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关于持久性有机污染物的斯德哥尔摩公约

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持久性有机污染物审查委员会
第二十二次会议
2026 年 9 月 21 日至 25 日，罗马
临时议程*项目 4 (b) (二)

技术工作：审议拟议列入《公约》附件 A、B 和/或 C 的化学品：四溴邻苯二甲酸双（2-乙基己基）酯（TBPH），涵盖其任何单个异构体和/或其组合

关于将四溴邻苯二甲酸双（2-乙基己基）酯（TBPH）（涵盖其任何单个异构体和/或其组合）列入《关于持久性有机污染物的斯德哥尔摩公约》附件 A、B 和/或 C 的提案**

秘书处的说明

一、 导言

1. 欧洲联盟已根据《关于持久性有机污染物的斯德哥尔摩公约》第 8 条第 1 款提交了一项关于将四溴邻苯二甲酸双（2-乙基己基）酯（TBPH）（涵盖其任何单个异构体和/或其组合）列入《关于持久性有机污染物的斯德哥尔摩公约》附件 A、B 和/或 C 的提案（见本说明附件）。该提案按提交的原文分发，未经正式编辑。与该提案相关的更多信息，载于欧洲联盟提交的 UNEP/POPS/POPRC.22/INF/6 号文件。秘书处对该提案是否包含《公约》附件 D 所规定信息的核实情况，载于 UNEP/POPS/POPRC.22/INF/7 号文件。

二、 建议采取的行动

2. 委员会不妨：

(a) 审议本说明中提供的信息；

(b) 决定其是否认为该提案符合《公约》第 8 条和附件 D 的要求；

* UNEP/POPS/POPRC.22/1。

** 本文件英文原文未经正式编辑。

(c) 如果决定该提案符合以上第 2 (b)分段中提到的要求，则制定并商定一项根据《公约》第 8 条第 6 款编写风险简介草案的工作计划。

附件*

关于将四溴邻苯二甲酸双（2-乙基己基）酯（TBPH）（涵盖其任何单个异构体和/或其组合）列入《关于持久性有机污染物的斯德哥尔摩公约》附件 A、B 和/或 C 的提案

1. 导言

1. 四溴邻苯二甲酸双（2-乙基己基）酯（TBPH）是一种溴化邻苯二甲酸盐衍生物，在芳环上有四个溴原子和两个二酯取代基。TBPH 由三种立体异构体组成：两种对映异构体（R,R 和 S,S）和内消旋异构体（R,S）。它们具有相同的分子式和键合元素序列，仅在结构的 3D（原子在空间中的取向）几何形状上有所不同。没有单个立体异构体的可用数据，因此假设性质相似。

2. TBPH 是一种新型溴化阻燃剂（NBFR），1987 年至 1994 年间首次报告了商业用途（加拿大环境与气候变化部（ECCC）、加拿大卫生部（HC），2019）。其主要用作非反应型阻燃添加剂，也用作增塑剂（美国环保局，2015a）。TBPH 已作为多溴二苯醚（PBDE）（如商用五溴二苯醚（pentaBDE）和八溴二苯醚（octaBDE）配方）阻燃剂的替代品销售（Knudsen 等人，2017）。TBPH 可单独使用，或与 2,3,4,5-四溴苯甲酸-2-乙基己酯（TBB，化学文摘社编号 183658-27-7）组成商业混合物使用。后者还可能包括有机磷酸盐阻燃剂（加拿大环境与气候变化部和加拿大卫生部，2019）。TBPH 的用途包括用于电线和电缆绝缘的柔性聚氯乙烯（PVC），建筑行业的硬质聚氨酯（PUR）和家具装饰应用中的柔性聚氨酯（加拿大环境与气候变化部和加拿大卫生部，2019；美国环保局，2015b 和瑞典主管部门，2022）。

3. 在欧洲联盟（欧盟），该物质根据《化学品注册、评估、许可和限制条例》（REACH）注册。TBPH 生产和/或进口到欧洲经济区的数量为 100−1 000 吨/年。在美利坚合众国（美国），TBPH 是一种高产量（生产或进口到美国的数量≥100 万磅（即≥450 吨/年）化学品（美国环保局，2015c）。根据 2020 年化学品数据报告（CDR）数据库，[1] 2016 年至 2019 年间，美国 TBPH 的全国总产量在 1 000 000 至<10 000 000 磅（相当于 453.6 至<4 536 吨/年）之间。有证据表明 TBPH 在一些国家仍在使用。然而，根据溴科学与环境论坛（BSEF）的数据，大多数国家（甚至所有国家）均不再生产和使用 TBPH（溴科学与环境论坛，2025）。美国商用混合物 Firemaster® 550 和 Uniplex™ FRP 45 的主要制造商之一似乎已于 2022 年停止生产 TBPH。[2] 相反，有证据表明 Uniplex™ FRP 45 在美国的制造仍在进行。[3]

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* 本附件英文原文未经正式编辑。本文件中提到的研究和其他信息不一定反映秘书处、联合国环境规划署（环境署）或联合国的观点。这些研究和参考文献中所用名称及材料的编制方式并不意味着秘书处、环境署或联合国对任何国家、领土、地区、城市或其当局的地缘政治局势或法律地位表达任何意见。

[1] https://www.epa.gov/chemical-data-reporting/access-chemical-data-reporting-data#2020。

[2] https://lanxess.com/en/sustainability/material-topics/sustainable-products/elimination-of-critical-substances。

[3] https://www.hallstarindustrial.com/product/uniplex-frp45/。

4. 虽然TBPH没有已知的自然来源，但已在所有环境区间中检测到该物质，其中包括空气、地表水、沉积物、生物群（包括野生动物）和人类。此外，有证据表明 TBPH 存在于偏远地区，但本地来源不详。根据北极监测和评估方案（2017），北极空气中 TBPH 的含量与多溴二苯醚的含量相当，并已显示出增加的迹象。结合在大湖区观察到的增长趋势，这可能反映了之前预计的 TBPH 作为五溴二苯醚替代品的使用数量增加情况（北极监测和评估方案，2017）。

5. 建模研究表明，TBPH 在释放到环境中时主要分布在土壤和沉积物区间中（欧洲化学品管理局，2022）。TBPH 预计将主要通过废水从工业来源和制成品释放到环境中（加拿大环境与气候变化部和加拿大卫生部，2019）。在向农业和牧场土地施用废水生物固体时，该物质也可能释放到土壤中（加拿大环境与气候变化部和加拿大卫生部，2019）。供消费者使用的产品也可能释放大量TBPH。作为添加型阻燃剂（而不是化学键合到聚合物上的反应型阻燃剂），TBPH 从消费品释放到环境中的可能性更大（Guerra 等人，2011，转引自加拿大环境与气候变化部和加拿大卫生部，2019）。加拿大环境与气候变化部和加拿大卫生部（2019）总结表明，TBPH 可以通过多种方式从消费品中释放到环境中，即从处理后的产品中挥发和浸出、吸附于室内灰尘以及在废物阶段释放。预计普通人群接触 TBPH 的主要来源来自环境媒介（空气、灰尘、土壤和水）、食物（包括母乳）以及使用含泡沫的家具等消费品（加拿大环境与气候变化部和加拿大卫生部，2019）。

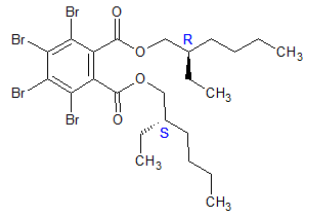
6. 欧盟已根据《化学品注册、评估、许可和限制条例》将TBPH确定为高度关注物质（SVHC），并因其具有高持久性和高生物积累性（vPvB）而于 2022 年 11 月将其列入授权候选名单[4]。欧洲化学品管理局（ECHA）评估了一组芳香族溴化阻燃剂，用于根据《化学品注册、评估、许可和限制条例》酌情提出限制提案，TBPH 属于其中之列（欧洲化学品管理局，2024a）。

7. 本提案专门针对《关于持久性有机污染物的斯德哥尔摩公约》附件 D 的信息要求和筛选标准，并总结了与持久性、生物积累性、远距离环境迁移和不利影响的筛选标准相关的证据。本提案依据的是根据《化学品注册、评估、许可和限制条例》（欧洲化学品管理局，2022）编写的欧盟高度关注物质档案、来自同行评审科学期刊的信息以及灰色文献。

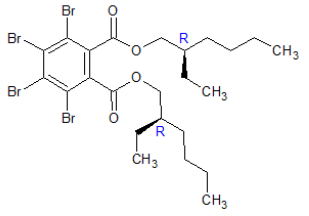
2. 化学特性

8. 本提案系关于四溴邻苯二甲酸双（2-乙基己基）酯，涵盖其任何单个立体异构体和/或其组合：

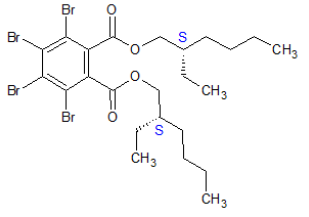
图 1：可能的立体对称体的结构式



四溴邻苯二甲酸[(2R)-2-乙基己基(2S)-2-乙基己基]酯



四溴邻苯二甲酸双[(2R)-2-乙基己基]酯



四溴邻苯二甲酸双[(2S)-2-乙基己基]酯

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

9. 四溴邻苯二甲酸双（2-乙基己基）酯是一种非对映异构体，由两种立体异构体组成（产生三种可能形式）。

10. 表 1 提供了与 TBPH 相关的可用识别信息。欧盟委员会编号和化学文摘社编号对应于一种多成分物质，其中包括四溴邻苯二甲酸双（2-乙基己基）酯的所有可能的异构体形式。

表 1：四溴邻苯二甲酸双（2-乙基己基）酯的化学特性

欧盟委员会编号：	247-426-5
欧盟委员会名称：	四溴邻苯二甲酸双（2-乙基己基）酯
化学文摘社编号：	26040-51-7
国际化联名称：	3,4,5,6-四溴苯-1,2-二甲酸双（2-乙基己基）酯
分子式：	$C_{24}H_{34}Br_4O_4$
分子量范围：	706.14 克/摩尔
同义名称或首字母缩略词：	TBPH、BEHTP、BEHTBP、BEHTEBP 和 BEH-TEBP
商品名：	BZ 45、DP 45、FRP 45、Firemaster® BZ-54、Firemaster® 550 (FM 550)、Firemaster® 552、Firemaster® 600、Pyronil 45 和 Uniplex™ FRP 45

11. TBPH 的物理化学性质信息见表 2。通过实验确定了该物质（但不是分别三种异构体）物理化学性质的数值。考虑到化学结构非常相似，即 2-乙基己基链的 R,R、R,S 或 S,S 立体异构体，可以合理地假设各个异构体的物理化学性质相似。

表 2：TBPH 的已知物理化学性质概述

性质	关键信息说明	数值[单位]	参考资料/信息来源
20°C 和 101.3 千帕时的物理状态	实验	20°C 和 101.3 千帕时为液态	实验研究（肉眼检查）[5]
熔点/凝固点	实验	101.3 千帕时-27°C，（未报告大气压力，系假设环境条件）	准则研究（德国标准化学会 ISO 3016；倾点），无详细记录[6]
沸点	实验	1 013 百帕时>300°C	准则研究（欧盟方法 A.2-沸腾温度；差示扫描量热法），无详细记录[7]
蒸汽压	（定量）结构—活性关系预测	25°C 时 2.28×10^{-9} 帕（修正 Grain 法）	MPBPWIN v1.43[8]

[5] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.。

[6] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.。

[7] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.。

[8] EPI 套件（http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm）。

性质	关键信息说明	数值[单位]	参考资料/信息来源
		25°C 时 2.12×10^{-9} 帕	COSMOtherm 2020，转引自 Glüge 和 Scheringer（2023）
密度	实验	20°C 时 1.541 千克/立方米	准则研究（欧盟方法 A.3-相对密度；U 型管法），无详细记录[9]
水溶性	实验	20°C 时<0.05 微克/升（在没有增溶剂的情况下检测不到） 20°C 时为 794 微克/升（使用 1%乙腈作为增溶剂）	准则研究（欧盟方法 A.6-水溶性；烧瓶法），大体相当于经合组织 TG 105[10]
正辛醇/水分配系数（对数值）	实验	25°C 时 10.2	准则研究（经合组织 TG 117，高效液相色谱法）[11]
有机碳/水分配系数（对数值）	实验	25°C 时 7.3	准则研究（经合组织 TG 121，高效液相色谱法）[12]
有机碳/空气分配系数（对数值）	（定量）结构-活性关系预测	15.114 20°C 时 15.489	KOAWIN v1.10，使用测得的正辛醇/水分配系数（10.2；美国环保局，2012） COSMOtherm 2020，转引自 Glüge 和 Scheringer（2023）
空气/水分配系数（对数值）	（定量）结构-活性关系预测	-4.914 25°C 时-3.525	HenryWin（美国环保局，2012） COSMOtherm 2020，转引自 Glüge 和 Scheringer（2023）

3. 关于 TBPH 及其如何满足附件 D 筛选标准的信息

12. 有整个物质的实验信息可用，但没有各个异构体的实验信息。由于异构体结构相似，在没有其他证据的情况下，预计异构体的性质与已确定的整个物质性质相当类似（欧洲化学品管理局，2022）。

3.1 持久性

13. 根据欧盟注册档案中提供的经合组织 TG 111 准则，在初步水解测试中评估了 TBPH 的非生物水解转化情况。[13] 使用 0.4 毫克 TBPH/升的 1%乙腈水溶液

[9] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM。

[10] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM。

[11] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM。

[12] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM。

[13] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM。

进行了初步试验。仅在 50°C和 pH 4、7 和 9 下进行了初步阶段研究。在每个 pH 值下，研究期结束后，测试用品的消失率>91%。所得半衰期在 pH 4 下为 30.4 小时，在 pH 7 下为 44.1 小时，在 pH 9 下为 77.5 小时。注册人使用 van´t Hoff 方程将半衰期外推至 20°C 的温度，得出以下数值：pH 4 下为 10.1 天，pH 7 下为 14.7 天，pH 9 下为 25.8 天。在 60°C 和 pH 4 下进行的第二次筛选实验中，鉴定出一种转化产物四溴邻苯二甲酸。由于得到这些结果之后没有根据准则在至少三种不同温度下进行确定性研究，因此结果值得怀疑。

14. 加拿大环境与气候变化部和加拿大卫生部（2019）认为，从 TBPH 的化学结构来看，由于芳环上多个溴取代基具有吸电子特性，其酯基可能易发生非生物水解。反之，支化酯取代基的空间效应和 TBPH 在水中的微弱溶解度表明水解反应速度缓慢。关于 TBB 和 TBPH 的商业混合物的经验数据表明，水解反应实际上是缓慢的。一项非生物水解研究发现，在 pH 4、7 或 9 和 50°C 下，TBB/TBPH 混合物问发生可以测量的水解。根据测试方法中规定的标准（92/69/EEC C7，相当于经合组织 TG 111）得出结论：在每个 pH 值和 25°C 下，水解半衰期均大于 1 年（大湖化学有限公司 1997 年未发表的研究，转引自加拿大环境与气候变化部和加拿大卫生部，2019）。

