, it is noteworthy, that the capacity to eliminate BCPS might vary between species.

In summary, toxicokinetic data from rats indicate that BMF values higher than 1 can be anticipated for air-breathing organisms and the substance should be considered as vB.

4.2. Repeated dose toxicity

4.2.1 Non-human information

4.2.1.1 Repeated dose toxicity: oral

For the evaluation of the endpoint repeated dose toxicity, results from five animal experiments - two sub-chronic (14 weeks) studies with rat and mice, two chronic (2 years) combined repeated dose/carcinogenicity studies with rat and mice (NTP, 2001) and a sub-acute toxicity test with rat (Poon *et al.*, 1999) were reviewed.

Study details, main results and remarks are depicted in Table 43.

Table 43: Studies on repeated dose toxicity

Study/Method	Results	Remarks/ Reference
Test species: rat (Fischer 344) male/female Number of animals: 10/sex/dose Test material: BCPS Vehicle: no vehicle Study duration: subchronic – 14 weeks Dose levels: 0, 2, 6, 19, 65 and 200 mg/kg bw/d (corresponding tg to 0, 30, 100, 300, 1000 or 3000 ppm) Application route: Feed mixed with the test substance was available ad libitum equivalent or similar to OECD TG 408 (repeated dose 90-day oral toxicity in rodents)	Dose dependent liver weight increase (up to +135%), dose dependent increase in centrilobular hepatocyte hypertrophy, cytomegaly and karyomegaly Increased incidences in nephropathy Organ weight changes: absolute and relative thymus decrease (male), absolute thymus decrease (female), absolute and relative kidney increase (m), relative kidney increase (f), absolute and relative testis increase NOEL: 2 mg/kg bw (based on liver weight ↑ associated by hypertrophy of centrilobular hepatocytes at 6 mg/kg bw/d)	NTP (2001) Klimisch 2 Key study GLP - addition of neurobehavioural examination - test conducted prior to OECD TG update to include endocrine disruptor relevant endpoints - urine analysis lacking
Test species: mouse (B6C3F1) male/female Number of animals: 10/sex/dose Test material: BCPS Vehicle: no vehicle Study duration: subchronic – 14 weeks	Dose dependent liver weight increase (up to +107.3%), dose dependent increase in centrilobular hepatocyte hypertrophy and significant induced incidences of focal hepatocyte necrosis in males in the highest dose groups (165 and 480 mg/kg bw/d) Organ weight changes: relative testis increase, relative kidney weight increase (m, f), relative ovaries and uterus increase, absolute thymus	NTP (2001) Klimisch 2 Key study GLP - addition of neurobehavioual examination

Study/Method	Results	Remarks/ Reference
Dose levels: 0, 3.5, 15, 50 165, 480 mg/kg bw/d (corresponding to 0, 30, 100, 300, 1000 or 3000 ppm) Application route: Feed mixed with the test substance was available ad libitum equivalent or similar to OECD TG 408 (repeated dose 90-day oral toxicity in rodents)	increase (f) NOEL: 3.5 mg/kg bw (based on liver weight increase associated by centrilobular hepatocyte hypertrophy noted at 15 mg/kg bw/d) NOAEL: 50 mg/kg bw/d (focal hepatocyte necrosis at 165 mg/kg bw/d)	- test conducted prior to OECD TG update to include endocrine disruptor relevant endpoints - no clinical chemistry,urine analysis lacking
Test species: rat (Fischer 344) male/female Number of animals: 50/sex/dose Test material: BCPS Vehicle: no vehicle Dose levels: 0, 0.5, 1.5, or 5.0 mg/kg bw/day corresponding to 0, 10, 30, or 100 ppm (males) 0, 1.6, 5.4, or 17 mg/kg bw/d corresponding to 0, 30, 100, or 300 ppm (females) Study duration: 105 to 106 weeks Application route: Feed mixed with the test substance was available ad libitum equivalent or similar to OECD Guideline 453 (Combined Chronic Toxicity/ Carcinogenicity Studies)	Centrilobular hepatocyte hypertrophy (males and females), significant bile duct hyperplasia and centrilobular degeneration (females) NOAEL: 1.5 mg/kg bw/d (bile duct hyperplasia centrilobular degeneration noted in females at 5.4 mg/kg bw/d, for males and females hepatocyte hypertrophy at 5 and 5.4 mg/kg bw/d respectively	NTP (2001) Klimisch 2 Supporting study GLP - no haematological examination, no urin-analysis, no clinical chemistry - determination of BCPS in plasma
Test species: mouse (B6C3F1) male/female Number of animals: 50/sex/dose Test material: BCPS Vehicle: no vehicle	Centrilobular hypertroyphy, eosinophilic foci (only females) NOEL: 3 mg/kg bw/d (based on centrilobular hepatocyte hypertrophy noted in female rats at 13 mg/kg bw/d); no NOEL for males identified (≤ 4 mg/kg bw/d)	NTP (2001) Klimisch 2 Supporting study GLP

Study/Method	Results	Remarks/ Reference
Dose levels: 0, 4, 13 or 40 mg/kg bw/day corresponding to 0, 30, 100 or 300 ppm (males) 0, 3, 10 or 33 mg/kg bw/day corresponding to 0, 30, 100 or 300 ppm (females) Study duration: 105 weeks to 106 weeks Application route: Feed mixed with the test substance was available ad libitum equivalent or similar to OECD Guideline 453 (Combined Chronic Toxicity/ Carcinogenicity Studies)	NOAEL: 10 mg/kg bw/day (based on eosinophilic foci (female))	- no haematological examination, no urinanalysis, no clinical chemistry - determination of BCPS in plasma
Test species: rat (Sprague-Dawley), male Number of animals: 6 males/group, 10 groups Test substance: BCPS Dose levels: 0, 10, 100, or 1000 ppm in diet corresponding to 0, 0.8, 8.1, and 75.6 mg/kg bw/d Study duration: 28 days Application route: oral feed study Time course setting: administration of 75.6 mg/kg bw/d BCPS, animals were sacrificed at the end of week 1, 2 and 3, adipose tissue, liver, and kidneys were analysed for BCPS residues	Distribution: percentage of total dose in adipose >> liver > kidneys >> lung >spleen > brain remaining constant; in kidneys levels increased until end of study; retained substance in tissue increased with dose Induction of BROD and PROD (CYP2B related enzymes) and induction of GST and UDPGT, MROD (CYP1A2 related enzyme) even decreased Most pronounced toxic effect: liver (hepatomegaly), urinary ascorbic acid increase (metabolite of the glucuronic acid pathway), hypercholesterolemia, increased hepatic Thiobarbituric acid reactive substances (TBARS) NOAEL: 8.1 mg/kg bw/d (based on liver weight increase, increased blood cholesterol concentration)	Poon *et al.* (1999) Klimisch 2 - not guideline conform

Liver effects

The liver is the target organ of BCPS exposure in rats and mice. A negative impact on the liver was observed in all repeated dose toxicity studies. The effects are mainly characterised by marked liver weight increase and centrilobular hypertrophy. The severity of this lesion increased in a dose dependent manner and was characterised mostly minimal to mild.

