

## Weight-of-evidence in PBT assessment Examples from the [Candidate List](#)

Version	Changes	Date
Version 1	First edition	December 2023
Version 1.1	Minor editorial changes	January, 2024

Examples for substances that were identified as PBT/vPvB based on a complex *Weight-of-evidence* assessment.

Chemical name (Link)	EC No.	Conclusion	Year	Group	Basis for <i>Weight-of-evidence (WoE)</i> on selected endpoint(s)
<a href="#">Bis(4-chlorophenyl) sulphone (BCPS)</a>	201-247-9	vPvB	2023	N/A	<p><u>Bioaccumulation</u></p> <ul style="list-style-type: none"> <li>- Screening information (log <math>K_{ow}</math>=3.9) and QSAR predictions indicating low potential for bioaccumulation in fish, supported by experimentally derived <math>BCF_{ss}</math> (<math>BCF_{ss}</math> =82)</li> <li>- Screening information for air-breathing organisms (Log <math>k_{ow}</math> &gt;2 and Log <math>K_{oa}</math> &gt;5) met</li> <li>- Biomonitoring data indicating accumulation in humans and wildlife species over various trophic levels</li> <li>- Field BMFs &gt;1 (fish – guillemot, fish – cormorants, fish –seals)</li> <li>- Toxicokinetic studies in rats, showing high affinity to adipose tissue and long terminal half-life (elimination half-life=12 days)</li> <li>- Benchmark approach to concentrations of known structurally unrelated POP substances in species at the top of the food chain.</li> </ul>
<a href="#">Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-</a>	473-390-7	vPvB	2023	PFCs	<p><u>Persistence</u></p> <ul style="list-style-type: none"> <li>- Stability of the structure (C-F bond)</li> <li>- Screening information (OECD TG 310 showing 0% biodegradation over 28 days)</li> <li>- Structural similarity to analogue substances (perfluorocyclobutane) with long half-lives (&gt;1000 years) in the air compartment</li> </ul>

Chemical name (Link)	EC No.	Conclusion	Year	Group	Basis for <i>Weight-of-evidence (WoE) on selected endpoint(s)</i>
<a href="#">heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine</a>					<p><u>Bioaccumulation</u></p> <ul style="list-style-type: none"> <li>- Screening information based on calculated log <math>K_{ow}</math> (5.7) indicating high potential for bioaccumulation in aquatic organisms</li> <li>- Fish <math>BCF_K</math> and <math>BCF_{SS} &gt; 5000</math> and a low depuration rate constant (<math>K_2 = 0.0633 \text{ d}^{-1}</math>) derived based on a pilot OECD TG 305 study (aqueous exposure, without headspace due to high Henry's Law constant (<math>H=42400</math>)).</li> </ul>
<a href="#">Perfluoroheptanoic acid (PFHpA) and its salts</a>	243-518-4; 228-098-2; 206-798-9; 21049-36-5 (CAS no.)	PBT/vPvB/ ELOC (M)	2023	PFCs; PFHpA and salts	<p><u>Persistence</u></p> <ul style="list-style-type: none"> <li>- Stability of the structure (C-F bond).</li> <li>- Screening information on PFHxA, PFOA and PFNA and QSAR predictions, simulation tests (non-standard aerobic and anaerobic simulation studies on PFOA in water, sediment, and soil;) and comparison with previous conclusions on structural analogues (including PFOA<sup>1</sup> and other PFCAs identified as SVHC)</li> <li>- Monitoring data in remote areas</li> </ul> <p><u>Bioaccumulation</u></p> <ul style="list-style-type: none"> <li>- Toxicokinetic study and elimination half-lives in air-breathing organisms. Half-life 74 days and &gt; 76 days in pigs and humans respectively)</li> <li>- Highest measured elimination half-life in humans of 3.3 years. Observed build up over the years in humans</li> <li>- BMF for pigs of 2.7</li> </ul> <p>Fish bioaccumulation study (BCF), food web studies (BAF) and trophic magnification studies (TMF) showing low bioaccumulation or biomagnification in aquatic organisms <u>Mobility (ELOC)</u></p> <ul style="list-style-type: none"> <li>- Low adsorption potential (<math>\log K_{oc}=1.63-1.7</math>), high water solubility (&gt;1000 mg/L) for salts and dissociated forms of PFHpA</li> <li>- Monitoring data in groundwater and drinking water.</li> </ul>
<a href="#">Bis(2-ethylhexyl) tetrabromophthalate covering any of the individual isomers and/or combinations thereof</a>	247-426-5	vPvB	2023	brominated phthalates	<p><u>Persistence:</u></p> <ul style="list-style-type: none"> <li>- Screening information; 7% degradation in 28 days observed in an inherent degradation test OECD TG 302C and QSAR predictions</li> <li>- Estimated half-lives from a non-guideline outdoor mesocosm study with an artificial sediment (<math>DT50 &gt; 200</math> days)</li> <li>- Monitoring data in all environmental compartments and in remote areas</li> </ul> <p><u>Bioaccumulation</u></p> <ul style="list-style-type: none"> <li>- Screening information (<math>\log K_{ow}=10.2</math> and <math>\log K_{oa}=15.4</math>) indicating high potential for bioaccumulation in aquatic and air-breathing organisms</li> <li>- Fish dietary bioaccumulation studies and benchmarking (depuration rate constants and BMF)</li> <li>- In vitro biotransformation assay (liver microsomes) indicating low metabolism potential</li> <li>- Toxicokinetic information in rats and humans</li> </ul>

