Weight-of-evidence in PBT assessment

Examples from the Candidate List

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

<table>
<thead>
<tr>
<th>Chemical name (Link)</th>
<th>EC No.</th>
<th>Conclusion</th>
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<th>Basis for Weight-of-evidence (WoE) on selected endpoint(s)</th>
</tr>
</thead>
</table>
| Bis(4-chlorophenyl)sulphone (BCPS)       | 201-247-9  | vPvB       | 2023 | N/A   | **Bioaccumulation**  
|                                          |            |            |      |       | - Screening information (log $K_{ow}=3.9$) and QSAR predictions indicating low potential for bioaccumulation in fish, supported by experimentally derived $BCF_{ww}$ ($BCF_{ww}=82$)  
|                                          |            |            |      |       | - Screening information for air-breathing organisms ($Log \ K_{ow} >2$ and $Log \ K_{ow} >5$) met  
|                                          |            |            |      |       | - Biomonitoring data indicating accumulation in humans and wildlife species over various trophic levels  
|                                          |            |            |      |       | - Field BMFs >1 (fish – guillemot, fish – cormorants, fish –seals)  
|                                          |            |            |      |       | - Toxicokinetic studies in rats, showing high affinity to adipose tissue and long terminal half-life (elimination half-life=12 days)  
|                                          |            |            |      |       | - Benchmark approach to concentrations of known structurally unrelated POP substances in species at the top of the food chain.  
| Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,2,3,3,3- | 473-390-7  | vPvB       | 2023 | PFCs  | **Persistence**  
|                                          |            |            |      |       | - Stability of the structure (C-F bond)  
|                                          |            |            |      |       | - Screening information (OECD TG 310 showing 0% biodegradation over 28 days)  
|                                          |            |            |      |       | - Structural similarity to analogue substances (perfluorocyclobutane) with long half-lives (>1000 years) in the air compartment  
|                                          |            |            |      |       |  

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### Weight-of-evidence in PBT assessment

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</table>
| bis(2-ethylhexyl) tetra bromophthalate covering any of the individual isomers and/or combinations thereof | 247-426-5 | vPvB | 2023 | brominated phthalates | Persistence:  
- Screening information; 7% degradation in 28 days observed in an inherent degradation test OECD TG 302C and QSAR predictions  
- Estimated half-lives from a non-guideline outdoor mesocosm study with an artificial sediment (DT50=200 days)  
- Monitoring data in all environmental compartments and in remote areas  
Bioaccumulation:  
- Screening information (log $K_{ow}$=10.2 and log $K_{oa}$=15.4) indicating high potential for bioaccumulation in aquatic and air-breathing organisms  
- Fish dietary bioaccumulation studies and benchmarking (depuration rate constants and BMF)  
- In vitro biotransformation assay (liver microsomes) indicating low metabolism potential  
- Toxicokinetic information in rats and humans |
| Perfluoroheptanoic acid (PFHpA) and its salts | 243-518-4; 228-098-2; 206-798-9; 21049-36-5 (CAS no.) | PBT/vPvB/ELoC (M) | 2023 | PFCs; PFHpA and salts | Bioaccumulation:  
- Screening information based on calculated log $K_{ow}$ (5.7) indicating high potential for bioaccumulation in aquatic organisms  
- Fish BCFs and BCFs$\geq$5000 and a low depuration rate constant ($K_2=0.0633 \text{d}^{-1}$) derived based on a pilot OECD TG 305 study (aqueous exposure, without headspace due to high Henry’s Law constant (H=42400)). |