Beside liver weight increase and centrilobular hypertrophies, following liver toxicity related findings were observed in the repeated dose toxicity studies:

In the 14-week mouse study, significantly increased incidences of focal hepatocyte necrosis were detected in males in the higher dose groups (165 and 480 mg/kg bw/day). In the 14-week rat study changes in sorbitol dehydrogenase activity and bile acid concentrations were consistent with the liver lesions observed histopathologically in rats. Alkaline phosphatase activity decreased in an exposure-related manner. Alanine aminotransferase activity, another marker of hepatocellular health, was not affected similarly and, in fact, demonstrated decreased activity in the lower dose groups. In the chronic (2 years) mouse toxicity study, centrilobular degeneration of the liver significantly increased only in females at 5.4 mg/kg bw/d (10 out of 50) and 17 mg/kg bw/d group (7/50). It is noteworthy, that the incidence of centrilobular degeneration and severity in male rats was generally high (control group: 18 out of 50) irrespective of BCPS administration. In the chronic (2 years) rat toxicity study significant increased incidence of eosinophilic foci were observed only in females in the high dose group (33 mg/kg bw/d). In the 28-day toxicity study of Poon *et al.* (1999) it was demonstrated that BCPS induces hepatic enzyme activities already at very low doses (0.8 mg/kg bw/d). A clear increase of BROD and PROD, which are CYP2B related microsomal enzymes was observed already at a dose level of 0.8 mg/kg bw/d. Whereas EROD activity, enzyme associated with the CYP1A1 level, has not changed and MROD activities (related to CYP1A2) even decreased. In this study significant increase of the phase II enzymes UDPGT and GST has been observed at a dose level of 8.1 mg/kg bw/d and above. Urine analysis reveals an increase in ascorbic acid (up to 16.7-fold) already significant at the lowest dose group (0.8 mg/kg bw/d).

A three-fold increase in serum cholesterol levels was observed at the highest dose (75.8 mg/kg bw/d), which demonstrates a serious perturbation in homeostasis of lipids and lipoproteins. The increase is considered as adverse since hypercholesterinemia has an impact on the development of coronary arterial diseases. Also, the increase in hepatic thiobarbituric acid reactive substances (TBARS) indicates dysfunction in lipid metabolism. According to the study authors, the significance of the dose related decrease in serum LDH is not clear. Adverse effects such as liver disease, myocardial infarcts and hemolysis is rather associated with increase and not decrease of the enzyme. In the study of Poon *et al.* (1999) BCPS application had no significant influence on N-acetylglucosaminidase (NAG), protein and haemoglobin levels in the urine. Hepatic liver enzyme induction was also observed in the study of Mathews *et al.* (1996). However, comparison of the results does not allow a clear pattern of enzyme induction to be identified (e.g., which types of CYP450 are induced).

Other relevant observations:

In the 14-week rat study (NTP, 2001) the thymus weight reductions were statistically significant in both absolute and relative thymus weight, with the top dose being relatively severe and adverse (66% of control absolute weight, 82% of control as relative weight). In the female rats, there were statistically significant reductions in absolute thymus weight (77% of control at top dose), but the values for relative weight (93% of control at top dose) were not significantly different. These effects have been considered in the study design of the planned EOGRTS.

In the 14-week study in rat the only neurotoxicological finding observed was a statistically significant decrease in landing hindlimb footsplay of male rats in the 65 mg/kg bw/day dose group (-14.8%, $p \leq 0.01$), a similar effect was not evident in female rats. No data for 200 mg/kg bw/day (top dose) were presented in this study. In the 14-week study in mice the only neurotoxicological finding observed was a statistically significant decrease in hindlimb grip strength in males at 6 mg/kg bw/day. However, no significant changes were observed at 19 mg/kg bw/day and 65 mg/kg bw/day. The top dose was not examined.

Moreover, it is noted that there is a concern for neurotoxicity based on neurotoxic effects of structural analogues like polychlorinated biphenyls.

In the 14-week rat study also the incidence of nephropathy was increased in females at dose levels of 65 or 200 mg/kg bw/d. Dose-related increase in severity of nephropathy was also observed in male rats. The male rats had also statistically significant relative and absolute right kidney weight increase at the highest two groups, whereas the female rats had only relative right kidney weight increase at the highest two dose groups.

In the oral 14-week rat study a statistically significant increase was observed at 19 mg/kg bw/d for relative testis weight (7.9%, $p \leq 0.01$) and for the relative and absolute testis weight at 65 mg/kg bw/day (17.1% for relative weight, $p \leq 0.01$, and 5.3% for absolute weight, $p \leq 0.05$) and 200 mg/kg bw/d (30% for relative weight, $p \leq 0.01$, and 3.4% for absolute weight, $p \leq 0.05$). In female rats, ovaries and uterus weight were not changed. In the 14-week toxicity study in mice also a significant increase of relative right testis weight was observed in the two highest dose groups (165 mg/kg bw/d: 9.2%, 480 mg/kg bw/d: 17.6 %, both $p<0.01$). Relative weight of ovaries was significantly increased from 50 mg/kg bw/d onwards (16.9% at 50 mg/kg bw/day, $p<0.05$). The relative weight of uterus was increased in the two highest dose groups (47.1% at 165 mg/kg bw/d and 40.4% at 480 mg/kg bw/d, both $p<0.01$).

Conclusion:

It is concluded that the main target organ of BCPS toxicity is the liver. Liver weight increase in absence of pathological changes (such as degenerative lesions, cell proliferation and necrosis) is considered to be an adaptation. Increased liver weight and centrilobular hypertrophy might be considered as adaptive response (CLP Annex I, 3.9.2.8.1 (d)).

The reviewed data also indicate some histopathological evidence of structural degeneration and necrotic changes. Based on the current data set it cannot be unambiguously excluded that other mechanisms might lead to adverse effects e.g., oxidative stress. For example, it is mentioned in the NTP report (NTP, 2001) that adverse effects may possibly arise from increased mixed-function oxidase activities that cause altered sensitivities toward hepatotoxins or carcinogens.

However, comparing the effect levels with the limit for classification, it can be summarised that adverse effects (e.g., liver necrosis) occur mostly above the limit for classification and if effects were observed below the limit of classification (e.g., centrilobular degeneration in 2-year rat study, females) the severity was only minimal to mild and therefore not considered adverse.

Furthermore, organ weight changes of the thymus and of testis have been observed and there is some concern for neurotoxicity. An EOGRTS with the cohorts 1A and 1B (Reproductive toxicity) and cohort 3 (Developmental immunotoxicity: due to observed effects on thymus) is pending.

5. Environmental hazard assessment

Not relevant for the identification of the substance as SVHC in accordance with Article 57 point (e) of REACH.

6. Conclusions on the SVHC Properties

6.1 CMR assessment

Not relevant for this assessment.

6.2 PBT and vPvB assessment

6.2.1 Assessment of PBT/vPvB properties

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

According to the ECHA guidance (ECHA 2017a, R.11), the weight-of-evidence determination by expert judgement enables the use of all (screening and assessment) information types listed in Section 3 of Annex XIII of the REACH Regulation in the PBT/vPvB assessment for comparing with the criteria, although not all of these information types can be directly (numerically) compared with the criteria.