<sup>1</sup> Listed as POP under the Stockholm Convention.

Chemical name (Link)	EC No.	Conclusion	Year	Group	Basis for <i>Weight-of-evidence (WoE) on selected endpoint(s)</i>
<a href="#">1,1'-[ethane-1,2-diy]bisoxy]bis[2,4,6-tribromobenzene]</a>	253-692-3	vPvB	2023	brominated flame retardants	<ul style="list-style-type: none"> <li>- Field and biomonitoring data (TMF, BMF)</li> <li>- Ubiquitous presence in biota (mussel, fish, birds, mammals (including in human plasma) also in Arctic species such as ringed seal and polar bear)</li> </ul> <p><u>Persistence</u></p> <ul style="list-style-type: none"> <li>- Non-standard screening study with pre-adapted inoculum as screening study</li> <li>- Mesocosm studies in soil and water-sediment compartments</li> <li>- Benchmarking with other higher brominated flame retardants (PBDE, HBB and PBEB)</li> <li>- Monitoring data from sediment cores (20-40 year old sediment layers) and detection in remote areas</li> </ul> <p><u>Bioaccumulation</u></p> <ul style="list-style-type: none"> <li>- Log K<sub>ow</sub> (7.88-9.39, predicted).</li> <li>- Non-standard fish dietary bioaccumulation study with low depuration rate constant (0.0128day<sup>-1</sup>), long depuration half-life in fish (54 days) in fish muscle tissues, the derived BCF value from the OECD TG 305 BCF estimation tool and benchmarking (Dechlorane Plus (EC 236-948-9) and MCCP (EC 287-477-0)) as indication of slow depuration in fish</li> <li>- Field studies indicating biomagnification (TMF and BMF &gt;1)</li> <li>- Monitoring data from human serum, hair, and breast milk and from wildlife (including predatory species like polar bears) and remote areas</li> </ul>
Medium-chain chlorinated paraffins ( <a href="#">MCCP</a> )	287-477-0	PBT/vPvB	2021	Chlorinated Organics	<p>The PBT/vPvB assessment was performed at the congener group level but the tested materials were UVCB substances/block of substances/specific congener groups. When the congener groups were not individually monitored a Gaussian distribution was used to determine the congener groups present in the testing material in order to be able to conclude on the P, B and/or T properties at the congener group level..</p> <p><u>Persistence</u></p> <ul style="list-style-type: none"> <li>- OECD TG 308 on C<sub>14</sub> chlorinated n-alkane, 50 % Cl. Wt.</li> <li>- Modelling data for individual congener groups</li> <li>- Screening tests on different UVCB substances/Block of substances</li> <li>- Monitoring data (including in remote areas), including sediment core studies</li> </ul> <p><u>Bioaccumulation</u></p> <ul style="list-style-type: none"> <li>- OECD TG 305 (dietary) on C<sub>14</sub> chlorinated n-alkane, 50 % Cl. Wt. and OECD TG 305 (aqueous exposure) on C<sub>14</sub> chlorinated n-alkane, 45 % Cl. Wt. and on C<sub>15</sub> chlorinated n-alkane, 51 % Cl. Wt.</li> <li>- Toxicokinetic data on mammals</li> <li>- Bioaccumulation in aquatic invertebrates (daphnia), mussels, terrestrial species</li> <li>- BMFs (in muscles and livers) &gt;1 for snake-frog predator-prey relationship</li> <li>- TMFs &gt;1 and &lt;1</li> <li>- Modelling data for individual congener groups</li> <li>- Monitoring data (widespread in wildlife at all trophic levels (including predatory species) and in humans: blood, milk samples, umbilical cord blood and placenta which indicates that MCCP are</li> </ul>