15. 此外，邻苯二甲酸双（2-乙基己基）酯（或 DEHP；TBPH 的未溴化骨架）的估计水解半衰期约为 2000 年（Giam 等人，1984，转引自 Pakalin 等人，2008）。这表明 TBPH 的水解可能并不快。此外，考虑到 TBPH 的水溶解度低而有机碳/水分配系数高，TBPH 对悬浮固体、沉积物和土壤中的有机物有高度吸附性，这种吸附可能会限制自然水体中的水解速度。此外，溴科学与环境论坛（BSEF）提到，由于其庞大的溴化原子和酯结构，TBPH 的非生物水解极其缓慢，因此 TBPH 在环境条件下不会分解（溴科学与环境论坛，2025）。

16. BIOWIN 模型（美国环保局，2012 年）预测 TBPH 不易生物降解；Biowin 2 或 Biowin 6 和 Biowin 3 模型预测的组合（如《化学品注册、评估、许可和限制条例》PBT 评估指南[14]R.11 章所述；欧洲化学品管理局，2023）表明，TBPH 在生物降解方面经筛查可能具有持久性或高度持久性。该物质可认为处于结构域内，但需注意，对于 Biowin 2 和 Biowin 3 的参数域而言，该物质的分子量已处于（或略高于）分子量范围的上限。Körner 等人（2024）的快速生物降解分类模型预测，TBPH 不容易生物降解（预测不容易生物降解的概率[15]=0.991）。美国环保局（2015b）参考的两项易生物降解性试验表明，TBPH 不易生物降解（降解率<4%）。此外，Li 等人（2025）使用经合组织 TG 301F，在 22±1°C 下持续 28 天评估了 TBPH 等其他新型溴化阻燃剂的生物降解性。使用了苯胺作为参比化合物。TBPH 在经合组织 TG 301F 条件下表现出有限的生物降解性，28 天后生物降解率为 1.4%。根据经合组织 TG 302C 在 25°C 下进行的两项固有降解性试验的结果证实了这一点；这两项测试发现在 28 天内产生了 7%和 12.9%的降解，表明 TBPH 不易生物降解，亦无固有生物降解性（欧洲化学品管理局，2022 和 Li 等人，2025）。根据《化学品注册、评估、许可和限制条例》PBT 评估指南 R.11 章（欧洲化学品管理局，2023），“如果在相当于经合组织 TG 302 系列的固有生物降解性试验中发现缺乏降解性（降解率<20%），即可能提供足够的信息来确认持久性标准（降解半衰期>120 天）已得到满足，而无需为持久性、生物积累性、毒性/高持久性和高生物积累性评估之目的进行进一步模

[14] 持久性、生物积累性、毒性。

[15] https://biodegradability-prediction-app.streamlit.app/，2025 年 5 月 27 日访问。

拟试验。此外，在特定情况下，如有其他具体信息支持，则可能得出该结果满足高度持久性标准（降解半衰期>180 天）的结论。”

17. 尚无针对 TBPH 的降解模拟研究。然而，de Jourdan 等人（2013）完成了一项未按测试指南进行的户外中观生态系统研究，其中研究了四种新型溴化阻燃剂（包括 TBPH）的归宿（欧洲化学品管理局，2022）。这项研究（2008 年 7 月至 9 月和 2009 年 7 月至 9 月）在安大略省（加拿大）的夏季进行，气温范围 15–22°C。中观生态系统的深度为 1.2 米，直径为 3.9 米，注水深度约 1 米。中观生态系统的供水系统是由现场的一口井供水的灌溉池。将含有富含有机物的土壤（表层土、粪肥、堆肥的 1:1:1 混合物，有机含量为 11.6%干总碳（1.6%干无机碳和 10.0%干有机碳））的人造沉积物置于托盘上，托盘置于每个中观生态系统的底部，以覆盖>50%的底部表面。归宿研究进行了两年（2008 年和 2009 年），其中第一年用于制定方法。中观生态系统于 2008 年 5 月建立，于 2008 年 7 月投加试验物质，2009 年 7 月再次投加。第一年，通过水下注入将 Firemaster® BZ-54（TBPH:TBB 1:4）投加于三个中观生态系统的水相。预计同时投加 TBPH 和 TBB 不会影响本研究的结果。在中观生态系统的数个位置，将溶解于二甲基亚砜（DMSO；体积分数为 0.001%）的 25 毫升商用 BZ-54 注入五次。目的是实现该化合物的均匀分布，标称浓度为 0.03 毫克/升，以便在其分配到沉积物中后，在上层 5 厘米中达到 500 纳克 TBPH/克沉积物的目标浓度，这与旧金山湾区的污水污泥中观察到的浓度一致。在第二年（2009 年 7 月 16 日），对每次投加的两个中观生态系统以相同的浓度重新投加，但不另外加水。分析方法的平均回收率为 77.4%（范围为 60%–88%，标准差为 5.9%）。

18. 在整个研究过程中，颗粒物中 TBPH 浓度波动较大，而沉积物中的浓度波动并不相同，最大浓度几乎等于整个采样期间的平均浓度。颗粒物中的 TBPH 降解半衰期估计为 25 天，95%置信区间（CI）为 7–44 天。颗粒物中可能发生了一些降解。色谱图中有一个大的未知峰值，与三溴代酸酐的预计质量相当一致。de Jourdan 等人（2013）提到，这可能是通过酯基水解为四溴邻苯二甲酸，随后形成酸酐而形成的。作者推测，这可能是由于颗粒区间中的光解造成的，因为 Davis 和 Stapleton（2009；见第 3.3 节关于光解的段落）在一项光解研究中检测到了 TBPH 的脱溴类似物。对于沉积物，回归方程不显著，表明没有显著下降。该研究的作者报告结果为，沉积物相的降解半衰期>200 天。实际降解半衰期估计（回归分析）给出的值为 9 303 天，95%置信区间为 1 330–17 280 天。沉积物中的 TBPH 浓度几乎与研究期间的最大浓度相同，因此表明沉积物区间中 TBPH 没有耗散/降解。此外，在沉积物中未发现降解产物。作者提到，在沉积物中检测到了少量的溴化降解产物，但由于基质干扰，无法准确确定。这项研究强烈表明 TBPH 在沉积物中具有持久性（降解半衰期>200 天）。表明 TBPH 存在于沉积物中的监测数据也佐证了 TBPH 的持久性（欧洲化学品管理局，2022），包括西太平洋远离点源的偏远地区（在深海海沟的超深渊表面沉积物样本中 100%检测到；Xie 等人，2023）。

19. 此外，TBPH 存在于所有环境区间中，包括空气、地表水、地下水、海水、沉积物、土壤以及北极、青藏高原、白令海、东格陵兰海、西太平洋、南大西洋、南半球海洋区域和南极等偏远地区，这进一步支持该物质极难降解的结论（见附件一中的监测数据——欧洲化学品管理局欧盟档案的环境和人类监测数据（欧洲化学品管理局，2022；Han 等人，2022 和第 3.3 节）。

3.1.1 根据附件 D 标准得出的持久性结论

20. 认为符合附件 D 第 1 (b) (i)和(ii)段所列的持久性标准。TBPH 在沉积物中的降解半衰期超过六个月（即 180 天；沉积物中降解半衰期>200 天）。表明 TBPH 存在于沉积物中的监测数据也支持 TBPH 的持久性，包括西太平洋远离点源的偏远地区（在超深渊表面沉积物样本中检测到，见第 3.3 节）。

3.2 生物积累

21. TBPH 符合附件 D 筛选标准，生物积累性的正辛醇/水分配系数（log K_{ow}）大于 5，具体数值为 10.2（欧洲化学品管理局，2022）。

22. 在根据经合组织 TG 305 进行的一项研究中，调查了幼体虹鳟（Oncorhynchus mykiss）体内 TBPH 的生物积累潜力（饮食接触；未发表，2018）。TBPH 经生长和脂质校正的动力学生物放大系数（BMF_{kgL}）为 0.038（未经修正的动力学生物放大系数为 0.0048）。根据《化学品注册、评估、许可和限制条例》PBT 评估指南 R.11 章（欧洲化学品管理局，2023），即使在经合组织 TG 305 饮食生物积累研究中发现生物放大系数低于 1，也不能认为这是断定物质不具有（高度）生物积累性的良好指标。该物质吸收率很低，同化效率为 0.011。在这项研究中，鱼类净化缓慢，经生长和脂质校正的净化速率常数（k_{2gL}）为 0.018/天，经生长校正的净化速率常数（k_{2g}）为 0.015/天，净化速率常数（k_2）为 0.044/天，TBPH 经生长校正的半衰期为 46.2 天（未经生长校正则为 15.6 天）。Brooke 和 Crookes（2012）认为，脂质标准化净化速率常数为 0.085/天或更短，表明生物浓缩系数（BCF）高于 5 000 升/千克。在用虹鳟进行的喂养研究中观察到的低净化速率（k_{2gL} 为 0.018/天）与 TBPH 的生物浓缩系数>5 000 升/千克相符。使用方法 1 和方法 2 模型（如经合组织 TG 305 指南所述；经合组织，2017）预测的所有生物浓缩系数值，除一种（方法 3 模型）外均高于 5 000 升/千克的生物浓缩系数，在 5 878–167 655 升/千克范围内。方法 3 模型给出的 TBPH 生物浓缩系数估计值为 881 升/千克。然而，方法 3 模型仅是针对鲤鱼推导而得的，因此尚不清楚其是否适用于虹鳟等其他鱼类。考虑到生物积累研究中观察到的低吸收率，这些方法很可能高估了吸收率，从而高估了 TBPH 的生物浓缩系数。还需要注意的是，TBPH 的正辛醇/水分配系数高于这些模型的指示性适用域。然而，经合组织 TG 305 生物浓缩系数估算工具是经合组织 TG 305 中唯一推荐的从饮食生物积累研究中得出生物浓缩系数值的工具。

23. 在将 TBPH 认定为欧盟高度关注物质的佐证文件中，将虹鳟体内的 TBPH 实验室净化速率常数和生物放大系数值同已知的持久性、生物积累性、毒性/高持久性和高生物积累性/持久性有机污染物质进行了比较（欧洲化学品管理局，2022）。TBPH 在虹鳟中的 BMF_{kgL} 为 0.038，k_{2g} 为 0.015/天，与两种持久性有机污染和生物积累性物质相似，分别为：得克隆（反式异构体 BMF_{kgL} 为 0.023，k_{2g} 为 0.010–0.013/天；顺式异构体 BMF_{kgL} 为 0.046–0.062，k_{2g} 为 0.017–0.023/天）；甲氧滴滴涕（生物放大系数为 0.16，k_{2g} 为 0.124/天）。得克隆和甲氧滴滴涕符合附件 D 的生物积累标准（生物浓缩系数>5 000 升/千克），这进一步表明 TBPH 具有生物累积性。

24. Burkhard 等人（2023）根据经合组织 TG 305 方法，使虹鳟（Oncorhynchus mykiss）通过饮食接触疏水性物质混合物（其中包括 TBPH），为期 28 天。TBPH 经生长和脂质校正的动力学生物放大系数（BMF_{kgL}）为

0.0018（未经修正的动力学生物放大系数为 0.0009）。该物质吸收率很低，同化效率为 0.004。在这项研究中，鱼类净化缓慢，经生长和脂质校正的净化速率常数（k_{2gL}）为 0.054/天，经生长校正的净化速率常数（k_{2g}）为 0.047/天，净化速率常数（k_2）为 0.056/天，TBPH 经生长校正的半衰期为 14.8 天（未经生长校正则为 12.3 天）。Brooke 和 Crookes（2012）认为，脂质标准化净化速率常数为 0.085/天或更短，表明生物浓缩系数（BCF）高于 5 000 升/千克。在用虹鳟进行的喂养研究中观察到的低净化速率（k_{2gL} 为 0.054/天）与 TBPH 的生物浓缩系数>5 000 升/千克相符。使用方法 1 和方法 2 模型（如经合组织 TG 305 指南所述；经合组织，2017）预测的生物浓缩系数值大多高于 5 000 升/千克（13 个模型中有 9 个预测生物浓缩系数>5 000；生物浓缩系数在 1 295 至 55 595 升/千克之间，见 UNEP/POPS/POPRC.22/INF/6 号资料文件表 A1）。方法 3 模型给出的 TBPH 生物浓缩系数估计值为 71.6 升/千克。然而，方法 3 模型仅是针对鲤鱼推导而得的，因此尚不清楚其是否适用于虹鳟等其他鱼类。这些生物浓缩系数估计值的不确定性与未发表的 2018 年研究（见上文）中所述的不确定性相似。

25. Nacci 等人（2018）进行的一项生物积累研究按照与经合组织 TG 305 研究（饮食接触）类似的设计，调查了一种河口鱼类，即大西洋鳉鱼（Fundulus heteroclitus）对 TBPH 的吸收和净化。将一种多氯联苯（多氯联苯 153）用作生物积累性的阳性对照物。根据 Nacci 等人（2018）的研究，TBPH 在低接触水平（139 毫克 TBPH/千克干重）下的生物放大系数为 0.02，在高接触水平（4 360 毫克 TBPH/千克干重）下的生物放大系数为 0.005，而多氯联苯 153 在 13 毫克/千克干重接触水平下的生物放大系数为 1.08。TBPH 经生长和脂质校正的动力学生物放大系数（BMF_{kgL}）为 0.01625（未经修正的动力学生物放大系数为 0.0291）。鱼类似乎对 TBPH 有一个临界吸收量，在高 TBPH 浓度下，并非所有 TBPH 都被吸收。在低浓度下或缓慢给药时，TBPH 将出现更高的吸收率，因此生物放大系数更高。这种浓度依赖性表明生物利用率随着接触量的增加而降低。该研究表明，TBPH 代谢不佳，在 F. heteroclitus 体内的净化速率常数（k_2）较低，为 0.0696，生长修正半衰期较长，为 10.4 天（未经生长修正的半衰期为 9.96 天）。使用方法 1 和方法 2 模型预测的大多数生物浓缩系数值低于 5 000 升/千克（13 个模型中有 11 个预测生物浓缩系数<5 000；生物浓缩系数范围为 445–13 017 升/千克；见 UNEP/POPS/POPRC.22/INF/6 号资料文件中的表 A2）。方法 3 模型给出的 TBPH 生物浓缩系数估计值为 435 升/千克。然而，方法 3 模型仅是针对鲤鱼推导而得的，因此尚不清楚其是否适用于大西洋鳉鱼等其他鱼类。这些生物浓缩系数估计值的不确定性与未发表的 2018 年研究（见上文）中所述的不确定性相似。值得注意的是，净化速率常数（k_2）与零没有统计学差异（p=0.1768），因此不能排除该物质在 F. heteroclitus 中确实存在生物积累性。

26. Hou 等人（2022）在 Epinephelus fasciatus 和 Plectorhynchus orientalis 两种鱼类的肝微粒体中使用七种新型溴化阻燃剂进行了体外孵育，以评估生物转化清除率。将微粒体在 25°C 下孵育了 0、0.5、1、2、4 和 6 小时，而不是经合组织 TG 319B 中推荐的 2 小时（最多 4 小时），因此只有 5 个时间点与推导清除率相关，而不是推荐的 6 个时间点。此外，还评估了肝微粒体催化与 TBPH 代谢最相关的第一阶段反应的能力。孵育混合物为3微升溶于二甲基亚砜的TBPH溶液（5微摩尔/升）。测试使用1毫克/毫升的蛋白质。实验进行了三次重复。微粒体样品的回收率约为 90%。两种鱼类的肝微粒体中的生物转化均符合一级