6.2.1.1 Persistence

BCPS is hydrolytically stable. The QSAR calculations indicate a half-life of BCPS in the atmosphere (gas-phase) of 54.7 days (12-hours) with OH radicals, this value might be an underestimation considering that a fraction is sorbed to airborne particles and resistant to atmospheric oxidation by hydroxyl radicals. For phototransformation in other media no data are available. Abiotic degradation is not expected to occur and it is not considered a relevant route for degradation.

For the persistence assessment of bis(4-chlorophenyl) sulphone, most weight is given to half-lives measured within the water-sediment simulation test according to OECD TG 308 and GLP (Unpublished study report, 2014). The test is considered reliable without restrictions with a Klimisch score of 1. Half-lives from such tests can be directly compared with the P/vP criteria stated in Annex XIII of REACH. Based on the half-life data, the vP criterion is fulfilled for the sediment (degradation half-lives > 180 days).

Under the applied conditions the $DT_{50,deg}$, 20°C half-life values were 394.3 and 1287.2 days in the Goose and Tilft water-sediment system, respectively. Temperature-corrected $DT_{50,\ deg}$, 12°C were 842 and 2748 days. Based on this water-sediment simulation study (OECD TG 308), it can be concluded that BCPS is very persistent in sediment (degradation half-lives >180 days).

The composition of non-extractable residues (NER) in sediment is unknown. In this particular case, when calculating the $DT_{50,deg}$, NER was not added to the parent substance concentration (i.e., it was assumed that NER represented irreversibly bound residues), as it would not change the vP conclusion. Noteworthy, the amount of NER increased over time and reached a maximum of 15.2% of the applied radioactivity. Assuming intact BCPS as part of NER would increase the half-lives.

The negligible degradability of BCPS in the simulation test is substantiated by the very low mineralisation rate (volatile CO_2) of max 0.5%AR after 100 days.

Results from a ready biodegradability screening test (NITE, 1999) are used as supporting information, which show negligible degradation. BIOWIN predictions are in line with the experimental data as they indicate that BCPS fulfils the screening criteria and it can be considered as potentially P or vP. Further monitoring data show the presence of the substance in various environmental media (e.g., Norström, 2010; UK Environment Agency's National Laboratory Service, unpublished).

6.2.1.2 Bioaccumulation

Based on all lines of evidence and taking into consideration the uncertainties of the monitoring data, sample size and limited data for other air-breathing organisms, it is concluded that BCPS is very bioaccumulative, and thus qualifies as vB.

Aquatic bioaccumulation

- The screening criterion for bioaccumulation for aquatic organisms based on measured log Kow of 3.9 (OECD TG 107) is not fulfilled. Additionally, the predicted BCF values indicate a low to moderate bioaccumulation potential of BCPS in fish.

- An experimentally derived BCF value of 82 (NITE, 2001) is considered to be reliable with restriction.

Biomagnification

- Field BMF values significantly higher than 1 have been found for BCPS thus indicating a very high bioaccumulation potential. In total, three food chains in the Baltic region and in Austria (fish - guillemot, fish – cormorants, fish - grey seals) were identified with BMFs >1.

- Field BMF values (fish, bird)

Fish, guillemots: The concentrations of BCPS in herring between 1998 and 2008 were in the range between 17 – 58 ng/g l.w., concentration seems to stay at a constant level of around 30 ng/g l.w. in herring obtained from Sweden, Poland and Lithuania (Norström *et* al., 2004 and 2010). The concentration in herring muscle in 1998 was between 29-31 ng/g l.w. (Norström *et* al., 2004, Sweden, n=20). There was no obvious trend between country or sampling location (Norström *et* al., 2010). Therefore, it seems reasonable to take the fish muscle BCPS level of around 30 ng/g l.w. and to compare it with the BCPS concentrations found in guillemot breast muscle of 1600 ng/g l.w. (n=5) and 1900 ng/g l.w. (in 1989) from the Baltic region (Norström et al., 2004). Calculated field **$BMF_{guillemot\ breast\ muscle,\ herring\ muscle}$ of 53 to 63**, indicate biomagnification of BCPS over food chains. It needs to be noted, that location and time of sampling varied. However, based on the consistent measured levels in fish from the Baltic Sea over several years, it is reasonable to conclude that BCPS biomagnifies over food chains. Further support for biomagnification comes from avian eggs (Table 38), which are used as matrix to investigate contaminants, as its composition directly reflects that of maternal tissues (e.g., Drouillard and Norstrom, 2001). As mentioned within the Drouillard and Norstrom (2001) publication egg-to-maternal tissue concentration is often less than one (typically in the order of 0.3 – 0.7), but depends on fat reserves of the female, clutch size and physico-chemical factors of the substances. Based on the analysed concentration in eggs, the BCPS concentration in female's tissue such as muscle would have been very likely in the same order or even higher. In total, 45 eggs have been analysed between 1971 – 2003, showing a geometric mean BCPS concentration of 1118 ng/g l.w. using the values from Jörundsdóttir *et* al.

(2006 and 2008). Herring was taken between 1998 – 2008, showing a concentration of around 30 ng/g l.w. (Norström *et* al., 2004 and 2010), this would yield a field **$BMF_{guillemot\ eggs,\ herring\ muscle}$** of **37**.

Fish, cormorants: The BCPS concentration was higher in fish-eating cormorants (breast muscle arithmetic mean: 16.3 ng/g fat, n=6, sample date: 2019) than in fish (mean whole fish: 4.9 ng/g fat, n = 8, sample date: 2019), which indicates that BCPS biomagnifies. In this case the field **$BMF_{cormorant\ breast\ muscle,\ whole\ fish}$ value** is **3.2**, which is significantly higher than 1 and can therefore be considered as an indication for very high bioaccumulation (ECHA, 2017). Further when comparing the whole fish concentration with liver concentration this would yield a field **$BMF_{cormorant\ liver,\ whole\ fish}$** of **10.9**. One cormorant had ingested fish, with a BCPS level of 5.5 ng/g fat, the BCPS level in the cormorant breast muscle was 23 ng/g fat, suggesting a BMF of 4.2.

- Field BMF values (herring, seals)

Fish, grey seals: The concentrations of BCPS in herring muscle between 1998 and 2008 were in the range between 17 – 58 ng/g l.w., concentration stays in herring at a certain level of around 30 ng/g l.w. obtained from Sweden, Poland and Lithuania (Norström *et* al., 2004 and 2010). It is therefore reasonable to take the fish level of around 30 ng/g l.w. and to compare it with the concentrations found in liver (median concentration: 200 ng/g l.w; sample date: 2000-2001) and blubber (concentration: median 60 ng/g l.w.; sample date: 1997) from grey seals from the Baltic region. A field BMF values results in **$BMF_{herring\ muscle,\ seals\ liver}$ values of 6.7** and a field **$BMF_{herring\ muscle,\ seals\ blubber}$** of **2**. However, location and time of sampling varied but based on the consistent measured levels in fish form the Baltic Sea over several years, BCPS biomagnifies in seals.