Chemical name (Link)	EC No.	Conclusion	Year	Group	Basis for <i>Weight-of-evidence (WoE) on selected endpoint(s)</i>
					absorbed to some extent in humans and transfer to foetus), including biota from remote regions like the Arctic <u>Toxicity</u> Aquatic toxicity on the commercial C14-17, 52% CI wt. substance with determination of the congener groups present in the testing material supported by bioavailability for the test organisms (daphnia), structural similarity and mode(s) of action
<a href="#">Fluoranthene</a>	205-912-4	PBT/vPvB	2019 (2009 CTPHT )	PAH	<u>Bioaccumulation</u> 2000 < BCF fish < 5000 BCF mollusc > 5000
<a href="#">Pyrene</a>	204-927-3	PBT/vPvB	2019 (2009 CTPHT )	PAH	<u>Bioaccumulation</u> - BCF fish < 2000, - BCFs > 5000 for molluscs, crustaceans, oligochaete See also similar WoE approaches for B in <a href="#">Chrysene</a> (EC 205-923-4), <a href="#">Benzo[k]fluoranthene</a> <sup>2</sup> (EC 205-916-6) and <a href="#">Benzo[ghi]perylene</a> (EC 205-883-8)
<a href="#">D4</a>	209-136-7	PBT/vPvB	2018	Cyclic Siloxanes	<u>Persistence</u> - MSC opinion on P based on simulation and monitoring studies (2015) on D4 and D5 - OECD TG 308 Simulation tests (water-sediment; half-life=356 days and 242 days in anaerobic and aerobic sediment respectively) - Estimated degradation half-lives in sediment based on multimedia and fugacity modelling data and monitoring studies (half-life of 1 year in sediment). <u>Bioaccumulation</u> - MSC opinion on B (2015) - Fish bioconcentration studies - Fish dietary studies, elimination half-lives - Field data, monitoring data (D4-6 in predatory freshwater fish, various bird eggs, confidential long-term monitoring data on D4 and D5; cyclic volatile methyl siloxanes in blood of turtles, cormorants and seals in Canada, seafood and freshwater fish in Spain and in Norwegian fish See also <a href="#">D5 (EC 208-764-9)</a> . D5 identified as vPvB. When it contains ≥ 0.1%w/w D4 (EC No. 209-136-7) also PBT
<a href="#">D6</a>	208-762-8	PBT/vPvB	2018	Cyclic Siloxanes	<u>Persistence</u>

<sup>2</sup> Polycyclic aromatic hydrocarbons (PAHs) are listed in Annex III of the POPs Protocol and in Annex III of the POPs Regulation. PAHs are subject to release reduction provisions under (Art 6 of the POPs regulation). For the purposes of emission inventories, the following four indicator compounds shall be used: benzo(a)pyrene, benzo(b)fluoranthene, benzo(k)fluoranthene, and indeno(1,2,3-cd)pyrene.