动力学，两种鱼类的测量值没有显著差异。在厚唇鱼中，TBPH 与六溴苯（HBB）的体外生物转化率并列最低（0.017±0.004 毫升/毫克蛋白质/小时，r^2=0.803）；在石斑鱼中，TBPH 的体外生物转化率唯一最低（0.016±0.002 毫升/毫克蛋白质/小时；r^2=0.964）。这项研究表明，鱼类对 TBPH 的代谢非常差。

27. 在寡毛类生物（Lumbriculus variegatus）中确定了 TBPH 的生物群-沉积物积累因子（BSAF）为 0.254 千克有机碳/千克脂质（美国环保局测试方法 100.3（美国环保局，2000）；Burkhard 等人，2021）。沉积物接触试验进行了 56 天的时间：一组虫体连续接触 TBPH，另一组虫体先接触 TBPH 沉积物 28 天，然后接触清洁沉积物 28 天，以此进行净化评估。研究期间没有按照美国环保局测试方法（美国环保局，2000 年）喂养这些生物。未报告在 28 天内达到 TBPH 吸收的稳态条件，因此表明如果达到稳态，生物群-沉积物积累因子还会更高。TBPH 在 L.variegatus 中表现出双相消除，94%的身体负荷在消除的前 12 小时内消耗完毕（即半衰期为 1.2 小时或更短），其余 6%在此后非常缓慢地消除（半衰期为 15 天），缓慢消除速率常数为 0.0461（±0.00485）/天。根据 Burkhard 等人（2021）的研究，L.variegatus 体内 TBPH 等高度疏水性化学物质的双相吸收和消除动力学机制不详。作者推测，原因可能是生物体内的残留沉积物、与胃肠道膜或黏液相关的化学物质，也可能是由于清洁沉积物的物理置换。几乎没有证据表明 L.variegatus 会对 TBPH 进行生物转化。这些结果表明 TBPH 可能在 L.variegatus 体内积累。

28. 实地研究似乎表明，在海底食物网中，TBPH 有可能发生生物放大作用：

29. 2020 年 10 月和 11 月，Hou 等人（2022）测量了中国南海西沙群岛珊瑚礁水域的 TBPH 浓度。在海水（平均浓度=0.037 皮克/升，检出频率=12.5%，n=8）、沉积物（平均浓度=0.181 微克/千克干重，检出频率=62.5%，n=8），以及 29 种不同类型的水生生物（检出频率=78.4%，所有生物体 n=109（每个物种 n=3–6））中发现了 TBPH，浓度范围为<方法检出限[16]到 0.369 微克/千克脂重。据报道，营养级较高的底栖物种（食肉物种或顶级捕食者物种）体内浓度最高。生物群中的 TBPH 浓度指的是无脊椎动物全身和鱼类肌肉中的测量结果。根据这些测得浓度，发现 TBPH 的实地生物群-沉积物积累因子[17]数值范围为海参的 0.11±0.01 至贝壳的 0.86±0.32 和鱼类（石斑鱼）的 0.86±0.61。根据《化学品注册、评估、许可和限制条例》R.11 章（见附录 R.11—3；欧洲化学品管理局，2023），以孔隙水浓度计，脂肪和有机碳标准化的生物群-沉积物积累因子值达到或高于 0.5，则表明生物积累性较高（生物浓缩系数>5 000）。TBPH 在贝类和鱼类中的生物群-沉积物积累因子值表明其具有很高的生物积累潜力。此外，这些生物群-沉积物积累因子值表明，沉积物中的 TBPH 向底栖无脊椎动物和底栖鱼类的转移程度相同。然而，由于沉积物不是鱼类体内 TBPH 的直接来源，因此认为观察到的 TBPH 的生物积累是食物链放大的结果。

30. 针对以螃蟹为食物来源的鱼类，计算了鱼和蟹的捕食者与猎物关系中的生物放大系数[18]估计值。估计的生物放大系数表明 TBPH 在鱼类中具有生物放大作用，鱼和蟹的捕食者与猎物关系中的生物放大系数范围为 4.2 至 24（中位数=6.8）（Hou 等人，2022 年）。人们承认，这些估计的生物放大系数只是粗

[16] 生物群中 TBPH 的方法检出限为 0.012 微克/千克脂重或纳克/克脂重。

[17] 生物群-沉积物积累因子是标准化脂质含量中物质浓度与标准化碳含量中物质浓度的比率。

[18] 这些生物放大系数是通过将捕食者体内的脂质标准化浓度除以捕食者饮食中的脂质标准化浓度来计算的。

略的，并且可能高估了 TBPH 的潜在生物放大作用，因为鱼不仅仅以螃蟹为食。例如，根据 FishBase 鱼类数据库，成年 Cephalopholis argus 主要以鱼类为食（75–95%）。[19] 该物种在这项研究的所有采样鱼类物种中具有最高的 TBPH 浓度（0.369±0.066 微克 TBPH/千克脂重），其营养级值为第二高。根据这些物种体内的 TBPH 平均浓度和所有采样鱼类体内的 TBPH 平均浓度（0.129TBPH/千克脂重），得出生物放大系数为 2.9。据认为，这是对鱼类中 TBPH 生物放大作用的比较现实的估计。公认的是，该生物放大系数值也存在很大的不确定性；例如，C. argus 体内 TBPH 平均浓度的依据仅为三个个体。然而，综合来看，这项研究的证据表明 TBPH 在鱼类中具有生物放大作用。值得注意的是，分析的样本指的是无脊椎动物的全身和鱼的肌肉，而不是猎物和捕食者的全身，因此所发现的含量可能无法反映整条鱼体内的含量。因此，这些生物放大系数的可靠性尚不清楚。

31. 由于测得正辛醇/水分配系数为 10.2，正辛醇/空气分配系数估计为 15.1 或 15.5（KOAWIN v1.10，美国环保局，2012；COSMOtherm 2020，转引自 Glüge 和 Scheringer（2023）），TBPH 符合《化学品注册、评估、许可和限制条例》针对呼吸空气生物的生物积累性筛选标准（正辛醇/水分配系数≥2，正辛醇/空气分配系数≥5；Kelly 等人，2007，转引自欧洲化学品管理局，2023）。使用人肝微粒体和肠道亚细胞组分进行了 TBPH 代谢的体外研究（Roberts 等人，2012）。在人肝微粒体实验中，没有观察到 TBPH 的显著减少，也没有检测到代谢物。向实验体系中加入猪肝羧酸酯酶后，缓慢形成了 TBPH 的代谢物四溴邻苯二甲酸单（2-乙基己基）酯（TBMEHP）。Roberts 等人（2012）提到，TBPH 代谢形成 TBMEHP 可能会影响 TBPH 的毒性，但可能不够迅速，不足以影响 TBPH 的生物积累性。现有的大鼠体内毒代动力学数据表明，TBPH 吸收不良、代谢不良，在口服接触后主要通过粪便以原样排出（Knudsen 等人，2017；罗伯茨等人，2012；Silva 等人，2015）。然而，静脉给药后，大部分 TBPH 在粪便中作为母体物质（30%）和代谢物 TBMEHP（70%）的混合物被消除，但相当一部分剂量保留在组织中（Knudsen 等人，2017）。事实上，在单次接触后，20%的经口和静脉给药的 TBPH（0.1 微摩尔/千克）保留在大鼠组织中，包括肝脏 7%、肌肉 5%、皮肤 3%、脂肪 2%和肾上腺 1%（Knudsen 等人，2017）。重复口服接触研究显示了类似结果，并表明虽然只有少量 TBPH 被吸收，但 TBPH 在肝脏和肾上腺组织中的浓度显著增加。这些结果表明，TBPH 有可能在肾上腺和肝脏组织中积累，主要是母体物质形式。从现有监测数据中可以明显看出这一点，其表明 TBPH 会在呼吸空气的动物体内积累。

32. 监测数据已检测到多种鸟类肝脏中的 TBPH（2010 年至 2011 年浓度范围<0.75 至 803 微克/千克脂重；n=69）、卵中的 TBPH（2011 年至 2013 年<0.4–31.3 微克/千克湿重，检出频率=25%（3/12），n=12）和血浆中的 TBPH（2011 年至 2013 年未检出–98.3 微克/千克湿重，检出频率=40%，n=15），这些鸟类包括捕食陆地物种的猛禽以及以北极水生生物为食的鸟类（Jin 等人，2016，Lazarus 等人，2016 和 Fernie 等人，2017）。报告显示，在所评估的新型溴化阻燃剂（1,2-双（2,4,6-三溴苯氧基）乙烷，即 BTBPE 和十溴二苯乙烷，即 DBDPE）中，TBPH 在鸟类肝脏中检出率最高（所有鸟类组织中的检出率为 54%；十种鸟类，n=69）（Jin 等人，2016）。此外，检测到 TBPH 还有海豚等海洋哺乳动物的脂肪（Zhu 等人，2014）和江豚脂肪（2003 年至 2008 年<0.04–

[19] https://www.fishbase.se/search.php。

3 859微克/千克脂重，n=33，TBPH浓度高于HBCDD浓度，Lam等人，2009），以及北极环斑海豹的血浆（2010年平均值0.04微克/升（平均值），检出频率=10%，n=10；Harju等人，2013）和肝脏（2007年<0.138–0.876微克/千克湿重，检出频率=60%，n=10；Sagerup 等人，2010），还有北极熊的脂肪组织和血浆（血浆中平均值 0.15 纳克/毫升，脂肪中<0.128–0.402 微克/千克湿重；Harju等人，2013和Vorkamp等人，2015）。

33. 在妊娠期间接触过TBPH的大鼠的胎盘中检测到TBPH（浓度最高达31.5毫克/千克体重/天）；Baldwin等人，2017）。此外，检测到TBPH还有人的血清（成人/母亲/儿童体内浓度范围为n.d.[20]–260微克 TBPH/千克脂重；检出频率=16–83%）、母乳（n.d.–6.6微克TBPH/千克脂重；检出频率=32.4–50%）、毛发[21]（13–2 600纳克/克，检出频率=94%）、指甲[21]（4.21–1 120微克TBPH/千克，检出频率=86–100%）和趾甲[21]（18–1 990纳克/克，检出频率=80%），来自 2008 年至 2016 年在加拿大、中国、英国和美国收集的样本（He 等人，2013；Zhou等人，2014；Liu等人，2016；Tao等人，2017；Guo等人，2018和Chen等人，2019）。指甲中的TBPH与室内灰尘之间存在显著正相关（p<0.001，r=0.37），这表明室内灰尘在通过摄入/吸入灰尘和接触灰尘等途径接触 TBPH方面起到重要作用（Chen等人，2019年）。

34. 人类可能通过饮食接触TBPH。例如，食用含有TBPH的食物是普通人群的潜在接触途径。Tao等人（2017）在2015年5月和6月期间检验了英国伯明翰代表全国连锁店的两家超市和一个当地市场的14组复合食品样本中TBPH的存在情况，涵盖肉、肝脏、油性鱼、鸡蛋和奶酪。在 63%的样本中检测到TBPH，浓度范围为肉类中0.20–0.57纳克/克脂重，肝脏中0.69–5.8纳克/克脂重，鱼类中<0.1–1.1 纳克/克脂重，鸡蛋和乳制品中 0.22–1.8 纳克/克脂重。然而，Tao 等人（2017）得出的结论是，摄入灰尘在导致英国成年人的 TBPH 身体负荷方面起到更重要的作用。

35. Xiong等人（2021）研究了九种新型溴化阻燃剂在南极陆地植物中的生物积累潜力。作者于2014年1月在南极长城站、菲尔德斯半岛和阿德利岛采集植物。TBPH 在苔藓/土壤中的积累因子（BAF）[22]为 5.01（平均值；最大值为12.55），是所研究的9种新型溴化阻燃剂中第二高的积累因子，表明TBPH很可能会从土壤转移到南极苔藓（Sanionia uncinate）。这是值得关切的，因为植物中的富集可能会导致其他生物中的富集。

36. 哺乳动物（包括人类）、植物和水生物种的监测数据提供了佐证，证明TBPH可以被环境中的生物吸收。

3.2.1 根据附件 D 标准得出的生物积累性结论

37. 由于TBPH的生物浓缩系数值超过5 000升/千克且其正辛醇/水分配系数大于5，因此认为TBPH符合附件D第1 (c) (i)和(iii)段中列出的生物积累性标准。实验室实验表明，几乎没有证据表明鱼类、寡毛类生物、大鼠和人类会对TBPH 进行生物转化，因此表明其具有生物积累潜力。毒代动力学数据表明，

[20] n.d.意为“未检出”。

[21] 考虑到验证方法中毛发中TBPH的平均回收率为120%，指甲中TBPH的平均回收率为141%（Liu等人，2015），Liu等人（2016）报告的毛发和指甲中的浓度可能高估了。

[22] 生物积累因子（BAF）的计算方法是将苔藓中的浓度（皮克/克干重）除以土壤中同一地点的浓度（皮克/克干重）。

虽然只有少量的 TBPH 被吸收，但其有可能在大鼠的肾上腺和肝脏组织中积累。实地研究似乎表明，在海底食物链中，TBPH 具有生物放大潜力。此外，TBPH 在贝类和鱼类中的实地生物群-沉积物积累因子值高于 0.5，表明其具有很高的生物积累潜力。比较 TBPH 和具有持久性有机污染物性质的物质（例如得克隆和甲氧滴滴涕）的实验室净化速率常数和生物放大系数值的基准方法会提供进一步证据，证明 TBPH 具有生物积累性。生物监测数据佐证了 TBPH 的生物积累潜力，表明 TBPH 被多种生物（鱼类和水生无脊椎动物，还有鸟类和哺乳动物，包括人类）广泛吸收，也存在于环斑海豹和北极熊（濒危物种）等北极物种和南极苔藓中。TBPH 可以在敏感的生命阶段通过鸟蛋、人类母乳转移，并且可以通过胎盘进入后代。

3.3 远距离环境迁移潜力

3.3.1 物理化学性质筛选

38. TBPH 的亨利定律常数估计值在 25°C 时为 3.02×10^{-2} 帕.立方米/摩尔（键合法，HENRYWIN v3.20；美国环保局，2012），估计蒸汽压为 25°C 时 2.28×10^{-9} 帕（MPBPVP v1.43；美国环保局，2012）或 25°C 时 2.12×10^{-9} 帕（COSMOtherm 2020，转引自 Glüge 和 Scheringer，2023），这些数值表明 TBPH 挥发到大气中的可能性较低。然而，在偏远地区发现的 TBPH 浓度表明已经发生了大气迁移。蒸汽相 TBPH 将主要通过与光化作用产生的氢氧自由基反应在大气中降解。25°C 时，TBPH 与氢氧自由基发生蒸气相反应的速率常数估计为 21.82×10^{-12} 立方厘米/分子/秒（AOPWIN v1.92；美国环保局，2012）。根据 12 小时光周期和 1.5×10^{6}OH/立方厘米这些数值，TBPH 在空气（气相）中的估计半衰期为 5.883 小时或 0.490 天（AOPWIN v1.92；美国环保局，2012）。由于吸收的部分可能耐大气氧化，因此根据与氢氧自由基反应得出的 AOPWIN 半衰期值很可能低估了空气中的半衰期。模型预测，空气中的大部分 TBPH 可能吸附到颗粒物上（TBPH 吸附到大气颗粒物上的比例为 99.7%至 100%；AEROWIN v1.00；美国环保局，2012）。由于 TBPH 蒸气压低，正辛醇/空气分配系数高（15.1），预计 TBPH 将与大气中的颗粒物产生关联。TBPH 吸附到空气中颗粒物，可能会增加其停留时间和远距离迁移的潜力。空气颗粒物的大气迁移会提供远距离迁移的潜在途径，这得到了在北极和南极等偏远地区采集的空气样本（气相和颗粒相或仅颗粒相）中检测到 TBPH 的佐证（Halvorsen 等人，2023；Lee 等人，2016；Möller 等人，2011a 和 2012；Rauert 等人，2018；Salamova 等人，2014；Xiao 等人，2012a；Zhao 等人，2020）。