Field data

Several field studies measuring the concentration of BCPS are available from 1971 – 2019 (ref. Annex I). There is evidence, that BCPS was taken up and detected above Limit of Detection (LOD) in different wildlife species (marine and freshwater fish, grey seals, birds, mink, otters) throughout aquatic food chains, including top predatory fish, as well as grey seals *Halichoerus grypus* and fish-eating birds (like e.g., white tailed-sea eagle, guillemot, cormorants). Data were mostly generated for the Baltic region, but also include remote areas (Arctic) and data from North America, Austria, Black Sea and Danube delta.

- Highest BCPS levels constant over 30 years were detected in fish-eating bird eggs (high trophic level)

From all biota samples analysed so far, the BCPS levels detected were highest in guillemot eggs from the island Störa Karlsö, Sweden (760 - 2600 ng/g l.w., geometric mean: 1118 ng/g l.w., period: 1971 - 2003). BCPS was found in an at least constant level in eggs of the fish-feeding bird guillemot from 1971 to 2003 (Jörundsdóttir *et* al., 2006 and Jörundsdóttir *et* al., 2008).

- High BCPS levels in seals

The highest BCPS value (=480 ng/g l.w.) was found in grey seal blubber in an unhealthy 11-year old individual (Norström et al., 2004). Larsen *et* al., 2004 investigated lung, liver and blubber from grey seals from Sweden. The target organ of BCPS is the liver, exhibiting the highest concentrations (median = 200 ng/g l.w.; range 55 – 700 ng/g l.w., n=10). The concentration in the blubber was lower than in liver, which was in the range of 41 – 240 ng/g l.w (median 60 ng/g l.w., n=10).

- Recent data (Hornek-Gausterer *et* al., 2021)

In predatory fish species (2019, Austria, Danube) and cormorant samples (2019, Austria, samples from liver and breast muscle) BCPS was detected with 100% detection frequency. Levels in freshwater fish ranged between 1.3 and 9.3 ng/g fat. BCPS levels in cormorants breast muscle were in the range of 4.3 to 40 ng/g fat (arithmetic mean: 16.3 ng/g fat, n=6) and 28 to 86 ng/g fat (arithmetic mean: 53.5 ng/g fat, n=6) in the liver samples. But comparing the BCPS concentrations of cormorants' breast muscle from 2019 (mean: 16 ng/g fat, n=6) to the concentrations from 2001 – 2005 (mean: 8.9 ng/g fat, n=5), indicates that BCPS level is increasing, despite the small sample size and unknown food intake during the migration route of the individuals. Further, the mean BCPS concentration in sub-adult cormorants was 8.85 ng/g fat and the concentration in adults revealed mean BCPS concentrations of 17.7 ng/g fat, indicating an increase in BCPS concentration in breast muscle with age. But due to the low sample size and as the results are not statistically significant, no final statement can be made.

Bioaccumulation in air-breathing organisms

- BCPS is taken up by organisms and humans and detected in various wildlife species.
- Screening criteria for bioaccumulation in air-breathing organisms are fulfilled

  Screening criteria[24] for air-breathing organisms have been established based on log K_{OW} > 2 and log K_{OA} > 5. The measured log K_{OW} of 3.9 (OECD TG 107) and the estimated log K_{OA} value of 9.2 (KOAWIN v.1.10) indicating, despite the low to moderate bioaccumulation potential in fish, a bioaccumulation potential for BCPS in air-breathing terrestrial and marine wildlife, as well as humans. Kelly *et* al. (2004) mentioned BCPS as an example for a hydrophilic compound to exhibit such bioaccumulation potential.
- BCPS exhibits a very long half-life in rats, which exceeds the recently established threshold values, and has a high affinity to adipose tissue.

  A very long terminal half-life of 12 days was observed in adipose tissue in rats after single i.v. application (ref. to 4.1 Toxicokinetics). BCPS is mainly distributed to adipose tissue and the affinity to adipose tissue is high. Accelerated clearance was observed after repeated dosing and a steady state was observed after 2-3 weeks. This observation can be attributed to liver enzyme induction and enhanced clearance. Liver metabolism might vary between species, e.g., it is known that the half-lives for polychlorinated biphenyls are much shorter in rats than in humans mostly due to a higher metabolism rate in rats.
- BCPS detected in human liver

  BCPS has been detected in human liver samples (Ellerichmann *et* al., 1998) while liver is a target organ of BCPS toxicity in rats and mice.
- In a benchmark approach, the concentrations of known structurally unrelated POP substances (with known vB properties) were compared with BCPS in species at the top of the food chain. The results for BCPS lie within the range of known POPs.

To conclude, while screening information and a measured, very limited BCFss value indicate a low to moderate bioaccumulation potential for fish, there is sufficient evidence that BCPS bioaccumulates in air-breathing organisms. Rat toxicokinetic data demonstrate that BCPS is rapidly distributed out of the blood into tissues, with adipose tissue as major storage site and the elimination is slow. Based on the derived terminal half-life in adipose

[24] https://echa.europa.eu/documents/10162/13632/information_requirements_r7c_en.pdf

tissue a BMF higher than 1 is anticipated for air-breathing mammals.
Monitoring data further supports findings from toxicokinetic data by the fact that the substance has been found in well detectable and partly very high concentrations in predatory organisms at the top of food-chains (e.g., fish-eating birds) and also in human liver samples. Further lower line of evidence comes from field BMF values in three food-webs (fish – guillemot, fish – cormorants, fish – seals), which show BMF values significantly higher than 1 and BCPS concentrations in biota, which are in the range of known POPs (see Table 39).

6.2.2 Summary and overall conclusions on the PBT and vPvB properties

A weight-of-evidence determination according to the provisions of Annex XIII of REACH is used to identify bis(4-chlorophenyl) sulphone (referred to hereinafter as BCPS) as vPvB. All available relevant information (such as the results of standard tests, monitoring and modelling, and (Q)SAR results) was considered together in a weight-of-evidence approach.

According to the ECHA guidance (ECHA 2017a, R.11), the weight-of-evidence determination by expert judgement enables the use of all (screening and assessment) information types listed in Section 3 of Annex XIII of the REACH Regulation in the PBT/vPvB assessment for comparing with REACH Annex XIII criteria, although not all of these information types can be directly (numerically) compared with the criteria.

Persistence

Based on the weight-of-evidence assessment of all available relevant information BCPS fulfils the P and vP criteria of REACH Annex XIII.

The following lines of evidence were considered in the assessment:

- BCPS is considered as hydrolytically stable. Furthermore, photodegradation in air for BCPS is unlikely to be a significant degradation pathway in the environment (atmospheric half-life is expected to be higher than 54.7 days).

- BCPS is not readily biodegradable according to a reliable OECD TG 301C study and meets the screening criteria P and vP. BIOWIN predictions are in line with the experimental data as they also indicate that BCPS screens as potentially P or vP.

- Based on a water-sediment simulation test according to OECD TG 308 (reliable without restrictions), the vP criterion is fulfilled for the sediment. Under aerobic conditions at 20°C, the $DT_{50,\ deg}$ values were 1287.2 and 394.3 days in the Tilft and Goose water-sediment systems, respectively. Temperature corrected $DT_{50,\ deg}$ values at 12°C are between 842 – 2748 days.