Chemical name (Link)	EC No.	Conclusion	Year	Group	Basis for <i>Weight-of-evidence (WoE) on selected endpoint(s)</i>
					<ul style="list-style-type: none"> <li>- Screening tests: OECD TG 310 (4.5 % degradation after 28 days) and in-vitro non-guideline study on the anaerobic degradation in a municipal waste water treatment plant (30-18 % degradation after 60 days)</li> <li>- Read across from D4 and D5: modified OECD TG 308 study with minimised head-space volume and D5 (estimated half-life of 1200 days and 3100 days at 24 °C under biotic aerobic and anaerobic conditions respectively) and a similar simulation study with D4 ((degradation half-life 242 days in aerobic sediment and 365 days in anaerobic sediment); <u>Bioaccumulation</u></li> <li>- Fish BCF studies (BCF<sub>SS</sub>=1160 L/kg and BCF<sub>K</sub>=4419-12632 L/kg)</li> <li>- BCF up to ~2 400 L/Kg in aquatic invertebrates</li> <li>- Field data (TMF&gt;1): biomagnification and trophic magnification data.</li> <li>- Benchmarking with other known biomagnifying substances with TMF&gt;1</li> </ul> <p>D6 identified as vPvB due to its intrinsic properties. D6 is additionally identified as PBT when it contains ≥ 0.1% weight by weight (w/w) D4 (EC No. 209-136-7) D6 is furthermore identified as vPvB when it contains ≥ 0.1% (w/w) D4 (EC No: 209-136-7) or D5 (EC No. 208-764-9)</p>
<a href="#">Dechlorane Plus<sup>1</sup></a>	236-948-9; 135821-03-3 (CAS no.); 135821-74-8 (CAS no.)	vPvB	2018	Chlorinated Organics	<p><u>Persistence</u></p> <ul style="list-style-type: none"> <li>- Read-across to structural analogues (e.g. heptachlor and chlorendic acid)</li> <li>- Substance properties (hydrophobicity)</li> <li>- QSAR predictions: benchmarking the predictions with those for other POPs and biodegradation pathway considerations</li> <li>- Monitoring data in sediments (Sediment core from central Lake Ontario, fresh water and marine sediments)</li> <li>- Limited biotransformation in fish in fish bioaccumulation study.</li> <li>- Widespread detection in remote regions</li> </ul> <p><u>Bioaccumulation</u></p> <ul style="list-style-type: none"> <li>- Screening information based on estimated log K<sub>ow</sub> (&gt;9) and log K<sub>oa</sub> (&gt;5) indicating high potential for bioaccumulation in aquatic and air-breathing organisms</li> <li>- Long depuration half-life in fish dietary studies</li> <li>- Monitoring (widely dispersed in food chains (including predators), biota in concentration of concern, detected in human blood, placenta and breast milk)</li> </ul>
<a href="#">PFHxS &amp; salts<sup>1</sup></a>	-	vPvB	2017	PFCs: PFHxS & salts	<p><u>Persistence</u></p> <ul style="list-style-type: none"> <li>- Stability of the structure (C-F bond)</li> <li>- Screening and simulation tests with read-across (PFOS, PFOA)</li> </ul> <p><u>Bioaccumulation</u></p> <ul style="list-style-type: none"> <li>- Binding to proteins in blood and liver like other PFSA and PFCA</li> <li>- Field BMF &gt;1 in top predators (dolphins, glaucous gull, ringed seal, polar bear)</li> <li>- Detected in top predators (e.g. polar bear liver, human blood)</li> <li>- Toxicokinetic information, long elimination half-lives in humans (7-8 years) and other mammals (713 days in pigs, 141 d in male monkeys)</li> </ul>

Chemical name (Link)	EC No.	Conclusion	Year	Group	Basis for <i>Weight-of-evidence (WoE) on selected endpoint(s)</i>
<a href="#">PFDA &amp; salts<sup>3</sup></a>	206-400-3; 221-470-5; 3830-45-3 (CAS no.)	PBT	2016	PFCs: PFDA & salts	<p><u>Persistence</u></p> <ul style="list-style-type: none"> <li>- Stability of the structure (C-F bond).</li> <li>- Read-across with PFOA, PFNA and C<sub>11</sub>-C<sub>14</sub> PFCAs</li> </ul> <p><u>Bioaccumulation</u></p> <ul style="list-style-type: none"> <li>- Binding to protein and membrane phospholipids</li> <li>- Monitoring (in mammals, including polar bears, beluga whale and humans)</li> <li>- Long elimination half-lives in humans, blood concentrations increase with increasing age</li> <li>- Field BMFs &gt;1</li> <li>- TMF &gt;1</li> </ul> <p>See also similar WoE approach to <a href="#">PFNA &amp; salts</a> (EC 206-801-3)</p>
<a href="#">UV-350</a>	253-037-1	vPvB	2015	Benzo-triazoles	<p><u>Persistence</u></p> <ul style="list-style-type: none"> <li>- QSAR predictions</li> <li>- Screening data, read-across to UV-320, UV-328 and UV-327 (OECD TG 301B and C)</li> <li>- Water/sediment simulation test similar to OECD TG 308 (DT<sub>50</sub>, sed. &gt;&gt; 100 d); OECD TG 308 with read-across (EC 407-000-3); degradation product similar to UV-350</li> <li>- Field study (soil) and monitoring studies with read-across to UV-320 and UV-328</li> </ul> <p>Similar assessment as for <a href="#">UV-327</a></p>
<a href="#">UV-328<sup>1</sup></a>	247-384-8	PBT/vPvB	2014	Benzo-triazoles	<p><u>Persistence</u></p> <ul style="list-style-type: none"> <li>- Screening data (OECD TG 301B: 2-8% degradation after 28 days)</li> <li>- No water or sediment simulation tests on the substance</li> <li>- OECD TG 308 test with read-across substance M1</li> <li>- Field studies (DT<sub>50</sub> up to 223 days)</li> <li>- Monitoring data</li> </ul> <p>Similar WoE approach as for <a href="#">UV-320</a></p>
<a href="#">PFOA<sup>1</sup></a>	206-397-9	PBT	2013	PFCs: PFOA & salts	<p><u>Persistence</u></p> <ul style="list-style-type: none"> <li>- Stability of the structure (C-F)</li> <li>- Screening information (OECD TG 301C: 5% degradation after 28 days and OECD TG 301 F showing no degradation after 28 days)</li> <li>- Several non-standard tests (e.g. sewage sludge laboratory scale, mixed microbial cultures, microcosm, industrial site sediment, aerobic and anaerobic degradation)</li> <li>- Field monitoring data</li> </ul> <p><u>Bioaccumulation</u></p> <ul style="list-style-type: none"> <li>- Biomagnification in air-breathing mammals: TMFs &gt;1 and field BMFs &gt;1</li> <li>- Accumulation in humans, long half-lives in humans (2-4 years)</li> <li>- Detected in human blood and breast milk</li> </ul>