39. Davis 和 Stapleton（2009，转引自加拿大环境与气候变化部和加拿大卫生部，2019）报告了 TBB 和 TBPH 在太阳辐射下在一系列有机溶剂中的还原光脱溴反应。在所有溶剂中，TBB 和 TBPH 的降解速度都慢于十溴二苯醚和研究中包含的九溴二苯醚同系物。对于 TBB 和 TBPH 而言，均观察到二溴和三溴降解产物；就 TBPH 而言，大多数缺少两个酯支链。虽然没有查明空气区间中 TBB 和 TBPH 的光降解数据，但在努纳武特地区的阿勒特对颗粒相和气相 TBB 和 TBPH 的观察表明，空气区间中的光降解可能相对缓慢（Xiao 等人，2012b）。

3.3.2 远距离迁移模型预测

40. 加拿大环境与气候变化部和加拿大卫生部使用经合组织总体持久性和远距离迁移潜力筛选工具，通过建模得出 TBPH 的典型迁移距离（CTD）为 2 850

公里（2019；未报告模型的输入参数）。Xiao 等人（2012a）报告称，TBPH 的典型迁移距离为 2 900 公里，转移效率为 13%（模型输入参数：空气中半衰期为 5.9 小时，水中半衰期为 1 400 小时（即 58 天），土壤中半衰期为 2 900 小时（即 121 天）；分别使用 SPARC 和 EPI 套件估计降解半衰期）。远距离迁移潜力（LRTP）边界为 5 097 千米（PCB 28 的典型迁移距离）和 2.248%（PCB-28 的迁移效率）。因此，针对 TBPH 获得的这些建模结果表明其具有远距离迁移潜力较低，并具有向地表介质的转移潜力。由于输入参数的不确定性（水和土壤中的半衰期未知），建模结果具有不确定性。此外，经合组织工具不包含沉积物区间，而 TBPH 在沉积物中具有持久性。

41. 根据 Brown 和 Wania（2008）引用的标准，TBPH 的正辛醇/水分配系数（10.2）、正辛醇/空气分配系数（15.114）和空气/水分配系数（-4.914）值表明，TBPH 到达北极并在北极人类食物链中积累的潜力很大。事实上，Brown 和 Wania（2008）选择的北极污染和生物积累潜力（AC-BAP）偏高的地区包括以下标准：正辛醇/水分配系数≥3.5；正辛醇/空气分配系数≥6；0.5≥空气/水分配系数≥-7；空气/水分配系数≤-1.78×正辛醇/空气分配系数+14.56。

3.3.3 偏远地区的测量

42. 对偏远区域环境和生物群样本的监测研究和测量表明了 TBPH 的远距离迁移潜力（更多信息见附录中的表 A1 至表 A6）。值得注意的是，生物群和环境样本中报告的 TBPH 浓度值可能被低估，Papachlimitzou 等人（2012）也指出这一问题。资料文件（UNEP/POPS/POPRC.22/INF/6）进一步讨论了 TBPH 分析方面的挑战。

43. 2005 年至 2022 年期间，在北极的各种介质中检测到 TBPH，包括 Zeppelin、Ny-Ålesund 和 Longyearbyen（斯瓦尔巴）以及阿勒特（加拿大）的北极空气中（浓度范围为<0.025–14 皮克/立方米（气相和/或颗粒相）；Halvorsen 等人，2023；Lee 等人，2016；Salamova 等人，2014；Xiao 等人，2012a；Hung 等人，2013a，转引自北极监测和评估方案，2016）；2009 年至 2010 年期间，在北冰洋和东格陵兰海的空气中检测到 TBPH（气相和/或颗粒相浓度范围为<0.16–0.36 皮克/立方米；Möller 等人，2011a 和 2011b）；2009 年至 2010 年期间，在白令海和东格陵兰海的海水中检测到 TBPH（浓度范围为未检出–0.22 皮克/升（溶解分数）；Möller 等人，2011a 和 2011b）；2008 年至 2013 年期间，在格陵兰岛中东部、斯瓦尔巴和加拿大北极地区的陆地、鸟类和海洋生物群样本中检测到 TBPH，包括脆弱物种和顶级捕食者北极熊（Ursus maritimus）（浓度范围为<0.106–3.754 纳克/克湿重和<0.14–44.29 纳克/克脂重；Harju 等人，2013；Houde 等人，2017；Sagerup 等人，2010 和 Vorkamp 等人，2015）。

44. 北极监测和评估方案（2017）提到，加拿大高北极地区阿勒特的大容量空气采样显示，2008 年至 2012 年期间 TBPH 浓度不断增加。在大湖区的空气中也观察到了增加的趋势（Ma 等人，2012b，转引自北极监测和评估方案（2017））。

45. 2006 年至 2007 年期间，在青藏高原海拔 4 730 米的空气中检测到 TBPH（浓度范围为 0.049–1.7 皮克/立方米（气相和颗粒相）；Xiao 等人，2012a）。根据 Xiao 等人（2012a）的研究，尽管气团在不同季节来自截然不同的区域，但青藏高原纳木错包括 TBPH 在内的阻燃剂浓度并未表现出显著的季节性。作者认为，这表明阻燃剂没有区域性来源，但它们在西藏的浓度在相当程度上反

映了真正全球范围的背景污染（Xiao 等人，2012a）。这佐证了 TBPH 的远距离大气迁移潜力。

46. 2011 年至 2018 年期间，在南极洲也检测到了 TBPH，包括南极洲西部南设得兰群岛乔治王岛的空气中（浓度范围为未检出–0.098 皮克/立方米（气相和颗粒相）；Zhao 等人，2020）；2010 年至 2011 年间，在从印度洋到南大洋的南半球海洋区域的空气中检测到 TBPH（颗粒相浓度范围为<0.025–1.5 皮克/立方米；Möller 等人，2012）；2014 年，在南极洲西部长城站、菲尔德斯半岛和阿德利岛的土壤中检测到 TBPH（浓度范围为未检出–20.22 皮克/克干重；Xiong 等人，2021 年）；2014 年，在南极洲西部长城站、菲尔德斯半岛和阿德利岛的植物中检测到 TBPH（苔藓（Sanionia uncinata）中的浓度范围为未检出–484.1 皮克/克干重；Xiong 等人，2021）。

47. 监测数据表明，TBPH 可以通过空气和/或河流/洋流在各海洋中部进行远程迁移，包括海洋最深处（超深渊带）。2016 年，在南大西洋中部检测到 TBPH（Sobotka 等人，2021）。此外，检测到 TBPH 的还有 19%的超深渊端足类动物（Alicella gigantea；n=10；甲壳、肌肉和内脏）以及 2016 年 12 月至 2019 年 1 月期间采集自西太平洋深海海沟（马里亚纳海沟、穆绍海沟和新不列颠海沟，水深达 10 853.2 米）的 100%的超深渊表面沉积物（0–2 厘米）样本（n=8）（Xie 等人，2023）。作者提到，包括 TBPH 在内的新型溴化阻燃剂可能会通过远距离大气迁移和洋流到达海沟表面海水。超深渊沉积物中的新型溴化阻燃剂一般通过海洋或陆地来源的沉积物颗粒的沉降来迁移，而在端足类动物体内，这些物质通过摄食食物网中的动物腐肉而积累（Xie 等人，2023）。作者进一步指出，超深渊沉积物中的新型溴化阻燃剂可能来源于吸附于塑料表面的这些物质。此外，还有人提出，沉积物会随着浊流发生远距离迁移（Kneller 等人，2016 年）。因此，含有 TBPH 的沉积物（该物质在沉积物中具有持久性）可能会通过浊流沿着海底远距离迁移。

48. 在远离已知点源的地点（如斯瓦尔巴的 Kongsfjord、Tempelfjord 和 Bjørnøya、挪威斯瓦尔巴群岛和加拿大北极地区），测得 TBPH 在以下样本中的含量为：海鸟和北极鸥（Larus hyperboreus）等海洋迁徙物种血浆（2012 年为 0.026±0.001 纳克/毫升，检出频率=17%，n=12；Harju 等人，2013）；三趾鸥（Rissa Tridactyla）肝脏（2009 年浓度范围为<0.171–1.398 纳克/克湿重和 14.62 纳克/克脂重（平均值），检出频率=50%，n=10；Sagerup 等人，2010）；欧绒鸭（Somateria mollissima）肝脏（2009 年浓度范围为<0.142–3.754 纳克/克湿重和 44.29 纳克/克脂重（平均值），检出频率=60%，n=10；Sagerup 等人，2010）；厚嘴海鸦（Uria lomvia）卵（2008 年浓度范围为<0.106–3.414 纳克/克湿重和 19.17 纳克/克脂重（平均值），检出频率=70%，n=10；Sagerup 等人，2010）；毛鳞鱼（Mallotus villosus）全身（2009 年浓度范围为<0.120–1.306 纳克/克湿重和 33.65 纳克/克脂重（平均值），检出频率=90%，n=10；Sagerup 等人，2010）；环斑海豹（Pusa/Phoca hispida）血浆（2012 年为 0.04 纳克/毫升，检出频率=10%，n=10；Harju 等人，2013）、肝脏（2007 年浓度范围为<0.138–0.876 纳克/克湿重和 16.36 纳克/克脂重（平均值），检出频率=60%，n=10；Sagerup 等人，2010）和脂肪（2009 年至 2013 年为<方法检出限–0.34 纳克/克脂重（几何平均值）；Houde 等人，2017），表明这种物质有可能通过迁徙物种转移到偏远环境中。

49. 此外，2012 年在格陵兰岛中东部，在黑海鸦（Cepphus grylle）卵中检测到 TBPH（0.05–0.066 纳克/克湿重或 0.024–0.025 纳克/克脂重；n=3）

（Vorkamp 等人，2015）。黑海鸦（Cepphus grylle）的迁徙受到限制，因为其在格陵兰岛过冬，仅从繁殖地到无冰地区进行短途迁移。因此，对黑海鸦体内污染物负荷的分析将反映格陵兰岛环境中的污染物接触情况（Vorkamp 等人，2004）。此外，检测到TBPH的还有北极地区特有物种北极熊（Ursus maritimus）的脂肪组织（<0.128–0.402 纳克/克湿重或<0.14–0.44 纳克/克脂重，n=5；Vorkamp等人，2015）和血浆（2012年0.15±0.16纳克/毫升，检出频率=95%，n=20；Harju 等人，2013）。在黑海鸦卵以及北极熊脂肪组织和血浆中观察到TBPH，这表明其来自北极以外来源的远距离迁移。

50. 用一种基准方法比较了偏远地点的空气、海水和生物群（例如黑海鸦卵和北极熊脂肪组织）中 TBPH 和具有持久性有机污染物特性的物质（例如十溴二苯醚（BDE-209）、五溴二苯醚、八溴二苯醚和得克隆）浓度，其结果表明，TBPH 的浓度范围与纳入《关于持久性有机污染物的斯德哥尔摩公约》之前的持久性有机污染物浓度范围相同（更多信息见附录表 A1、A2 和 A6 中的基准评估；Möller 等人，2011a；2011b 和 2012；Xiao 等人，2012a；Salamova 等人，2014；Vorkamp 等人，2015；北极监测和评估方案，2017 和 Sobotka 等人，2021）。这佐证了 TBPH 的远距离迁移潜力。此外，在 Salamova 等人（2014）的研究中，TBB 和 TBPH 是北极空气样本中测量的主要非多溴二苯醚溴化阻燃剂，在所分析的 45 种溴化阻燃剂中，分别占溴化阻燃剂总浓度的约 46%和 17%。

3.3.4 根据附件 D 标准得出的远距离环境迁移结论

51. 虽然模型预测表明远距离迁移的可能性很低，并有可能转移到地表介质，但监测数据表明，TBPH已经迁移到偏远地区（北极和南极）。TBPH的物理化学性质表明其有可能到达北极并在北极人类食物链中积累。监测数据佐证了这一点，表明已经在偏远区域（北极和南极）的环境和生物群样本中测量到了TBPH。北极、青藏高原和南极空气中存在 TBPH，表明发生了大气迁移。在南极洲苔藓和土壤发现了 TBPH，这佐证了 TBPH 的大气迁移，其主要与大气颗粒结合，并沉积到地表介质。此外，白令海、东格陵兰海和南大西洋海水中 TBPH 的测得含量表明，存在通过空气和/或水进行的远距离迁移。在西太平洋远离点源的深海沉积物（水深达 10 853.2 米）中检测到 TBPH，表明 TBPH 有可能通过吸附到悬浮物上发生远距离迁移，然后通过河流和洋流中的水迁移到沉积物中。此外，远离已知点源地点的迁徙物种和北极特有物种体内存在 TBPH，表明 TBPH 有可能通过候鸟转移到偏远环境。因此得出结论认为，TBPH 符合附件 D 第 1 (d) (i)、(ii)和(iii)段中列出的潜在远距离环境迁移标准。

3.4 不利影响

3.4.1 对人类健康和其他生物的不利影响

52. TBPH 对人类健康的主要不利影响与其在小鼠中观察到的神经行为影响及其对甲状腺系统的影响有关。本节中指出和介绍的其他影响可能导致 TBPH 的不利影响。

53. 神经行为影响：Bao 和 Jing（2021）研究了 TBPH 对五周大小鼠的神经行为影响。三组小鼠（对照组，20 毫克/千克体重/天和 200 毫克/千克体重/天；每组 n=8）通过经口灌胃接触 TBPH 28 天。使用莫里斯水迷宫测试评估了空间学习和记忆情况。通过测量丙二醛（MDA）、超氧化物歧化酶（SOD）和谷胱甘肽（GSH）评估了海马体中的氧化应激。该研究还测量了内质网（ER）应激

相关蛋白（葡萄糖调节蛋白 78-kDa（GRP78）、PKR 样内质网激酶（PERK）和 C/EBP 同源蛋白（CHOP））以及参与记忆的海马生物标志物，包括突触后致密物蛋白 95（PSD-95）、脑源性神经营养因子（BDNF）和磷酸化 cAMP 反应元件结合蛋白（p-CREB）。研究表明对空间学习和记忆没有影响。

54. 然而，20 和 200 毫克/千克/天的 TBPH 接触均显著改变了氧化应激标志物（$p<0.05$），增加了丙二醛并降低了超氧化物歧化酶和谷胱甘肽水平，表明海马体中脂质过氧化和氧化损伤增强。在 200 毫克/千克/天剂量下，内质网应激标志物（GRP78、PERK 和 CHOP）显著上调（$p<0.01$），表明内质网应激参与了 TBPH 诱导的神经毒性。在相同剂量下，TBPH 也显著降低了脑源性神经营养因子和突触后致密物蛋白 95 水平（分别为 $p<0.05$ 和 $p<0.01$），而磷酸化 CREB（p-CREB）没有受到有统计学意义的影响。由于这些生物标志物对于记忆形成至关重要，因此研究结果表明，尽管不存在行为影响，但 TBPH 可能会损害认知相关分子途径。