- In the OECD TG 308 study no degradation products of BCPS ≥5% of applied radioactivity (AR) at two consecutive sampling intervals were observed and $^{14}CO_2$ formation was ≤ 0.5 % of AR.

- Monitoring data showed the presence of the substance in environmental media (e.g., data from UK).

For the persistence assessment of BCPS, most weight is given to half-lives measured from reliable and well documented GLP and OECD conforming studies. Half-lives from such tests can be directly compared with the P/vP criteria and clearly result in very high persistence. Screening tests, QSAR data and monitoring data support the findings from the simulation test.

As an overall conclusion, based on the above information used in a weight-of-evidence approach, it is concluded that BCPS meets the 'persistent' 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 its persistent and very persistent (P/vP) properties in sediment (degradation half-lives > 180 days).

Bioaccumulation

Using a weight-of-evidence assessment of all the data available, BCPS meets the B and vB criteria according to Annex XIII of REACH.

The assessment is based on the following lines of evidence:

- The screening criterion for bioaccumulation for aquatic organisms based on measured log K_{OW} of 3.9 (OECD TG 107) is not fulfilled. Additionally, the predicted BCF values indicate a low to moderate bioaccumulation potential of BCPS in fish. An experimentally derived BCFss value of 82 (NITE, 2001) is considered to be reliable with restriction . There is no evidence for a significant bioaccumulation in fish.

- Screening criteria for air-breathing organisms have been established based on log K_{OW} > 2 and log K_{OA} > 5. The measured log K_{OW} for BCPS is 3.9 and the estimated log K_{OA} value is 9.2 (KOAWIN v.1.10), indicating, despite the low to moderate bioaccumulation potential in fish, a biomagnification potential for BCPS in air-breathing terrestrial and marine wildlife, as well as humans.

- BCPS is taken up by organisms and humans and detected in various wildlife species.

- High BCPS levels were detected in fish-eating bird eggs (geometric mean: 1118 ng/g l.w. period: 1971 -2003) and seals (liver median: 200 ng/g l.w.; blubber median: 60 ng/g l.w.).

- Results from toxicokinetics studies in rats demonstrate, that BCPS is readily adsorbed and rapidly distributed to lipid-rich tissues. The substance is very slowly excreted and exhibits a very long terminal half-life of 12 days in adipose tissue (after single intra-venous application in rats) which is indicative that BCPS is very bioaccumulative in adipose tissue. Based on this observation a biomagnification factor (BMF) value higher than 1 is anticipated for air-breathing mammals.

- A BMF value significantly higher than 1 can be considered as an indication for very high bioaccumulation. Field BMF values significantly higher than 1 have been found for BCPS. In total, three food chains (fish – guillemot, fish – cormorants, fish – seals) were identified with BMFs >1. The locations of these food webs are in the Baltic region and in Austria.

- In a benchmark approach, the concentrations of known structurally unrelated POP substances (with known vB properties) were compared with BCPS in species at the top of the food chain. Results for BCPS are in the range of known POPs.

- BCPS was investigated in post-mortem human liver samples and detected in all of them while liver is a target organ of BCPS toxicity in rats and mice.

- The applied QSAR predictions for half-lives in humans, birds and fish are considered more uncertain for the B assessment than experimental or monitoring data and they are given a low weight.

To conclude, while screening information and a measured BCFss value indicate a low to

moderate bioaccumulation potential for fish, there is sufficient evidence that BCPS bioaccumulates in air-breathing organisms. Rat toxicokinetic data demonstrate that BCPS is rapidly distributed out of the blood into tissues, with adipose tissue as major storage site and the elimination is slow. Based on the derived terminal half-life in adipose tissue a BMF higher than 1 is anticipated for air-breathing mammals.

Monitoring data further supports findings from toxicokinetic data by the fact that the substance has been found in well detectable and partly very high concentrations in predatory organisms at the top of food-chains (e.g., fish-eating birds) and also in human liver samples. Further but lower line of evidence comes from field BMF values in three food-webs (fish – guillemot, fish – cormorants, fish – seals), which show BMF values significantly higher than 1 and BCPS in biota concentrations, which are in the range of known POPs.

Overall, taking all available information together in a weight-of-evidence determination, thereby considering high concentrations of BCPS in biota with a potential of biomagnification in certain food chains and a long half-life in rats, a high bioaccumulation potential of BCPS has been identified. Annex XIII, points 3.2.2. (b) and (c) of the REACH Regulation require that: detection of elevated levels in biota compared to levels in their surrounding environment, data from the toxicokinetic behaviour of the substance and information on the ability of the substance to biomagnify in the food chain are considered. Therefore, it is concluded that the 'bioaccumulation' criterion (B) and the 'very bioaccumulative' criterion (vB) of REACH Annex XIII are fulfilled.

Conclusion on vPvB properties

In conclusion, BCPS is identified as a vPvB substance 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.

6.3 Assessment under Article 57(f)

Not relevant for the identification of the substance as SVHC in accordance with Article 57 point (e) of REACH.

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Annex I – Monitoring data in biota

Table 44: BCPS levels in different organisms from 1971 until 2019 reported in literature, * median levels

Species/ No. ind. (n)	Age or gram /length	Tissue	Trophic level	BCPS ng/g l.w.	Average values ng/g l.w.	LOD/LOQ	Location	Year	Reference	Trend
FISH										
salmon (*Salmo salar*) 1 pool, n=10	-	muscle	low/ middle	8.7	**8.7**	LOD = 0.2 ng; LOQ = 3 * LOD	Gotland, Sweden	1971	Norström *et al.*, 2004	
salmon (*Salmo salar*) 2 pool, n=4, total 8	-	muscle	low/ middle	31; 33	**32**	LOD = 0.2 ng; LOQ = 3 * LOD	Gotland, Sweden	1996	Norström *et al.*, 2004 in Norström et *al.*, 2010, in Norström PhD thesis 2006	⇧
arctic char (*Salvelinus alpinus*) n=10	-	muscle		n.d	**n.d**	LOD = 0.47 ng/g l.w.	Fresh water lake (Vättern), Sweden	1972	Norström *et al.*, 2004	
arctic char (*Salvelinus alpinus*) n=5	-	muscle		-	**1.8**	LOD = 1.1 ng/g l.w.	Fresh water lake (Vättern), Sweden	1996	Norström *et al.*, 2004	⇧
arctic char (*Salvelinus alpi nus*) n=10	-	muscle		n.d.	**n.d.**	LOD = 0.2 ng; LOQ = 3 * LOD	Remote area, Lake, Abiskojaure, Sweden	1999	Norström *et al.*, 2004	
perch (*Perca fluviatilis*) n=30	2 years old	muscle	low/ middle	40-100	-	n.i; recovery study and blank samples analysed	Latvia	1994	Olsson and Bergmann, 1995 in Norström *et al.*, 2004 and Norström PhD	