1 Listed as POP under the Stockholm Convention.
### Weight-of-evidence in PBT assessment

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<tr>
<td>1,1'-[ethane-1,2-diylbisoxoy]bis[2,4,6-tribromobenzene]</td>
<td>253-692-3</td>
<td>vPvB</td>
<td>2023</td>
<td>Brominated flame retardants</td>
<td>- Field and biomonitoring data (TMF, BMF)&lt;br&gt; - Ubiquitous presence in biota (mussel, fish, birds, mammals (including in human plasma) also in Arctic species such as ringed seal and polar bear&lt;br&gt; <strong>Persistence</strong>&lt;br&gt; - Non-standard screening study with pre-adapted inoculum as screening study&lt;br&gt; - Mesocosm studies in soil and water-sediment compartments&lt;br&gt; - Benchmarking with other higher brominated flame retardants (PBDE, HBB and PBEB)&lt;br&gt; - Monitoring data from sediment cores (20-40 year old sediment layers) and detection in remote areas&lt;br&gt; <strong>Bioaccumulation</strong>&lt;br&gt; - Log Kow (7.88-9.39, predicted).&lt;br&gt; - Non-standard fish dietary bioaccumulation study with low depuration rate constant (0.0128day⁻¹), 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&lt;br&gt; - Field studies indicating biomagnification (TMF and BMF &gt;1)&lt;br&gt; - Monitoring data from human serum, hair, and breast milk and from wildlife (including predatory species like polar bears) and remote areas</td>
</tr>
</tbody>
</table>
| Medium-chain chlorinated paraffins (MCCP) | 287-477-0 | PBT/vPvB | 2021 | Chlorinated Organics | 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..<br> **Persistence**<br> - OECD TG 308 on C14 chlorinated n-alkane, 50 % Cl. Wt.<br> - Modelling data for individual congener groups<br> - Screening tests on different UVCB substances/Block of substances<br> - Monitoring data (including in remote areas), including sediment core studies<br> **Bioaccumulation**<br> - OECD TG 305 (dietary) on C14 chlorinated n-alkane, 50 % Cl. Wt. and OECD TG 305 (aqueous exposure) on C13 chlorinated n-alkane, 45 % Cl. Wt. and on C15 chlorinated n-alkane, 51 % Cl. Wt.<br> - Toxicokinetic data on mammals<br> - Bioaccumulation in aquatic invertebrates (daphnia), mussels, terrestrial species<br> - BMFs (in muscles and livers)>1 for snake-frog predator-prey relationship<br> - TMFs >1 and <1<br> - Modelling data for individual congener groups<br> - 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...
Weight-of-evidence in PBT assessment

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</table>
| Fluoranthene         | 205-912-4  | PBT/vPvB   | 2019 (2009 CTPHT) | PAH   | Bioaccumulation  
Aquatic toxicity on the commercial C14-17, 52% Cl 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  
absorbed to some extent in humans and transfer to foetus), including biota from remote regions like the Arctic |
| Pyrene               | 204-927-3  | PBT/vPvB   | 2019 (2009 CTPHT) | PAH   | Bioaccumulation  
- BCF fish < 2000,  
- BCFs > 5000 for molluscs, crustaceans, oligochaete  
See also similar WoE approaches for B in Chrysene (EC 205-923-4), Benzo[k]fluoranthene (EC 205-916-6) and Benzo[ghi]perylene (EC 205-883-8) |
| D4                   | 209-136-7  | PBT/vPvB   | 2018        | Cyclic Siloxanes | Persistence  
- 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).  
Bioaccumulation  
- 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 D5 (EC 208-764-9). D5 identified as vPvB. When it contains ≥ 0.1%w/w D4 (EC No. 209-136-7) also PBT |
| D6                   | 208-762-8  | PBT/vPvB   | 2018        | Cyclic Siloxanes | Persistence |

2 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.
### Weight-of-evidence in PBT assessment

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</table>
| Dechlorane Plus¹     | 236-948-9; 135821-03-3 (CAS no.); 135821-74-8 (CAS no.) | vPvB | 2018 | Chlorinated Organics | - 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)  
- 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)); **Bioaccumulation**  
- Fish BCF studies (BCF up to ~2 400 L/kg in aquatic invertebrates)  
- Field data (TMF >1): biomagnification and trophic magnification data  
- Benchmarking with other known biomagnifying substances with TMF >1  
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) |
| PFHxS & salts¹      | -      | vPvB       | 2017 | PFCs; PFHxS & salts | **Persistence**  
- Stability of the structure (C-F bond)  
- Screening and simulation tests with read-across (PFOS, PFOA)  
**Bioaccumulation**  
- Binding to proteins in blood and liver like other PFSAs and PFCAs  
- Field BMF >1 in top predators (dolphins, glaucous gull, ringed seal, polar bear)  
- Detected in top predators (e.g. polar bear liver, human blood)  
- Toxicokinetic information, long elimination half-lives in humans (7-8 years) and other mammals (713 days in pigs, 141 d in male monkeys) |
## Weight-of-evidence in PBT assessment