55. Xiong 等人（2024）通过腹腔注射施用 TBPH（20 毫克/千克体重/天；二甲基亚砜对照；每组 n=10）60 天，以进一步探究 TBPH 造成的神经毒性。使用莫里斯水迷宫和跳台被动回避测试评估了神经行为表现。此外，还评估了多个机制性终点，包括：海马氧化应激标志物（活性氧（ROS）和谷胱甘肽；凋亡相关指标（细胞色素 C（Cyt C）、凋亡蛋白酶激活因子-1（Apaf-1）、半胱天冬酶-3（Casp-3）、半胱天冬酶激活的脱氧核糖核酸酶（CAD）、N-甲基-D-天门冬氨酸受体 2B（NMDAR2B）和磷酸化 CREB（p-CREB））、免疫组化变化以及海马蛋白水平磷酸化细胞外信号调节激酶（p-ERK）、FOS 和 JUN。

56. 接触 TBPH 的小鼠在两项行为测试中表现均显著受损，逃避潜伏期和错误率增加，表明学习、记忆和认知功能存在缺陷。莫里斯水迷宫是一种广泛用于在实验性神经毒性研究（如经合组织 TG 426（发育神经毒性研究））中评估学习和记忆情况的测试。尽管与完整的（发育）神经毒性研究相比存在局限性，但观察到的神经行为影响提供了生物学相关信息，并可用作确定不利影响的证据权重方法中的证据。

57. 组织病理学和免疫组织化学分析显示海马体和背外侧前额叶皮层存在明显的结构损伤。接触 TBPH 显著增加了活性氧、谷胱甘肽、Cyt C、Apaf-1、Casp-3、CAD、p-ERK、FOS 和 JUN 的水平（$p<0.05$），同时显著减少了 NMDAR2B 和 p-CREB（$p<0.05$）。这些改变表明存在明显的氧化应激和细胞凋亡通路激活情况，特别是在海马体的齿状回内。综合来看，这些结果表明 TBPH 会通过氧化损伤和 ERK1/2–FOS 通路激活来诱导神经毒性，最终破坏神经元完整性和认知功能。

58. 现有研究表明，在低至 20 毫克/千克体重/天的剂量下，TBPH 会在小鼠腹腔注射接触后引起不良神经行为影响。这些影响似乎是由氧化应激增加、细胞凋亡通路激活和 ERK1/2–FOS 信号级联反应的过度激活介导的。Bao 和 Jing（2021）报告的神经行为变化缺乏可能与接触时间较短（28 天，而不是 60 天）和给药途径的差异（口服灌胃，而不是腹腔注射）有关。腹腔注射会确保几乎完全的全身吸收，而 TBPH 表现出的口服生物利用率较低（Knudsen 等人，2017）。此外，腹腔给药绕过了肝脏首过代谢，可能会导致更高的循环浓度和脑内浓度。

59. 尽管存在这些方法上的差异，但这两项研究都一致证明海马体中的氧化应激增加。实验设计之间的这种趋同现象强化了 TBPH 具有神经毒性潜力的结论。

60. 据《化学品注册、评估、许可和限制条例》档案报道，[23] 在根据经合组织 TG 408 对大鼠进行的 90 天重复经口给药毒性研究中，在高达 1 000 毫克/千克体重/天的剂量下，没有发现大脑中与给药相关的组织病理学变化，也未发现对脑重量的影响。这些研究结果不一定与 Bao 和 Jing（2021）以及 Xiong 等人（2024）的小鼠研究结果相矛盾，因为经合组织 TG 408 研究之目的不是检测神经功能性或机制性影响。此外，经合组织 TG 408 研究不包括对空间学习和记忆的评估，而这些评估是在小鼠研究中专门研究的，因此结果不具有直接可比性。还应注意的是，经合组织 TG 408 研究不包括专门针对周围神经（例如坐骨神经）的评价，因此未评估对周围神经系统结构的潜在影响。

61. 对动物的肺部影响：Xing 等人（2024）报告了体外和体内模型中接触 TBPH 与肺损伤标志物之间的关联。

62. 在体外，使小鼠 TC-1 和 MRC-5 细胞接触 TBPH（0–20 毫克/升）48 小时。接触 TBPH 导致以下水平升高：促炎细胞因子（肿瘤坏死因子 TNF-α）、白细胞介素-1β（IL-1β）、白细胞介素-6（IL-6）、白细胞介素-17（IL-17）、干扰素-γ（IFN-γ）、趋化因子（嗜酸性粒细胞趋化因子、单核细胞趋化蛋白-1（MCP-1））、单核细胞趋化蛋白-2（MIP-2），以及活化后受调控、由正常 T 细胞表达并分泌的趋化因子（RANTES）。此外，细胞增殖标志物 Ki67 减少，而 p16 和 p21 表达增加，表明出现了细胞周期停滞。TBPH 还上调了纤维连接蛋白（FN）、α-平滑肌肌动蛋白（α-SMA）和转化生长因子-β（转化生长因子-β）等细胞外基质（EM）标志物，同时下调 E-cadherin 并增加胶原沉积。活性氧和丙二醛水平上升，同时抗氧化标志物（谷胱甘肽、超氧化物歧化酶、过氧化氢酶）减少，表明氧化应激明显。

63. 在体内，8 周大的 C57 小鼠通过经口灌胃接触 TBPH（0（植物油对照）、10、30 和 60 毫克/千克体重/天；每组 n=5），持续 28 天。组织病理学检查均显示所有测试剂量下均出现肺泡毛细血管充血和炎症细胞浸润。在 10–60 毫克/千克体重/天剂量下，肺组织中的促炎细胞因子（TNF-α、IL-1β、IL-6、白细胞介素-8（IL-8）、IFN-γ）显著升高（$p<0.05$）。氧化应激标志物（活性氧、丙二醛）增加（$p<0.05$），而抗氧化酶（谷胱甘肽、超氧化物歧化酶、过氧化氢酶）减少（$p<0.05$），特别是在 30–60 毫克/千克体重/天剂量下。在 30 和 60 毫克/千克体重/天剂量下，转化生长因子-β 表达和胶原纤维含量也显著升高（$p<0.05$），表明肺纤维化的早期迹象。

64. 目前还没有通过吸入途径进行的研究。《化学品注册、评估、许可和限制条例》档案 [23] 中提供的一项大鼠 90 天口服毒性研究（经合组织 TG 408）报告称，在剂量最高达 1 000 毫克/千克体重/天时，肺部没有组织病理学变化。与 Xing 等人（2024）研究之间的差异，原因可能是物种敏感性和研究设计上的差异。Xing 等人（2024）观察到的分子变化可能代表早期或适应性反应，如果持续下去，可能发展为纤维化。这些研究结果表明，即使在相对较低的剂量下，TBPH 也可能启动促炎性信号通路。

[23] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM。

65. 肺部影响流行病学：Mendy 等人（2023、2024）在俄亥俄州大辛辛那提大都市区进行了两项前瞻性流行病学研究，调查了早期接触溴化阻燃剂（包括 TBPH）与儿童呼吸系统健康影响之间的关系。

66. 在 2023 年的研究中，跟踪了 234 名儿童的同期出生群。孕妇根据特定的标准入选（例如，年满 18 岁，英语流利，居住在当地且无搬迁计划，怀孕 16 周以下，没有某些疾病）。使用大容量小型表面采样器从孩子 1 岁时的卧室和主要活动室收集了沉降灰尘样本。将粉尘过筛（300 微米）、纯化并通过 HPLC-MS 进行分析，以确定有机磷酸盐阻燃剂（TCEP、TCIPP、TDCIPP、TPHP）和替代溴化阻燃剂（TBB 和 TBPH）的数量。所有有机磷酸盐阻燃剂的几何平均浓度为 10.27 微克/克灰尘，灰尘负荷为 2.82 微克/平方米。TCIPP 是数量最多的有机磷酸盐阻燃剂。对于替代溴化阻燃剂而言，几何平均浓度为 0.48 微克/克灰尘，负荷为 0.13 微克/平方米，TBPH 水平（0.27 微克/克灰尘，负荷为 0.08 微克/平方米）高于 TBB。每两年通过照料者问卷评估呼吸系统健康，直至 5 岁。5 岁时，儿童接受肺量测定，测量 1 秒用力呼气量（FEV_1）和峰值呼气流量（PEF）。婴儿期接触有机磷酸盐阻燃剂和替代溴化阻燃剂与呼吸道症状的风险增加有关，TBPH 粉尘负荷与峰值呼气流量降低有关（$p<0.05$）。根据关键潜在混杂因素调整了 TBPH 粉尘负荷与 5 岁时峰值呼气流量降低之间的关系，这些因素包括儿童性别、种族/民族、出生体重、胎龄、体型（身高）、家庭收入、母乳喂养持续时间、产前接触烟草烟雾情况（血清可替宁）和家庭总粉尘重量；额外考虑住房清洁指标的敏感性分析不影响结果。

67. 2024 年的研究跟踪了 342 名孕妇组群（2003–2006 年）。在妊娠 20 周时收集了室内灰尘样本，并在妊娠 16 周和 26 周以及分娩时测量了母亲尿液中的有机磷酸酯（OPE）和替代溴化阻燃剂浓度。评估了产前接触与呼吸系统健康影响（每两年报告一次，直至 5 岁）和 5 岁时肺功能之间的联系。TBPH 粉尘浓度与儿童喘鸣风险增加有关（儿童呼吸困难；相对危险度（RR）：1.57，95% 置信区间：1.28–1.94，$p<0.0001$））。在这两项研究（Mendy 等人，2023 和 Mendy 等人，2024）中，尽管由于观察性研究设计而无法确定因果关系，但认为所观察到的与不良呼吸系统影响的关联对于认定不利影响具有参考意义和佐证作用。

68. 内分泌影响：Yuan 等人（2024）评估了 TBPH 对雄性 Sprague-Dawley 大鼠的内分泌干扰潜力。在一项为期 28 天的重复给药研究中，对 48 只大鼠（6 周大）经口灌胃施用 TBPH，剂量为 0（玉米油对照）、5、50 和 500 毫克/千克体重/天。收集了血液和甲状腺进行临床化学和组织病理学分析。在 500 毫克/千克体重/天剂量下，甲状腺明显变小（$p<0.05$），这一点得到了相对器官重量计算（$p<0.05$）的佐证，组织学变化包括滤泡上皮变平和滤泡腔扩张。50 和 500 毫克/公斤剂量组的血清总甲状腺素（TT4）和游离甲状腺素（FT4）水平显著升高（$p<0.05$），而促甲状腺激素（TSH）显着降低，表明下丘脑–垂体–甲状腺（HPT）轴紊乱。欧洲化学品管理局/欧洲食品安全局指南（2018）支持的解释是，当甲状腺器官重量和组织病理学的变化与内分泌活动相关时，即可认为是甲状腺介导的不利影响。相比之下，《化学品注册、评估、许可和限制条例》档案 [23] 中提供的一项符合准则的大鼠 90 天口服毒性研究（经合组织 TG 408）报告称，在高达 1 000 毫克/千克体重/天剂量下，甲状腺没有组织病理学变化（未测量甲状腺重量）。然而，未评估甲状腺组织病理学以外的内分泌终点。

69. 遗传毒性、生殖毒性和致癌性：根据现有信息，TBPH 可能对生殖没有毒性。由于缺乏数据，目前尚无法就其生殖毒性和致癌性得出结论。关于这些终点的进一步信息载于资料文件（UNEP/POPS/POPRC.22/INF/6）。

3.4.2 对环境的不利影响

70. 《化学品注册、评估、许可和限制条例》登记档案中未提供长期鱼类毒性研究。该档案[5]中提供了短期鱼类毒性研究（经合组织 TG 203）、长期水蚤繁殖测试（经合组织 TG 211）和藻类研究（经合组织 TG 201）。所有这些研究表明，在测试浓度下没有观察到任何毒性作用。资料文件（UNEP/POPS/POPRC.22/INF/6）进一步详细介绍和讨论了经合组织 TG 203、211 和 201 研究。

71. 《化学品注册、评估、许可和限制条例》登记档案[5]包括一项关于 TBPH 溶解度的研究，该研究根据欧盟理事会法规 A.6 方法，使用烧瓶法（基本相当于经合组织 TG 105）进行研究。在水中无法检测到该物质，表明 20°C 下的溶解度<0.05 微克/升，而使用 1%乙腈作为增溶剂时，溶解度极限报告为 794 微克/升。然而，鉴于经合组织 TG 105 建议使用柱洗脱法（而不是烧瓶法）来确定溶解度<10 毫克/升的测试化学品的水溶解度，上述研究的可靠性值得怀疑。此外，没有报告不同烧瓶中的 TBPH 浓度。因此，无法检查烧瓶之间的浓度差是否≤15%。此外，未报告试验期间的 pH 值。

72. 以下由 Fu 等人（2024a、b）、Hong 等人（2025）、Zhou 等人（2024）和 Guo 等人（2020）报告的研究是在高于纯水中溶解度极限的浓度下进行的，但研究使用二甲基亚砜作为溶剂。Zhou 等人（2024）指出，基于先前的 TBPH 实验（Guo 等人，2020；Zhou 等人，2021；Guo 等人，2021；Zhou 等人，2022），在其进行的斑马鱼研究中测试的浓度（标称 10 微克/升）低于二甲基亚砜和水混合物（使用 0.01%体积分数的二甲基亚砜）中的溶解度极限（2025 年 10 月 Zhou 个人通信）。在另一项斑马鱼研究（Guo 等人，2020 年）中，作者提到，TBPH 在 0.1%（体积分数）的二甲基亚砜中的最大浓度约为 2 微摩尔/升（即约 1 412 微克/升）；Guo 个人通信，2025 年 10 月）。据作者称，TBPH 完全溶解在 0.1%（体积分数）的二甲基亚砜中，TBPH 浓度最高达 141 微克/升（Guo 个人通信，2025 年 10 月）。Fu 等人（2024a、b）的研究作者在制备储备溶液时使用涡旋振荡和超声波处理，以确保 TBPH 在二甲基亚砜（0.005%）中发生完全分子水平溶解。在每日更新接触溶液时，将储备溶液缓慢添加到强烈通气和搅拌的稀释水中，确保二甲基亚砜在水中快速扩散和稀释，以促进 TBPH 以分子形式分散，从而最大限度地减少胶体或微晶体的形成（Fu 个人通信，2025 年 10 月）。进行目视检查，溶液保持清澈透明，未观察到浑浊、沉淀、乳浊或可见晶体/颗粒。此外，接触溶液中的 TBPH 浓度测量值与标称浓度一致（Fu 个人通信，2025 年 10 月）。

73. 在 Hong 等人（2025）的研究中，通过几项措施确保了测试期间接触方案的可靠性：鱼的游泳活动、接触介质每日更换，以及实际接触浓度的监测（Hong 个人通信，2025 年 10 月）。同样，Zhou 等人（2024）确保每天更新接触介质，以保持浓度一致并最大限度地减少潜在的聚集或沉降。基于之前关于 TBPH 的工作（Zhou 等人，2022；Zhou 等人，2021；Guo 等人，2021；Guo 等人，2020），作者证实测试浓度（标称 10 微克/升）低于二甲基亚砜和水混合物中的溶解度极限（Zhou 个人通信，2025 年 10 月）。为了确保 TBPH 完全溶解在接触介质中，在稀释前对二甲基亚砜（0.01%体积分数）中的储备溶液进行了超声和强烈涡旋处理（Zhou 个人通信，2025 年 10 月）。接触期间，接触