Species/ No. ind. (n)	Age or gram /length	Tissue	Trophic level	BCPS ng/g l.w.	Average values ng/g l.w.	LOD/LOQ	Location	Year	Reference	Trend
									Thesis, 2006	
perch n=10	2 years old, 15-18cm, app. 45g	muscle	low/ middle	70-88	**72**	n.i; recovery study and blank samples analysed	Daugavgriva (influenced by industrial discharge), Latvia	1994	Olsson and Bergmann, 1995	
perch n=10	2 years old 15-18cm, app. 45g	muscle	low/ middle	52-100	**76**	n.i; recovery study and blank samples analysed	Salacgriva (without local pollution), Latvia	1994	Olsson and Bergmann, 1995	
perch n=10	2 years old, 15-18cm, app. 45g	muscle	low/ middle	40-78	**56**	n.i; recovery study and blank samples analysed	Lielirbe (without local pollution), Latvia	1994	Olsson and Bergmann, 1995	
perch (*Perca fluviatilis*) n=62	2 years old	muscle	low/ middle	38 - 100	-	n.i; recovery study and blank samples analysed	Latvia	1994-95	Olsson *et al*. 1999 in Norström *et al.,* 2004 and Norström PhD Thesis, 2006	
perch (*Perca fluviatilis*)	2 years old	muscle	low/ middle	56-88	71	n.i., recovery analysed	Daugavgriva (influenced by industrial discharge), Latvia	1994	Olsson *et al.,* 1999	
perch (*Perca fluviatilis*)	2 years old	muscle	low/ middle	69-98	82	n.i., recovery analysed	Daugavgriva (influenced by industrial discharge), Latvia	1995	Olsson *et al.,* 1999	⇧
perch (*Perca fluviatilis*)	2 years old	muscle	low/ middle	52-100	75	n.i., recovery analysed	Salacgriva (without local	1994	Olsson *et al*., 1999	

Species/ No. ind. (n)	Age or gram /length	Tissue	Trophic level	BCPS ng/g l.w.	Average values ng/g l.w.	LOD/LOQ	Location	Year	Reference	Trend
							pollution) (=Kurmrags), Latvia			
perch (*Perca fluviatilis*)	2 years old	muscle	low/ middle	38-71	61	n.i., recovery analysed	Salacgriva (without local pollution) (=Kurmrags), Latvia	1995	Olsson *et al,* 1999	
perch (*Perca fluviatilis*)	2 years old	muscle	low/ middle	40-78	55	n.i., recovery analysed	Lielirbe (without local pollution), Latvia	1994	Olsson *et al.,* 1999	
perch (*Perca fluviatilis*)	2 years old	muscle	low/ middle	46-72	63	n.i., recovery analysed	Lielirbe (without local pollution), Latvia	1995	Olsson *et al.,* 1999	
perch (*Perca fluviatilis*) n=23	2-4 years old	muscle	low/ middle	28-190	**-**	n.i.	Latvia	1997	Valters *et al.,* 1999 *in* Norström al., 2004 and and Norström PhD Thesis, 2006	
perch (*Perca fluviatilis*) n=2	one 2 or 3 years old, one 4 years old	muscle	low/ middle	48-57	**53**	n.i	Lielupe, Emburga, Latvia	1997	Valters *et al.,* 1999	-
perch (*Perca fluviatilis*) n=4	three 2 or 3 years old, one 4 years old	muscle	low/ middle	74-120	**94**	n.i.	Lielupe, Kalnciems, Latvia	1997	Valters *et al.,* 1999	
perch (*Perca fluviatilis*) n=4	one 2 or 3 years old	muscle	low/ middle	140-190	**160**	n.i.	Lielupe, Sloka, Latvia	1997	Valters *et al.,* 1999	
perch (*Perca fluviatilis*) n=5	one 2 or 3 years old	muscle	low/ middle	39-58	**48**	n.i.	Daugava, Lielvarde, Latvia	1997	Valters *et al.,* 1999	
perch	one 2 or 3	muscle	low/ middle	28-38	**32**	n.i.	Dole, Latvia	1997	Valters *et al.,*	

Species/ No. ind. (n)	Age or gram /length	Tissue	Trophic level	BCPS ng/g l.w.	Average values ng/g l.w.	LOD/LOQ	Location	Year	Reference	Trend
(*Perca fluviatilis*) n=5	years old								1999	
perch (*Perca fluviatilis*) n=3	one 2 or 3 years old	muscle	low/ middle	38-50	**44**	n.i.	Daugavgriva, Latvia	1997	Valters *et al*., 1999	
perch	-	muscle	low/ middle	38	**38**	LOD = 3 times the SD of blank sample noise. LOQ was used.	Near river Daugava, Latvia	2008	Norström *et al*., 2010	
perch (*Perca fluviatilis*) n=5	-	muscle	low/ middle	-	**15**	LOD = 0.2 ng; LOQ = 3 * LOD	Northern baltic coast, Island Holmön, Sweden	1998	Norström *et al*., 2004	
perch (*Perca fluviatilis*) n=5	-	muscle	low/ middle	-	**16**	LOD = 0.2 ng; LOQ = 3 * LOD	Northern baltic coast, Island Holmön, Sweden	1998	Norström *et al.,* 2004	
Perch (*Perca fluviatilis*) n=5	-	muscle	low/ middle	-	**35**	LOD = 0.2 ng; LOQ = 3 * LOD	Souther Baltic coast, Kvädöfijärden, Sweden	1998	Norström *et al*., 2004	
perch (*Perca fluviatilis*) n=5	-	muscle	low/ middle	-	**37**	LOD = 0.2 ng; LOQ = 3 * LOD	Souther Baltic coast, Kvädöfijärden, Sweden	1998	Norström *et al*., 2004	
perch	-	muscle	low/ middle	-	**20**	LOD = 3 times the SD of blank sample noise. LOQ was used.	Kvädöfjarden, Sweden	?	Norström *et al*., 2010	
perch	-	muscle	low/ middle	-	**36**	LOD = 3 times the SD of blank sample noise. LOQ was used.	Holmön, Sweden	?	Norström *et al*., 2010	
perch	-	muscle	low/ middle	-	**42**	LOD = 3 times the SD of blank sample noise.	Western coast of Saaremaa Island, Estonia	2008	Norström *et al*., 2010	

Species/ No. ind. (n)	Age or gram /length	Tissue	Trophic level	BCPS ng/g l.w.	Average values ng/g l.w.	LOD/LOQ	Location	Year	Reference	Trend
						LOQ was used.				
perch	-	muscle	low/ middle	-	**69**	LOD = 3 times the SD of blank sample noise. LOQ was used.	Coastal area near Sillamäe, Estonia	2008	Norström *et al.,* 2010	
perch	-	muscle	low/ middle	-	**46**	LOD = 3 times the SD of blank sample noise. LOQ was used.	Szczecin, Lagoon, Poland	2008	Norström *et al.,* 2010	
pelagic Baltic herring (Clupea haengus) n=10		muscle	low/ middle	-	29	LOD = 0.2 ng; LOQ = 3 * LOD	Baltic sea, Landsort, Sweden	1998	Norström *et al.*, 2004 in Norström et *al.,* 2010	
pelagic Baltic herring (*Clupea haengus*) n=10		muscle	low/ middle	-	31	LOD = 0.2 ng; LOQ = 3 * LOD	Baltic sea, Landsort, Sweden	1998	Norström *et al.*, 2004 in Norström *et al.*, 2010	
herring	-	-	low/ middle	-	33	LOD = 3 times the SD of blank sample noise. LOQ was used.	Kvädöfjärden, Sweden	-	Norström *et al,* 2010	
herring	-	-	low/ middle	-	17	LOD = 3 times the SD of blank sample noise. LOQ was used.	Fladen, Sweden	-	Norström *et al,* 2010	
herring	-	-	low/ middle	-	58	LOD = 3 times the SD of blank sample noise. LOQ was used.	Utlängen, Sweden	2008	Norström *et. al,* 2010	
herring	-	-	low/ middle	-	32	LOD = 3 times the SD of blank sample noise. LOQ was used.	Gulf of Gdansk, Poland	2008	Norström *et. al,* 2010	