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<tr>
<td>PFDA &amp; salts$^3$</td>
<td>206-400-3; 221-470-5; 3830-45-3 (CAS no.)</td>
<td>PBT</td>
<td>2016</td>
<td>PFCs: PFDA &amp; salts</td>
<td>Persistence - Stability of the structure (C-F bond). - Read-across with PFOA, PFNA and C$_{11-14}$ PFCAs Bioaccumulation - Binding to protein and membrane phospholipids - Monitoring (in mammals, including polar bears, beluga whale and humans) - Long elimination half-lives in humans, blood concentrations increase with increasing age - Field BMFs &gt;1 - TMF &gt;1 See also similar WoE approach to PFNA &amp; salts (EC 206-801-3)</td>
</tr>
<tr>
<td>UV-350</td>
<td>253-037-1</td>
<td>vPvB</td>
<td>2015</td>
<td>Benzo-triazoles</td>
<td>Persistence - QSAR predictions - Screening data, read-across to UV-320, UV-328 and UV-327 (OECD TG 301B and C) - Water/sediment simulation test similar to OECD TG 308 (DT50, sed. &gt;&gt; 100 d); OECD TG 308 with read-across (EC 407-000-3); degradation product similar to UV-350 - Field study (soil) and monitoring studies with read-across to UV-320 and UV-328 Similar assessment as for UV-327</td>
</tr>
<tr>
<td>UV-328$^4$</td>
<td>247-384-8</td>
<td>PBT/vPvB</td>
<td>2014</td>
<td>Benzo-triazoles</td>
<td>Persistence - Screening data (OECD TG 301B: 2-8% degradation fater 28 days) - No water or sediment simulation tests on the substance - OECD TG 308 test with read-across substance M1 - Field studies (DT50 up to 223 days) - Monitoring data Similar WoE approach as for UV-320</td>
</tr>
<tr>
<td>PFOA$^1$</td>
<td>206-397-9</td>
<td>PBT</td>
<td>2013</td>
<td>PFCs: PFOA &amp; salts</td>
<td>Persistence - Stability of the structure (C-F) - Screening information (OECD TG 301C: 5% degradation after 28 days and OECD TG 301 F showing no degradation after 28 days) - Several non-standard tests (e.g. sewage sludge laboratory scale, mixed microbial cultures, microcosm, industrial site sediment, aerobic and anaerobic degradation) - Field monitoring data Bioaccumulation - Biomagnification in air-breathing mammals: TMFs &gt;1 and field BMFs &gt;1 - Accumulation in humans, long half-lives in humans (2-4 years) - Detected in human blood and breast milk</td>
</tr>
</tbody>
</table>

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$^3$ 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).
### Weight-of-evidence in PBT assessment

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<td>C11-PFCA&lt;sup&gt;3&lt;/sup&gt;</td>
<td>218-165-4</td>
<td>vPvB</td>
<td>2012</td>
<td>PFCs: C11&lt;sup&gt;-&lt;/sup&gt;-C14-PFCAs</td>
<td>See also similar WoE approach to APFO (EC 223-320-4)</td>
</tr>
<tr>
<td>C12-PFCA&lt;sup&gt;3&lt;/sup&gt;</td>
<td>206-203-2</td>
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<td></td>
<td>Persistence</td>
</tr>
<tr>
<td>C13-PFCA&lt;sup&gt;3&lt;/sup&gt;</td>
<td>276-745-2</td>
<td></td>
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<td></td>
<td>- Stability of the structure (C-F)</td>
</tr>
<tr>
<td>C14-PFCA&lt;sup&gt;3&lt;/sup&gt;</td>
<td>206-803-4</td>
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<td>- Read-across approach within C8-C14-PFCAs was applied for the persistence assessment.</td>
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<td>- structural similarity and the regular pattern of physico-chemical properties within the group of C11-14-PFCAs</td>
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<td><strong>Bioaccumulation</strong></td>
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<td>- BCF-values of C11-PFCA &gt; 5000</td>
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<td>- Read-across approach within C8-C14-PFCAs</td>
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<td>- Field BMFs</td>
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Weight-of-evidence in PBT assessment

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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 Article57(f)
K<sub>oa</sub> Octanol-air partition coefficient
K<sub>oc</sub> Organic carbon normalized adsorption coefficient
K<sub>ow</sub> 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  Perfluorochemicals
PFCA  Perfluoroalkyl carboxylic acid/ perfluoroalkyl carboxylate
PFDA  Perfluorodecanoic acid
PFHpA Perfluoroheptanoic acid
PFHxS Perfluorohexane-1-sulphonic acid
PFSA  Perfluorooctane 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