溶液中没有观察到可见的沉淀物、晶体或聚集体，测得 TBPH 浓度的一致性表明 TBPH 在很大程度上已经溶解（Zhou 个人通信，2025 年 10 月）。后来的研究没有报告测试介质中存在未溶解的供试品、浑浊现象、油膜的形成或该物质未溶解的其他指标。Guo 等人（2020）的研究作者指出，在最高浓度组（1 412 微克/升 TBPH）的试验中出现了白色薄雾，表明存在未溶解的 TBPH（Guo 个人通信，2025 年 10 月）。据作者称，仅在最高浓度组中观察到白色薄雾，该组中 TBPH 接近饱和。为了保持接触的一致性，每天更新溶液以尽量减少这种影响。在较低浓度组中，没有观察到此类沉淀，接触溶液在整个实验过程中保持清澈。因此，根据作者的说法（Guo个人通信，2025年10月），在较低浓度组（最高为0.2微摩尔/升或141微克/升）中，胚胎/幼虫仅接触了溶解的TBPH。因此，并根据上述分析监测信息，认为这些研究是可靠的。不利影响的评估重点是在测试生物仅接触溶解 TBPH 的浓度下观察到的影响。

74. 根据关于难溶试验化学品的水相水生毒性试验的经合组织 GD 23（经合组织，2019），溶剂会提供一种载体，可以将一些难溶的试验化学品溶解于其中，以产生更适合添加到测试介质中并与之混合的储备溶液。虽然上述对藻类（经合组织 TG 201）和无脊椎动物（经合组织 TG 211）的毒性研究不适合证明该物质在测试介质中的饱和浓度，但经合组织 GD 23 解释说，100 毫克/升的溶剂浓度不太可能显著改变测试溶液中可以达到的测试化学品最大溶解浓度。二甲基亚砜是已发现可有效用于水生毒性测试的溶剂之一。Hutchinson 等人（2006）回顾了使用溶剂进行的水生研究，并报告称浓度范围为 0.001–2%二甲基亚砜的研究没有引起任何影响，包括性腺组织学、产卵、肝脏卵黄蛋白原水平和其他组织学和生物标志物方面的影响，仅在 0.02%二甲基亚砜浓度下引起斑马鱼（Danio rerio）产生热休克蛋白以及在0.001%浓度下降低了胖头鳐（Pimephales promelas）的产卵量。根据 Hutchinson 等人（2006）基于使用二甲基甲酰胺所产生影响的建议，经合组织 GD 23 推荐使用 20 微升/升的最大溶剂浓度。

75. 本节所述研究并非标准试验，但可认为其中包含溶剂对照的数据是可靠的。Zhou等人（2024年）研究的作者表明，根据已发表的文献和斑马鱼毒理学研究的既定实验规范，广泛认为浓度≤0.1%的二甲基亚砜对斑马鱼胚胎和幼鱼无毒性，并且通常用作 TBPH 等疏水性化合物的溶剂（Zhou 个人通信，2025 年 10 月）。在其之前关于 TBPH 的工作中（Guo 等人，2020），将接触 0.1%DMSO 的斑马鱼胚胎或幼虫的发育、存活、神经毒性、肝脏转录组现象和行为与无溶剂对照组进行比较，没有发现显著差异，因此表明二甲基亚砜没有产生任何影响。Guo在个人通信（2025年10月）中提到，根据经合组织TG 236进行的研究也报告了二甲基亚砜浓度最高达 1%时没有出现明显的形态或发育异常，这佐证了 0.1%二甲基亚砜的适用性。鉴于 TBPH 的溶解性较差且二甲基亚砜对受试生物没有影响，因此认为在以下研究中使用该溶剂是可以接受的。

76. TBPH 的关键环境影响针对的是鱼类繁殖和鱼类甲状腺系统。以下段落介绍了对生殖的广泛不利影响（精子计数和畸形、成年生殖行为以及对早期幼鱼发育的影响）。佐证这些影响的，是暗示对甲状腺系统产生不利影响（眼部发育、与光/视觉相关的影响、肝脏脂肪变性和游泳速度）的机制性证据。

77. 生殖和内分泌影响：Fu 等人（2024a）的一项研究发现，TBPH 影响了斑马鱼（Danio rerio）的基因调节和生殖行为。使四个月大的雄性斑马鱼接触 0、1.4、14、140 和 1 400 微克/升的 TBPH（每剂量组 20 条鱼；组重复 3 次），含有 0.005%二甲基亚砜（体积分数；不使用无溶剂对照），在基于标称/测量浓度的半静态系统中持续 28 天。在这项研究中，选择了 24 条接触该物质的雄性

成鱼，然后将其与未接触的雌性成鱼配对，观察其行为，并评估所产生的胚胎和幼虫的发育参数。作者提到，化学分析表明，在西班牙巴塞罗那附近的流入废水样本中检测到 TBPH 浓度最高为 0.13 微克/升（Cristale 等人，2015）。因此，作者得出结论认为，1.4 微克/升是环境相关浓度。接触该物质对斑马鱼幼体的孵化成功率、存活率、体长和心率产生了显著的浓度相关影响。这些反应的方向、一致性和浓度依赖性，特别是存活率下降（≥14 微克/升；$p<0.05$）、生长减缓（≥1.4 微克/升；$p<0.05$）和心脏活动降低（≥1.4 微克/升；$p<0.01$），表明发生了发育和生理表现受损，而不是适应性调节。综合来看，这些研究结果证明了早期幼鱼发育过程中存在生物[24]相关的不利影响。幼鱼孵化率、存活率、生长率和心率降低会对种群产生直接影响。

78. 对于成鱼而言，观察到了内分泌活动。具体而言，雄性斑马鱼在所有接触浓度（1.4、14、140 和 1 400 微克/升）下大脑中雄激素受体（AR）的转录表达均显示最显著的降低（$p<0.001$），随后芳香酶（细胞色素 P450，cyp19b）在所有接触浓度下均出现上调（$p<0.05$）。雄激素受体是核受体家族的成员，在各种器官中表达，包括性腺和大脑，已证明其会在胚胎形成、精子形成和生殖行为中发挥作用（Chang 等人，2013）。此外，成年雄性的血液样本显示，在两个最高浓度下，11-酮睾酮在统计学上显著下降（$p<0.05$）。此外，在除了最低浓度（LOEC[25]为 14 微克/升）外的所有浓度下，与溶剂对照组相比，接触了该物质的雄性鱼的交配行为导致与雌性鱼的平均距离增加和接近度下降，并且在所有 TBPH 接触浓度下，每对鱼的接近频率均降低（$p<0.01$）。性腺组织病理学显示，在两个最高剂量组（140 和 1 400 微克/升；$p<0.01$）中，接触了该物质的成鱼的精原细胞出现了有统计意义的减少；在 140 微克/升处理组中，精母细胞（SPC）减少（$p<0.05$）。此外，接触 TBPH 后，精子畸形（体长缩短、心包囊肿、卵黄囊肿和尾部歪斜）的发生率呈浓度依赖性增加。TBPH 还导致精子活力下降（≥140 微克/升；$p<0.01$）。研究结果表明，TBPH 可以作为内分泌干扰物，在 LOAEC[26]为 1.4 微克/升时损害斑马鱼的繁殖并产生不利影响。

79. 内分泌影响：Hong 等人（2025）在一项使用稀有鮈鲫幼鱼（Gobiocypris rarus；两个月大）的 28 天接触毒性研究中评估了 TBPH 的甲状腺毒性。在一项使用幼年稀有鮈鲫（Gobiocypris rus rarus；驯化 14 天后，使鱼接触 0、0.1、100 和 1 000 微克/升 TBPH（含 0.01%二甲基亚砜（体积分数））的标称/测量浓度；Hong 个人通信，2025 年 10 月），为期 28 天。每天更换接触溶液并清洁养鱼缸，以去除食物残渣和粪便。在任何实验组（包括对照组）中均未观察到鱼类死亡（Hong 个人通信，2025 年 10 月）。根据作者传达的信息，氧饱和度约为 80%。在不利影响方面，TBPH 引起稀有鮈鲫幼鱼体重呈浓度依赖性下降，与对照组相比，TBPH 在 100 微克/升和 1 000 微克/升时显著减轻（$p<0.05$）。作者提到，在甲状腺功能亢进个体中观察到的普遍症状是体重减轻。

80. 接触期结束后，对脑、肝脏、甲状腺和肠道组织进行了采样，以便进行进一步组织病理学检查和转录组分析，并确定了鱼脑中的甲状腺激素水平。接触 TBPH 28 天后，鱼脑中甲状腺相关基因的转录水平表明，三种脱碘酶（dio1、dio2 和 dio3）在所有 TBPH 处理组中表现出相似的表达模式。脱碘酶基因 dio2

[24] 值得注意的是，根据欧洲食品安全局（2017），对于动物研究的连续数据而言，影响具有生物学意义指的是临界效应值（平均反应值的变化）达到 5%。

[25] LOEC 是指最低观测效应浓度。

[26] LOEC 是指最低观测不良效应浓度。

在 1 000 微克/升 TBPH 浓度下表现出显著增加（p<0.05），而 dio1 和 dio3 在 1 000 微克/升和 100 微克/升 TBPH 浓度下分别表现出显著下调（p<0.05）。观察到脑中苹果酸脱氢酶（me）、钠碘转运蛋白（nis）和甲状腺过氧化物酶（tpo）的表达显著增加（p<0.05）（0.1 微克/升 TBPH 浓度），表明存在组织特异异质性。对于肝组织而言，dio3 和甲状腺受体（tr）等甲状腺相关基因在 100 微克/升 TBPH 浓度下表现出显著下调（p<0.05），而转甲状腺素蛋白（ttr）在 1 000 微克/升 TBPH 浓度下表现出显著上调（p<0.05）。Hong 等人（2025）指出，化学诱导的甲状腺相关基因表达变化是功能障碍的关键指标。鱼脑组织中的甲状腺激素水平表明，接触 1 000 微克/升 TBPH 导致 T4 水平显著变化（p<0.05），但所有 TBPH 接触组中的 T3 水平与对照组相比没有差异（p>0.05）。T4 浓度的增加，加上脱碘酶和甲状腺激素通路基因的转录调节，表明甲状腺激素稳态受到直接干扰。组织病理学结果表明，在 0.1 微克/升和 1 000 微克/升 TBPH 浓度下，甲状腺组织出现明显的局灶性增生。在 1 000 微克/升 TBPH 浓度下，观察到上皮细胞脱落进入滤泡腔。甲状腺滤泡增生和上皮变性代表内分泌组织的不良结构改变。作者认为，甲状腺组织的病理损伤会扰乱其合成、储存和分泌甲状腺激素的功能，表明该物质有可能成为内分泌干扰物。

81. 对鸟类的影响：Goodchild 等人（2021）研究了卵内接触环境相关浓度的 TBPH 是否会影响美洲红隼（Falco sparverius）的生长、孵化成功率、氧化应激或甲状腺功能。红隼胚胎在胚胎期第 5 天接触 TBPH。具体而言，将 TBPH 注射到每只受精卵的气室中，TBPH（溶解在有机红花油中）标称浓度为 0 纳克/克卵重（n=23）、10 纳克/克卵重（n=23）、50 纳克/克卵重（n=25）、100 纳克/克卵重（n=24）。作者指出，卵内容物（孵化前）和卵黄囊残留物（孵化后）中的 TBPH 浓度远低于注射浓度（对于接触 100 纳克/克的卵，测量浓度为 1.8–9.5 纳克/克卵重（n=10））。结果显示，在雌雄雏鸟脑质量减少方面存在显著不利影响（100 纳克/克 TBPH；p<0.05），接触了 50 和 100 纳克/克 TBPH 的雄性雏鸟的心脏明显更重（p<0.05）。作者提到，心脏增大可能反映了在同样的雄性雏鸟中观察到的甲状腺变化，如下所述。

82. 此外，在 100 纳克/克 TBPH 浓度下接触 TBPH 后，两种性别的肝脏中不同氧化应激生物标志物（例如硫醇、硫化谷胱甘肽（GSSG）、总麸胱甘肽（总 GSH）和还原型谷胱甘肽（GSH）以及总硫醇和蛋白结合巯基（PBSH））均显著增加（p<0.05）。对雏鸟甲状腺的组织病理学检查显示，在 100 纳克/克 TBPH 浓度下，两种性别的胶质直径（CD）均显著降低（p<0.05）。由于胶质构成甲状腺激素的储存区间，这种结构变化表明甲状腺滤泡活性发生了变化，并可能表明甲状腺激素稳态失调。在这项研究中，还观察了在两种性别的内分泌活动：卵内接触 10 纳克/克 TBPH 的雏鸟血浆 T3:T4 比例显著降低（p<0.05），而接触 100 纳克/克 TBPH 的雏鸟腺体 T3:T4 比例显著增加（p<0.05）。后者表明接触 TBPH 会扰乱甲状腺激素平衡。这项研究表明，鸟类接触 TBPH 除了潜在发育影响外，还表现出几种氧化应激迹象（例如心脏质量增加（雄性仅在 50 纳克/克卵重下即有此影响）和雏鸟脑质量减少（在 100 纳克/克 TBPH 下））。研究进一步表明，TBPH 会影响鸟类的甲状腺发育和活性。

83. 对眼部发育的影响：在 Zhou 等人（2024）的一项研究中，斑马鱼胚胎（受精后 0.75 小时）接触 10 微克/升标称浓度的 TBPH，相当于接触 7 微克/升平均测得接触浓度 144 小时。每个对照组和处理组重复三次，含有 0.01%的二甲基亚砜（体积分数）作为溶剂。没有同时使用无溶剂对照组，因为在斑马鱼

研究中广泛认为≤0.1%的二甲基亚砜是无毒的；先前的研究工作（Guo 等人，2020）显示，二甲基亚砜和无溶剂对照组之间没有显著差异，从而可以明确识别 TBPH 本身的影响（Zhou 个人通信，2025 年 10 月）。转录组分析发现，在进行接触直至受精后 144 小时的胚胎中，共有 5 781 个基因发生显著变化（倍数变化>2，p<0.05），其中 2 734 个基因上调，3 047 个基因下调。接触 TBPH 后，晶状体中的标记蛋白 βB1-晶状体蛋白的免疫荧光染色显著减弱。接触还显著降低了晶状体蛋白相关基因和视蛋白基因（opn1mw4）的表达；前者是晶状体纤维细胞的关键蛋白质，这种细胞是晶状体的发育和正常功能所需的，后者负责对正常色觉必需的一种蛋白质进行编码。眼部的组织病理状况表明，接触 TBPH 导致神经节细胞层（GCL）（p<0.001）、内核层（INL）（p<0.05）和视网膜色素上皮（RPE）（p<0.001）区域发生显著变化。这项研究表明，接触 7 微克/升浓度的 TBPH 会对斑马鱼眼部发育产生不利影响。Zhou 等人（2024）指出，视觉系统的正常功能，尤其是感光器，对于鱼类的运动、捕食或躲避捕食者至关重要，视觉系统的破坏会对鱼类的生存和种群稳定造成严重危害。