Species/ No. ind. (n)	Age or gram /length	Tissue	Trophic level	BCPS ng/g l.w.	Average values ng/g l.w.	LOD/LOQ	Location	Year	Reference	Trend
herring	-	-	low/ middle	-	26	LOD = 3 times the SD of blank sample noise. LOQ was used.	Coastal area north from Klaipeda, Lithuania	2008	Norström *et. al,* 2010	
bream n=4	-	muscle	low/ middle	3,4 - 34	-	n.i.	Germany, freshwater (Elbe, Rhein)	1997	in Norström PhD Thesis 2006 and in Norström *et* al., 2004 and in Norström *et. al,* 2010	
SEALS										
grey seal n=3		blubber	high	53 - 88	70.5	n.i.	Hudiksvall, Sweden	1993	Olsson, 1995 in Norström,2006 and in PhD thesis Norström 2006	
grey seal 1 pool, n=5	-	blubber	high	-	68	LOD = 0.2 ng; LOQ = 3 * LOD	Swedish East coast, Sweden	1995 - 97	Norström *et* al., 2004 and in PhD thesis Norström 2006	
grey seal n=1	7 years old	blubber	high	49; 49	49	LOD = 0.2 ng; LOQ = 3 * LOD	Swedish East coast, Öxelösund, Sweden	1996	Norström *et al.,* 2004	
grey seal n=1	6 years old	blubber	high	73; 68	70.5	LOD = 0.2 ng; LOQ = 3 * LOD	Bothnian Bay, Sweden	1996	Norström *et al.,* 2004	
(Grey seal, n=1 unhealthy individual)	11 years old	blubber	high	470; 480	475	LOD = 0.2 ng; LOQ = 3 * LOD	Sthlm. Archipelago, Baltic coast, Sweden	1996	Norström *et al.,* 2004	
grey seal n=1	10 years old	blubber	high	98; 98	98	LOD = 0.2 ng; LOQ = 3 * LOD	Bothnian Sea, Sweden	1997	Norström *et al.,* 2004	
grey seal		blubber	high	41 - 240	60*; 140.5	LOQ for BCPS	Northern Baltic	2000-	Larsson *et al.,*	

Species/ No. ind. (n)	Age or gram /length	Tissue	Trophic level	BCPS ng/g l.w.	Average values ng/g l.w.	LOD/LOQ	Location	Year	Reference	Trend
n=10	6 – 16 years old					3.5 ng, calculated as 5 times the mean background amount (0.7 ng) in the blank solvent sample	sea, Bothanian Sea and Bay, Sweden	01	2004, cited in Norström,2006 and in PhD thesis Norström 2006	
grey seal n=10	6 – 16 years old	liver	high	55 - 700	200*, 377.5	LOQ for BCPS 3.5 ng, calculated as 5 times the mean background amount (0.7 ng) in the blank solvent sample	Northern Baltic sea, Bothanian Sea and Bay, Sweden	2000-01	Larsson *et* al., 2004 cited in Norström, 2006 and in PhD thesis Norström 2006	
grey seal n=10	6 – 16 years old	lung	high	21 - 98	29*, 59.5	LOQ for BCPS 3.5 ng, calculated as 5 times the mean background amount (0.7 ng) in the blank solvent sample	Northern Baltic sea, Bothanian Sea and Bay, Sweden	2000 - 2001	Larsson *et* al., 2004 in Norström, 2006 and in PhD thesis Norström 2006	
BIRDS										
black skimmer (*Rynchops niger*) n=4	unknown	egg	high	identified in 3 individuals	-	peak identified	Salt works colony, California, USA	2011	Millow *et al.,* 2015	Not possibl e
white-tailed sea eagle n=21	unknown	egg	high	n.d. - 16	-	n.i.	Baltic coast, Sweden	1971-76	Helander *et al.* 2002 in Norström et *al*., 2010	

Species/ No. ind. (n)	Age or gram /length	Tissue	Trophic level	BCPS ng/g l.w.	Average values ng/g l.w.	LOD/LOQ	Location	Year	Reference	Trend
white-tailed sea eagle n=21	unknown	egg	high	7.4 – 610	170 110	n.i.	Baltic coast, Sweden	1987 - 91	Helander *et* al. 2002, in PhD Thesis Norström 2006	↑
white-tailed sea eagle n=1	unknown	egg	high	500	-	n.i.	Söderköpnig, Sweden	1987	Olsson, 1995, in PhD Thesis Norström 2006	
guillemot (*Uria aalge*) n=5	unknown	replacement egg	high	1100 - 2600	1400*	Recovery 88% with amount of 0.06 µg, n=5	Stora Karlsö, island in the Baltic Sea, Sweden	1971	Jörunddsdottir *et al.* 2006	
guillemot (*Uria aalge*) n=5	unknown	replacement egg	high	1100 - 1900	1500*	Recovery 88% with amount of 0.06 µg, n=5	Stora Karlsö, island in the Baltic Sea, Sweden	1976	Jörunddsdottir *et al.* 2006	
guillemot (*Uria aalge*) n=5	unknown	replacement egg	High	810 – 1500	1200*	Recovery 88% with amount of 0.06 µg, n=5	Stora Karlsö, island in the Baltic Sea, Sweden	1981	Jörunddsdottir *et al.* 2006	
guillemot (*Uria aalge*) n=5	unknown	replacement egg	high	900 – 1400	1100*	Recovery 88% with amount of 0.06 µg, n=5	Stora Karlsö, island in the Baltic Sea, Sweden	1986	Jörunddsdottir *et al.* 2006	
guillemot (*Uria aalge*) n=5	unknown	replacement egg	high	780 – 1200	900*	Recovery 88% with amount of 0.06 µg, n=5	Stora Karlsö, island in the Baltic Sea, Sweden	1991	Jörunddsdottir *et al.* 2006	
guillemot (*Uria aalge*) n=5	unknown	replacement egg	high	770 – 980	890*	Recovery 88% with amount of 0.06 µg, n=5	Stora Karlsö, island in the Baltic Sea, Sweden	1996	Jörunddsdottir *et al*. 2006	
guillemot (*Uria aalge*) n=5	unknown	replacement egg	high	760 - 1400	1000*	Recovery 88% with amount of 0.06 µg, n=5	Stora Karlsö, island in the Baltic Sea, Sweden	2001	Jörunddsdottir *et al.* 2006	