<sup>3</sup> POPRC has recommended the listing of LC-PFCAs in Annex A to the Convention. The listing will be decided by the COP in its 12th meeting (2025).

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					See also similar WoE approach to <a href="#">APFO</a> (EC 223-320-4)
<a href="#">C<sub>11</sub>-PFCA<sup>3</sup></a>	218-165-4	vPvB	2012	PFCs: C <sub>11</sub> - C <sub>14</sub> -PFCAs	<u>Persistence</u> <ul style="list-style-type: none"> <li>- Stability of the structure (C-F)</li> <li>- Read-across approach within C8-C14-PFCAs was applied for the persistence assessment.</li> <li>- structural similarity and the regular pattern of physico-chemical properties within the group of C11-14-PFCAs</li> </ul> <u>Bioaccumulation</u> <ul style="list-style-type: none"> <li>- BCF-values of C<sub>11</sub>-PFCA &gt; 5000</li> <li>- Read-across approach within C8-C14-PFCAs</li> <li>- Field BMFs</li> </ul>
<a href="#">C<sub>12</sub>-PFCA<sup>3</sup></a>	206-203-2				
<a href="#">C<sub>13</sub>-PFCA<sup>3</sup></a>	276-745-2				
<a href="#">C<sub>14</sub>-PFCA<sup>3</sup></a>	206-803-4				

## Abbreviations

APFO	Ammonium pentadecafluorooctanoate
BAF	Bioaccumulation factor
BCF	Bioconcentration factor
BCF <sub>K</sub>	Bioconcentration factor, kinetic
BCF <sub>SS</sub>	Bioconcentration factor, steady-state
BCPS	Bis(4-chlorophenyl) sulphone
BMF	Biomagnification Factor
CTPHT	Coal tar pitch, high temperature
D4	Octamethylcyclotetrasiloxane
D6	Dodecamethylcyclohexasiloxane
ELoC	Equivalent Level of Concern under REACH Article 57(f)
K <sub>oa</sub>	Octanol-air partition coefficient
K <sub>oc</sub>	Organic carbon normalized adsorption coefficient
K <sub>ow</sub>	n-octanol/water partition coefficient
K <sub>2</sub>	Depuration rate constant
MCCP	Medium-chain chlorinated paraffins
OECD	Organisation for Economic Co-operation and Development
PAH	Polycyclic aromatic hydrocarbon
PBT	Persistent bioaccumulative and toxic
PFCs	Perfluorocarbons
PFCA	Perfluoroalkyl carboxylic acid/ perfluoroalkyl carboxylate
PFDA	Perfluorodecanoic acid
PFHpA	Perfluoroheptanoic acid
PFHxS	Perfluorohexane-1-sulphonic acid
PFSA	Perfluoroalkane sulfonic acid
PFNA	Perfluorononanoic acid
PFOA	Perfluorooctanoic acid
POP	Persistent Organic Pollutant
POPRC	Persistent Organic Pollutant Review Committee
vPvB	Very Persistent and very Bioaccumulative
SVHC	Substance of very high concern
TG	Test guideline
TMF	Trophic magnification factor
UV-320	2-benzotriazol-2-yl-4,6-di-tert-butylphenol
UV-327	2,4-di-tert-butyl-6-(5-chlorobenzotriazol-2-yl)phenol
UV-328	2-(2H-benzotriazol-2-yl)-4,6-ditertpentylphenol
UV-350	2-(2H-benzotriazol-2-yl)-4-(tert-butyl)-6-(sec-butyl)phenol
WoE	Weight-of-evidence
Wt.	weight