84. Zhou 等人（2024）的研究表明，这些眼部影响可能具有持久性。作者认为，在晶状体和视网膜迅速形成的早期发育期间产生的破坏，可能会导致永久性缺陷（Harding 等人，2008 和 Yi 等人，2023）。参与晶状体分化的基因（例如晶状体蛋白、mipa、lgsn）和光感受器功能（例如视紫红质、视蛋白）的下调佐证了这一点。先前的研究表明，早期视觉系统损伤通常无法恢复，导致终生损伤（Chen，2020）。总之，TBPH 会对斑马鱼造成持久的视觉损伤，对受污染环境中的个体健康和种群稳定产生严重影响。

85. 肝脏影响：Fu 等人（2024b）研究了 TBPH 对野生型斑马鱼的毒性。使性成熟鱼（20 条/性别/组；每组重复 3 次；4 个月大的鱼）在 20 升玻璃缸中接触标称浓度为 0、0.14、1.41、14.1 和 141 微克/升的 TBPH 两个月。对照组和接触组均加入 0.005%的二甲基亚砜，并且每天完全更换接触溶液。根据 Fu 等人（2024b）的研究，TBPH 的最低浓度（0.14 微克/升）与西班牙巴塞罗那废水中报告的含量（0.13 微克/升；Cristale 等人，2015），表明本研究中接触浓度具有环境相关性。最高浓度（141 微克/升）是根据作者之前研究（Guo 等人，2021）中的预实验结果选择的，该浓度在斑马鱼接触 28 天后对其产生了毒性作用。在本实验期间，进行了转录组、生化和组织病理分析。

86. 对对照组和 141 微克/升 TBPH 接触组的肝组织进行了转录组分析。在 141 微克/升 TBPH 浓度下观察到具有统计学意义（p<0.05）的性别特异性代谢紊乱：雌性鱼表现出脂质生物合成基因下调，表明脂质代谢受损，而在雄性鱼中观察到胰岛素信号和糖酵解基因上调，表明糖酵解活性增强和葡萄糖-脂质稳态紊乱。生化分析揭示了性别特异性肝脏生化变化。在雌性中，在 14.1 和 141 微克/升时观察到肝糖元升高（p<0.05）；在雄性中，在≥0.14 微克/升时观察到血胰岛素水平降低（p<0.05），在≥1.41 微克/升时观察到肝乳酸水平降低（p<0.05）。这些影响反映了葡萄糖代谢的显著失调。Fu 等人（2024b）提出，这些指标的变化可认为是某些肝脏疾病的信号。在雄性斑马鱼肝脏中，在≥1.41 微克/升 TBPH浓度下观察到超氧化物歧化酶和活性氧（ROS）显著增加（p<0.05），在 141 微克/升 TBPH 浓度下观察到过氧化氢酶显著增加（p<0.05），表明产生了氧化应激。在雄性斑马鱼肝脏中，在 141 微克/升 TBPH 浓度下肿瘤坏死因子 α 显著增加（p<0.05），在≥14.1 微克/升 TBPH 浓度下白细胞介素显著增加（p<0.05），表明产生了炎症反应。在雌性斑马肝脏中，在≥14.1 微克/升 TBPH 接触组中观察到活性氧水平显著升高（p<0.05）。

87. 以下所述影响在综合考虑时可认为属于不利影响。Fu 等人（2024b）发现，与溶剂对照组相比，在浓度≥14.1 微克/升 TBPH 时，雌性斑马的体重和肝体指数明显更高（p<0.05），而雄性斑马则无显著变化。肝体指数增加通常用于指示代谢应激或解毒活动。此外，组织病理学检查显示，在接触剂量为≥1.41 微克/升的情况下，雌性动物出现肝脏脂肪变性（p<0.001），在接触剂量为 141 微克/升的情况下，雄性动物出现肝脏脂肪变性（p<0.001），显示出明显的肝细胞气球化效应。肝细胞气球化是肝脏脂质积聚的一个关键特征，最终会导致肝细胞脂肪变性。同样，油红 O 染色显示经 TBPH 处理的肝细胞中细胞内脂滴呈剂量依赖性增加。炎症因子的改变表明雄性斑马鱼的肝脏受到了更严重的影响。Fu 等人（2024b）的研究表明，斑马鱼接触环境相关浓度的 TBPH 会导致内脏脂肪积聚增加，这表明潜在的肝脏功能异常。Fu 等人（2024b）发现，TBPH 在斑马鱼的肝脏中积聚最多，从大脑（雄性中的半衰期最长达 15.67 天）和肌肉（雌性中的半衰期最长达 14.52 天）的清除较慢，表明具有持久性影响。组织病理学检查显示剂量依赖性肝损伤，雄性鱼更严重。炎症标志物升高，尤其是雄性。这些影响发生在环境相关浓度下（Cristale 等人，2015），对野生种群构成风险。

88. 对能量稳态的影响：Guo 等人（2020）使斑马鱼胚胎（受精后 0.75 小时；n=~250）和幼鱼接触加入 0.1%（体积分数）二甲基亚砜、浓度为 0、0.14、1.4、14、141 和 1 412 微克/升 TBPH 直至受精后 72 小时（半静态条件，基于标称/测得浓度），研究了 TBPH 对其过氧化物酶体增殖物激活受体 γ（PPARγ）、脂质代谢和游泳行为的影响。每个溶剂对照组和接触组重复四次。据作者称，没有同时使用无溶剂对照组，因为 0.1%的二甲基亚砜已被广泛确定为用于斑马鱼胚胎/幼鱼研究的可接受溶剂浓度（Guo 个人通信，2025 年 10 月）。这项研究包括一种 PPARγ 激动剂罗格列酮（0.1 微摩尔/升）作为阳性对照，一种 PPARγ 拮抗剂 GW9662 作为阴性对照。通过持续接触，测量了受精后 120 小时幼鱼的三磷酸腺苷含量和运动行为，以评估能量稳态的可能改变情况。

89. Guo 等人（2020）发现，接触 TBPH 24 小时的胚胎在浓度≥141 微克/升时，会使 PPARγ 介导的脂质启动子出现显著的 DNA 去甲基化（p<0.05）；与此同时，在受精后 72 小时的幼鱼中，多个基因上调：TBPH 处理组中，PPARrγ（在≥141 微克/升的浓度下）显著上调（p<0.05），而在两个最高接触浓度（≥141 微克/升）下，tet 甲基胞嘧啶双加氧酶 2（tet2）基因转录也显著上调（p<0.05）。在与脂质代谢相关的下游基因中，脂肪酸结合蛋白（fabp11a）基因转录在浓度≥141 微克/升时以浓度依赖性方式显著上调（p<0.05）。细胞色素 P450（cyp11a1）基因转录在浓度为 141 微克/升时显著增加（p<0.05）。除最低接触浓度（≥1.4 微克/升）外的所有接触浓度下，受精后 72 小时的幼鱼体内的甘油三酸酯（p<0.05）浓度和总胆固醇（p<0.05）均显著降低。在≥14 微克/升 TBPH 中，受精后 72 小时的幼鱼总中性脂质含量显著（p<0.05）降低。在受精后 120 小时的幼鱼中，测量了三磷酸腺苷（ATP）浓度。在两个最高接触浓度（≥141 微克/升）下，三磷酸腺苷浓度显著增加（p<0.05），而在 15 分钟的连续黑暗刺激期间，在除最低处理组（≥1.4 微克/升）之外的所有处理组中，受精后 120 小时斑马鱼幼体的平均游泳速度显著增加（p<0.05）。根据欧洲化学品管理局关于应用 CLP 标准的指导意见（欧洲化学品管理局，2024b），在不利影响评估中必须考虑认为与种群相关的行为影响。研究结果表明，TBPH 会影响 PPARγ 启动子的甲基化（浓度≥141 微克/升），并且 TBPH 作为 PPARγ 激动剂发挥作用。这种改变随后通过 PPARγ 信号通路影响幼鱼的脂质代谢，导

致能量稳态破坏（通过三磷酸腺苷（≥141 微克/升）和游泳速度（≥1.4 微克/升）的变化观察到），这对生存有严重影响。

3.4.3 关于不利影响的结论

90. 认为 TBPH 符合附件 D 第 1 (e) (i)和(ii)段所列的不利影响标准。

91. 关于对人类健康的不利影响，实验研究表明，TBPH 有可能造成小鼠的神经行为影响（20 毫克/千克体重/天）以及小鼠和鸟类大脑发生变化等不利影响。一项动物研究中，对大鼠甲状腺系统（500 毫克/千克体重/天）的影响与甲状腺萎缩和甲状腺激素变化（50 毫克/千克体重/天）一致，表明可能产生内分泌干扰。已观察到其他可能导致 TBPH 不良效应的影响，例如对小鼠炎症和纤维化等肺损伤标志的影响（30–60 毫克/千克体重/天）。与肺部影响有关的流行病学证据还表明，生命早期接触 TBPH 与儿童呼吸系统影响之间可能存在联系。

92. 关于对环境的不利影响，有关水生生物的数据表明，TBPH 可对生殖造成环境不利影响，如影响早期幼体发育（最低观测不良效应浓度为 1.4 微克/升）、降低鱼类精原细胞和精母细胞的百分比（包括精子畸形和精子活力降低；最低观测不良效应浓度为 140 微克/升）。已观察到其他影响，表明对甲状腺系统产生不利影响，例如对幼鱼眼部发育的影响（最低观测不良效应浓度为 7 微克/升），幼鱼甲状腺增生（0.1 微克/升），对鱼肝的影响（雌性在 1.41 微克/升下脂肪变性，雄性在 141 微克/升下脂肪变性），以及幼鱼能量稳态受到破坏，影响游泳行为（1.4 微克/升）。这些不利影响可能导致正常功能受损并对猎物行为产生负面影响，两者最终都会影响种群的维持。

4. 关切的理由和采取全球行动的必要性说明

93. 根据现有数据，认为 TBPH 符合《斯德哥尔摩公约》附件 D 中关于持久性、生物积累性、远距离迁移和不利影响的筛选标准。

94. 由于 TBPH 在许多应用中的持续使用，TBPH 通过人类活动直接或间接排放到环境中。

95. TBPH 具有持久性、生物积累性，有证据表明对人类健康和环境产生不利影响，并且有可能在空气和水中进行远距离环境迁移，使该物质的排放成为越境污染问题。在全球范围内，TBPH 在野生动物和环境基质（空气、土壤、沉积物、水）中的出现和分布得到了证明，包括北极和南极等偏远地区的测量结果。此外，在淡水、地下水和海水以及废水处理厂（WWTP）的污泥中检测到了 TBPH，这些污泥在农业用地上的散布可能导致土壤污染，并随后污染用于食用的植物（见欧洲化学品管理局，2022，附件一）。在人类的指甲、毛发和（母亲）血清（包括学龄儿童的血清）中发现了 TBPH。TBPH 可以通过鸟蛋、人类母乳和胎盘转移到敏感的生命阶段。在供人类食用的食品和室内灰尘中也检测到了 TBPH。因此，人类可能通过饮食以及摄入或吸入灰尘和接触灰尘而接触 TBPH。

96. 在人类中，发现儿童时期接触 TBPH 与不良呼吸系统影响（尤其是喘鸣和峰值呼气流量降低）之间可能存在联系。

97. 动物研究中与野生动物和人类相关的影响包括神经毒性和对生殖的影响。已观察到其他影响，这些影响导致针对甲状腺系统的 TBPH 不利影响，例如对鱼类眼部发育的影响、甲状腺萎缩和增生、肺功能，以及对肝脏、脂质代谢和

能量稳态的影响。这些影响可能会导致生殖功能受损，并可能对猎物行为产生影响，这两者最终都会对生物体的种群数量产生负面影响。

98. 其他关切包括TBPH的持久性，这会增加接触野生动物的可能性、程度和持续时间。TBPH 会通过空气和/或水进行远距离迁移，可能导致区域或全球污染。因此，该物质的释放可能导致生物大面积长期接触该物质。TBPH 通过食物链发生生物积累和生物放大，导致顶级捕食者物种体内浓度增加。

99. 一项基准研究工作表明，偏远地点的空气、海水和生物群中发现的 TBPH 浓度与十溴二苯醚（BDE-209）、五溴二苯醚、八溴二苯醚和得克隆等持久性有机污染物物质在纳入《关于持久性有机污染物的斯德哥尔摩公约》之前的浓度范围相同。

100. 北极空气和大湖区的TBPH浓度有增加的迹象，这反映了其作为多溴联苯醚阻燃剂替代品的使用可能增加，令人关切。事实上，TBPH 已在偏远地区发现，应当保护这些地区免受人类活动产生的危险物质的进一步污染，因为原始环境的内在价值应当得到保护。

101. 根据TBPH的持久性、生物积累性、对水生生物和陆地生物（包括人类）的毒性以及在包括偏远区域在内的环境区间中的广泛存在，可以得出结论，TBPH 的使用可能对人类健康和环境产生不利影响，因而有必要采取全球行动。

5. References

AMAP [Arctic Monitoring and Assessment Programme] (2017). AMAP Assessment 2016: Chemicals of Emerging Arctic Concern. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway. xvi+353pp. https://www.amap.no/documents/download/3003/inline.

Baldwin, K.R., Phillips, A.L., Horman B., Arambula, S.E., Rebuli, M.E., Stapleton, H.M., Patisaul, H.B. (2017): Sex specific accumulation and behavioral effects of developmental Firemaster 550 exposure in Wistar rats. Scientific Reports 7, 7118. DOI:10.1038/s41598-017-07216-6.

Bao, Z. and Jing, Y. (2021). Brominated flame retardant TBPH induced oxidative damage and reduced the expression of memory-related proteins in mice, with no discernable impairment of learning and memory. *Human and Experimental Toxicology* 2021, Vol. 40(12S) S684–S692. https://doi.org/10.1177/09603271211058876.

Brooke, D. and Crookes, M. (2012). Depuration rate constant: growth correction and use as an indicator of bioaccumulation potential. Environment Agency, Horizon House, Deanery Road, Bristol, BS1 5AH. https://assets.publishing.service.gov.uk/media/5a7c778de5274a559005a103/LIT_7371_44228a.pdf.

Brown, T. and Wania, F. (2008): Screening chemicals for the potential to be persistent organic pollutants: a case study of Arctic contaminants. *Environmental Science & Technology*, 42, 5202–5209. https://doi.org/10.1021/es8004514.

BSEF [The international Bromine Council] (2025). BSEF's comments received during the stakeholder consultation on TBPH draft scientific dossier (Annex D) for an EU proposal. Consultation period: 18 June 2025 – 13 August 2025. The compilation of comments is available at: https://echa.europa.eu/list-of-substances-proposed-as-pops/-/dislist/details/0b0236e18bafb66b.

Burkhard, L.P., Lahren, T.J., Hanson, K.B., Kasparek, A.J., Mount, D.R. (2023). Dietary Uptake of Highly Hydrophobic Chemicals by Rainbow Trout (Oncorhynchus Mykiss). *Arch Environ Contam Toxicol.* 2023 Nov; 85(4):390-403. https://doi.org/10.1007/s00244-023-01038-6.

Burkhard, L.P., Lahren, T. J., Highland, T. L., Hockett, J. R., Mount, D. R., Norberg-King, T. J. (2021). Bioaccumulation of Bis-(2-ethylhexyl)-3,4,5,6-tetrabromophthalate and Mono-(2-ethylhexyl)-3,4,5,6-tetrabromophthalate by *Lumbriculus variegatus*. *Archives of Environmental Contamination and Toxicology*. 80, 579-585. https://doi.org/10.1007/s00244-021-00824-4.