Species/ No. ind. (n)	Age or gram /length	Tissue	Trophic level	BCPS ng/g l.w.	Average values ng/g l.w.	LOD/LOQ	Location	Year	Reference	Trend
guillemot (*Uria aalge*) n=10	unknown	egg	high	850-1300	1100*	Recovery 88% with amount of 0.06 µg, n=5	Stora Karlsö, island in the Baltic Sea, Sweden	2003	Values are from Jörunddsdottir et al. 2006 cited in Jörunddsdottir et al. 2008	⇧
Guillemot (*Uria aalge*) n=5	unknown	breast muscle	high	-	1900	LOD = 0.2 ng; LOQ = 3 * LOD	Stora Karlsö, island in the Baltic Sea, Sweden	1989	Norström *et al.,* 2004 in Norström *et al.,* 2010, in PhD Thesis Norström 2006	
guillemot (*Uria aalge*) n=5	unknown	breast muscle	high	-	1600	LOD = 0.2 ng; LOQ = 3 * LOD	Stora Karlsö, island in the Baltic Sea, Sweden	1989	Norström *et al*., 2004 in Norström *et* al., 2010, in PhD Thesis Norström 2006	
guillemot (*Uria aalge*) *n*=10	unknown	egg	high	5.1 – 8.8	6.4	LOQ = 3.2 ng/g fat	Vestmanna-eyjar Iceland	2002	Jörunddsdottir *et al*. 2009 Jörunddsdottir *et* al. 2008	
guillemot (*Uria aalge*) n=10	unknown	egg	high	4.5 - 16	6.7	LOQ = 3.2 ng/g fat	Sandøy, Faroe Islands	2003	Jörunddsdottir *et al*. 2009 Jörunddsdottir *et* al. 2008	
guillemot (*Uria aalge*) n=10	unknown	egg	high	3.3 - 10	6.2	LOQ = 3.2 ng/g fat	Bjørnøya, Norway	2005	Jörunddsdottir *et al.* 2009 Jörunddsdottir *et* al. 2008	
guillemot (*Uria aalge*) n=10	unknown	egg	high	6.3 - 17	10	LOQ = 3.2 ng/g fat	Hjelmsøya, Norway	2005	Jörunddsdottir *et al*. 2009 Jörunddsdottir *et* al. 2008	
guillemot (*Uria aalge*)	unknown	egg	high	n.d - 18	10	LOQ = 3.2 ng/g fat	Sklinna, Norway	2005	Jörunddsdottir *et al.* 2009	

Species/ No. ind. (n)	Age or gram /length	Tissue	Trophic level	BCPS ng/g l.w.	Average values ng/g l.w.	LOD/LOQ	Location	Year	Reference	Trend
n=10									Jörunddsdottir *et al.* 2008	
guillemot (*Uria aalge*) n=10	unknown	egg	high	850-1300	1100	LOQ = 3.2 ng/g fat	Stora Karlsö Sweden	2003	Jörundsdóttir *et al.,* 2008; Jörunddsdottir *et al.* 2009 Jörunddsdottir *et al.* 2008	
guillemot (*Uria aalge*)	unknown	egg	high	760 - 2600	1680	BCPS to 3.2 ng/g fat	Sweden	1971 - 2001	Jörunddsdottir *et al.,* 2009 in Norström *et* al., 2010	
guillemot (*Uria aalge*)	unknown	egg	high	5.1 – 8.8	7	BCPS to 3.2 ng/g fat	Vestmanna-eyjar, Iceland	2002	Jörundsdóttir *et al*., 2008; Jörunddsdottir *et* al., 2009 in Norström *et* al., 2010	
guillemot (*Uria aalge*)	unknown	egg	high	4.5 - 16	10.2	BCPS to 3.2 ng/g fat	Sandøy, Faroe Islands (remote)	2003	Jörundsdóttir *et al.,* 2008; Jörunddsdottir *et* al., 2009 in Norström *et al*., 2010	
guillemot (*Uria aalge*)	unknown	egg	high	3.3 - 10	6.5	BCPS to 3.2 ng/g fat	Bjørnøya = Bear Island, Norway	2005	Jörundsdóttir *et* al., 2008; Jörunddsdottir *et al*., 2009 in Norström *et al*., 2010	
guillemot (*Uria aalge*)	unknown	egg	high	6.3 -17	11	BCPS to 3.2 ng/g fat	Hjelmsøya, Norway	2005	Jörundsdóttir *et al*., 2008; Jörunddsdottir *et al*., 2009 in Norström *et al.,*	

Species/ No. ind. (n)	Age or gram /length	Tissue	Trophic level	BCPS ng/g l.w.	Average values ng/g l.w.	LOD/LOQ	Location	Year	Reference	Trend
									2010	
guillemot (*Uria aalge*)	unknown	egg	high	n.d. - 18	18	BCPS to 3.2 ng/g fat	Sklinna, Norway / North Sea	2005	Jörundsdóttir *et al.*, 2008; Jörunddsdottir *et al*., 2009 in Norström *et al.,* 2010	
herring gull (*Larus argentatus*) n=1	unknown	egg	high	identified	-	n.i.	Canada	1989	Letcher *et al*., 1995 cited in Norström *et al.,* 2006	
glaucous gull n=87		plasma	high	5.2 - 143	-	see below	Norway / North Sea	2002 and 2004	Verreault *et al.,* 2005 cited *in* Norström *et al*., 2010 and PhD thesis Norström 2006	
glaucous gull (male), n=42	unknown	blood (plasma)	high	8.15 – 143 ng/g wet weight	26.5 ± 10.8	LOD: 0.001 - 0.35 ng/g wet weight	Bear Island / Artic Norway	2002 and 2004	Verreault *et al.,* 2005	not possibl e
glaucous gull (female) n=42	unknown	blood (plasma)	high	5.24 – 58.8 ng/g wet weight	19.5 ± 3.56	LOD: 0.001 - 0.35 ng/g wet weight	Bear Island / Artic Norway	2002 and 2004	Verreault *et al*., 2005	not possibl e
common gull		eggs	high	ng/g w.w	0.20	n.i.	Urban area around Tromsø, Norway	2017	Screening program 2017 (2018)	
OTHER BIOTA										
mink		liver		ng/g w.w	0.53	n.i.	Arctic	2017	Screening program 2017 (2018)	

Species/ No. ind. (n)	Age or gram /length	Tissue	Trophic level	BCPS ng/g l.w.	Average values ng/g l.w.	LOD/LOQ	Location	Year	Reference	Trend
HUMAN										
human n=6		liver	high	~2-40 ng/g lipid	-	n.i.	Germany	-	Ellerichmann *et al.,* 1998 cited in Norström PhD Thesis 2006	

n.i. not indicated; * geometric mean concentrations

Annex II – Human health and Environmental hazard assessment

For detailed information on human health and environmental hazard assessment, see the SEV report finalised by the eMSCA in 2020 (Substance evaluation - CoRAP - ECHA (europa.eu)).