Chang, C., Lee, S.O., Wang, R.S., Yeh, S., Chang, T.M. (2013). Androgen receptor (AR) physiological roles in male and female reproductive systems: lessons learned from AR-knockout mice lacking AR in selective cells. *Biol. Reprod*., 89, 1−16. https://doi.org/10.1095/biolreprod.113.109132.

Chen L. (2020). Visual system: An understudied target of aquatic toxicology. *Aquatic Toxicology*. 225: 105542. https://doi.org/10.1016/j.aquatox.2020.105542.

Chen, Y., Cao Z., Covaci, A., Li, C., Cui, X. (2019): Novel and legacy flame retardants in paired human fingernails and indoor dust samples. *Environment International* 133, 105227. https://doi.org/10.1016/j.envint.2019.105227.

Cristale, J. and Lacorte, S. (2015). PBDEs versus NBFR in wastewater treatment plants: occurrence and partitioning in water and sludge. *AIMS Environmental Science*. 2, 533−546. DOI: 10.3934/environsci.2015.3.533.

Davis, E.F. and Stapleton, H.M. (2009). Photodegradation pathways of nonabrominated diphenyl ethers, 2-ethylhexyltetrabromobenzoate and di(2- ethylhexyl)tetrabromophthalate: identifying potential markers of photodegradation. *Environ Sci Technol.* 43(15), 5739-5746. https://doi.org/10.1021/es901019w.

de Jourdan, B.P., Hanson, M.L., Muir, D.C., Solomon, K.R. (2013). Environmental fate of three novel brominated flame retardants in aquatic mesocosms. *Environmental Toxicology and Chemistry* 32(5):1060-1068. DOI: 10.1002/etc.2165.

ECHA [European Chemicals Agency] and EFSA [European Food Safety Authority] with the technical support of the Joint Research Centre (JRC), Andersson N., Arena M., Auteri D., Barmaz S., Grignard E., Kienzler A., Lepper P., Lostia AM., Munn S., Parra Morte J.M., Pellizzato F., Tarazona J., Terron A. and Van der Linden S. (2018). Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009. EFSA Journal 2018;16(6):5311, 135 pp. . https://doi.org/10.2903/j.efsa.2018.5311.

ECHA (2022). Member State Committee support document for identification of bis(2-ethylhexyl) tetrabromophthlate covering any of the individual isomers and/or combinations thereof as a substance of very high concern because of its vPvB (Article 57E) properties. https://echa.europa.eu/documents/10162/170b9b2f-a1d0-9661-d36d-faf0846f6763.

ECHA (2023). Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.11: PBT/vPvB assessment. Version 4.0. December 2023. https://echa.europa.eu/documents/10162/17224/information_requirements_r11_en.pdf/a8cce23f-a65a-46d2-ac68-92fee1f9e54f.

ECHA (2024a). Investigation report on aromatic brominated flame retardants. European Chemicals Agency, December 2024.

https://echa.europa.eu/documents/10162/17233/rest_aromatic_brominated_flame_retardants_investigation_report_en.pdf.

ECHA (2024b). Guidance on the Application of the CLP Criteria. Part 4: Environmental hazards and Part 5: Additional Hazards. Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures. Version 4.0. November 2024. https://echa.europa.eu/documents/10162/2324906/clp_parts4-5_en.pdf/56ed0738-f7e9-6a6f-e9ca-c13af265ec6b?t=1730718888268.

ECCC and HC [Environment and Climate Change Canada, Health Canada] (2019). State of Science Report: Certain Organic Flame Retardants Substance Grouping Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester (TBB) and 1,2-Benzenedicarboxylic acid, 3,4,5,6-tetrabromo-, bis(2-ethylhexyl) ester (TBPH) (2019). https://www.canada.ca/content/dam/eccc/documents/pdf/pded/ofr-tbb-tbph/State-science-report-certain-organic-flame-retardants-substance-grouping-tbb-tbph.pdf.

EFSA [European Food Safety Authority] (2017). Guidance on the assessment of biological relevance of data in scientific assessments. EFSA Journal, 154(8):4970. https://doi.org/10.2903/j.efsa.2017.4970.

Fernie, K.J., Chabot, D., Champoux, L., Brimble, S., Alaee, M., Marteinson, S., Chen, D., Palace, V., Bird, D.M., Letcher, R.J. (2017). Spatiotemporal patterns and relationships among the diet, biochemistry, and exposure to flame retardants in an apex avian predator, the peregrine falcon. *Environmental research* 158, 43-53. http://dx.doi.org/10.1016/j.envres.2017.05.035.

Fu, K., Hua, J., Zhang, Y., Du, M., Han, J., Li, N., Wang, Q., Yang, L., Li, R., Zhou, B. (2024a). Integrated studies on male reproductive toxicity of bis (2-ethylhexyl)-tetrabromophthalate: *in silico, in vitro, ex vivo,* and *in vivo*. *Environmental Science & Technology*, 58(1), 194-206. https://pubmed.ncbi.nlm.nih.gov/38113192/.

Fu, K., Zhu, B., Sun, Y., Zhou, Y., Pang, H., Ren, X., Guo, Y., Shi, X., Han, J., Yang, L., Zhou, B. (2024b). Bis(2-ethylhexyl)-tetrabromophthalate poses a higher exposure risk and induces gender-specific metabolic disruptions in Zebrafish Liver. *Environ Sci Technol*. 58(11), 4937-4947. https://doi.org/10.1021/acs.est.4c00234.

Giam, C.S. *et al.* (1984). The handbook of the environmental Chem. 3:67-142. Hutzinger O ed. Berlin, Springer-Verlag.

Glüge, J. and Scheringer, M. (2023). Evaluation of physicochemical properties data in the ECHA database. *J. Phys. Chem. Ref. Data* 52, 043101 (2023). https://doi.org/10.1063/5.0153030.

Goodchild, C., Karouna-Renier, N.K., Henry, P.F.P., Letcher, R.J., Schultz, S.L., Maddox, C.M., Bean, T.G., Peters, L.E., Palace, V., Fernie, K.J. (2021). Thyroid disruption and oxidative stress in American kestrels following embryonic exposure to the alternative flame retardants, EHTBB and TBPH. Environment International, 157, 106826. https://doi.org/10.1016/j.envint.2021.106826.https://doi.org/10.1016/j.envint.2021.106826.

Great Lakes Chemical Corporation (1997). CN-2065: Abiotic degradation: hydrolysis as a function of pH. 1997 Sep 3. Huntingdon Life Sciences Ltd. Unpublished Study # GLC 042/970941.

Guerra, P., Alaee, M., Eljarrat, E., Barcelo, D. (2011). Introduction to Brominated Flame Retardants: Commercially Products, Applications, and Physicochemical Properties. In Eljarrat E, Barceló D. editors. 2011. Brominated Flame Retardants. Series: The Handbook of Environmental Chemistry. Volume 16. Heidelberg Berlin:Springer. 290 pp.

Guo W., Han J., Wu S., Shi X., Wang Q., Zhou B. (2020). Bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate Affects Lipid Metabolism in Zebrafish Larvae via DNA Methylation Modification. *Environ. Sci. Technol*. 54(1), 355-363. doi: 10.1021/acs.est.9b05796.

Guo, W., Lei, L., Shi, X., Li, R., Wang, Q., Han, J., Yang, L., Chen, L., Zhou, B (2021). Nonalcoholic Fatty Liver Disease Development in Zebrafish upon Exposure to Bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate, a Novel Brominated Flame Retardant. *Environ. Sci. Technol*. 55, 6926−6935. https://doi.org/10.1021/acs.est.1c01476.

Guo, L.C., Xiao, J., Zhang, Y., Yu, S., Lin, H., Su, G., Liu, T., Li, X., Lv, S., Rutherford, S., Ma, W. (2018). Association between serum polybrominated diphenyl ethers, new flame retardants and thyroid hormone levels for school student near a petrochemical complex, South China. *Chemosphere*, 202 (2018), pp. 476-482. https://doi.org/10.1016/j.chemosphere.2018.03.120.

Halvorsen, H., Pfaffhuber, K., Nipen, M., Bohlin-Nizzetto, P., Berglen, T., Nikiforov, V., Hartz, W. (2023). Monitoring of environmental contaminants in air and precipitation. Annual report 2022. (Norwegian Environment Agency, M-2543|2023) (NILU report, 18/2023). Kjeller:NILU. https://nilu.brage.unit.no/nilu-xmlui/bitstream/handle/11250/3100929/NILU-report-18-2023.pdf?sequence=1&isAllowed=y.

Han, F., Chen, G., Tao, G., Xu, J., Zhang, H., Zhang, L., Li, H., Zhao, Y., Tian, D., Kimura, S.Y., Wei, X., Ruan, Y., Wu, C., Xiao, S., Zhan, M., Zheng, W. (2022).Thyroid-disrupting effects caused by exposure to alternative flame retardants from groundwater contamination in rural central China, *Science of The Total Environment*, 839, 156300, ISSN 0048-9697, https://doi.org/10.1016/j.scitotenv.2022.156300.

Harding, R.L., Howley, S., Baker, L.J., Murphy, T.R., Archer, W.E., Wistow, G., Hyde, D.R., Vihtelic, T.S. (2008). Lengsin expression and function during zebrafish lens formation. *Exp Eye Res*. 86(5), 807-18. doi: 10.1016/j.exer.2008.02.009.

Harju, M., Herzke, D., Kaasa, H. (2013). Perfluorinated alkylated substances (PFAS), brominated flame retardants (BFR) and chlorinated paraffins (CP) in the Norwegian Environment Screening 2013. NILU OR 31/2013. https://www.miljodirektoratet.no/globalassets/publikasjoner/m40/m40.pdf.

He S., Li M., Jin J., Wang Y., Bu Y., Xu M., Yang X. & Liu A. (2013): Concentrations and trends of halogenated flame retardants in the pooled serum of residents of Laizhou Bay, China. *Environmental Toxicology and Chemistry,* 32, 1242–1247. https://doi.org/10.1002/etc.2172.

Hong X-S, Yan L., Sang W., Liu W., Li Z-T., Wang J., Yan S-H., Xin J-J., Zhao G-F., Ma X-F., Zha J-M. (2025). Environmental levels of bis(2-ethylhexyl)-tetrabromophthalate (TBPH) cause thyroid toxicity and early carcinogenic signals in juvenile fish, *Environmental Pollution,* 380, 126568. https://doi.org/10.1016/j.envpol.2025.126568.

Hou, R., Huang, Q., Pan, Y., Lin, L., Liu, S., Li, H., Xu, X. (2022). Novel brominated flame retardants (NFBRs) in a tropical marine food web from the South China Sea: the influence of hydrophobicity and biotransformation on structure-related trophodynamics. *Environmental Science & Technology,* 56(5), 3147–3158. https://doi.org/10.1021/acs.est.1c08104.

Houde, M., Wang, X., Ferguson, S., Gagnon, P., Brown, T., Tanabe, S., Kunito, T., Kwan, M., Muir, D. (2017). Spatial and temporal trends of alternative flame retardants and polybrominated diphenyl ethers in ringed seals (P*hoca hispida*) across the Canadian Arctic. *Environmental Pollution*, 223, 266-276. https://doi.org/10.1016/j.envpol.2017.01.023.

Hung, H., Kurt-Karakus, P., Ahrens, L., Bidleman, T., Evans, M., Halsall, C., Harner, T., Jantunen, L., Lee, S.C., Muir, D., Shoeib, M., Stern, G., Sverko, E., Su, Y., Vlahos, P., Xiao, H. (2013a). Occurrence and trends in the physical environment. In: Muir, D.C.G., P. Kurt-Karakas and J.E. Stow (eds.), Canadian Arctic Contaminants Assessment Report on Persistent Organic Pollutants III. pp. 147-272. Aboriginal Affairs and Northern Development, Canada.

Hutchinson TH, Shillabeer N, Winter MJ, Pickford DB. (2006). Acute and chronic effects of carrier solvents in aquatic organisms: a critical review. *Aquat Toxicol.*, 76(1):69-92. doi:10.1016/j.aquatox.2005.09.008.

Jin, X., Lee, S., Jeong, Y., Yu, J., Baek W.K., Shin, K-H., Kannan, K., Moon, H-B. (2016). Species-specific accumulation of polybrominated diphenyl ethers (PBDEs) and other emerging flame retardants in several species of birds from Korea. *Environmental Pollution.* 219, 191-200. http://dx.doi.org/10.1016/j.envpol.2016.10.040.

Kelly, B.C., Ikonomou, M.G., Blair, J.D., Morin, A.E., Gobas, F.A.P.C. (2007). Food web-specific biomagnification of persistent organic pollutants. *Science*, 317: 236-239. DOI: 10.1126/science.1138275.

Kneller, B., Nasr-Azadani, M.M., Radhakrishnan, S., Meiburg, E. (2016). Long-range sediment transport in the world's oceans by stably stratified turbidity currents. *JRG Oceans*, 121(12), 8608-8620. https://doi.org/10.1002/2016JC011978.

Knudsen, G.A., Sanders, M.J., Birnbaum, L.S. (2017). Disposition of the emerging brominated flame retardant, bis(2-ethylhexyl) tetrabromophthalate, in female Sprague Dawley rats: effects of dose, route, and repeated administration. *Xenobiotica*. 47(3), 245-254. doi: 10.1080/00498254.2016.1174793.

Körner, P., Glüge, J., Glüge, S., Sheringer, M. (2024). Critical insights into data curation and label noise for accurate prediction of aerobic biodegradability of organic chemicals. *Environ. Sci.: Processes Impacts*, 2024, 26, 1780. DOI: 10.1039/d4em00431k.

Lam, J.C., Lau, R.K., Murphy, M.B., Lam, P.K.S. (2009). Temporal trends of hexabromocyclododecanes (HBCDs) and polybrominated diphenyl ethers (PBDEs) and detection of two novel flame retardants in marine mammals from Hong Kong, South China. *Environmental Science and Technology*, 43, 6944-6949.

Lazarus, R.S., Rattner, B.A., McGowan, P.C., Hale, R.C., Karouna-Renier, N.K., Erickson, R.A., Ottinger, M.A. (2016). Chesapeake Bay Fish-osprey (Pandion Haliaetus) food chain: Evaluation of contaminant exposure and genetic damage. *Environmental Toxicology and Chemistry* 35, 1560-1575. https://doi.org/10.1002/etc.3386.

Lee, S.C., Sverko, E., Harner, T., Pozo, K., Schachtschneider, J., Zaruk, D., DeJong, M., Barresi, E., Narayan, J. (2016). Retrospective analysis of "new" flame retardants in the global atmosphere under the GAPS network. *Environmental Pollution*, 217, 62-69. http://dx.doi.org/10.1016/j.envpol.2016.01.080.

Li, H., Yang, H., Sun, S., Wang, Z., Bu, J., Liu, J., Xing, W., Wang, L. (2025). Aerobic simulated biodegradation of novel brominated flame retardants: Systems and mechanisms, *Biochemical Engineering Journal*, Volume 221, 2025, 109808, ISSN 1369-703X, https://doi.org/10.1016/j.bej.2025.109808.

Liu, L., He, K., Hites, R., Salamova A. (2016). Hair and nails as noninvasive biomarkers of human exposure to brominated and organophosphate flame retardants. *Environ. Sci. Technol*., 50 (6) (2016), pp. 3065-3073. DOI: 10.1021/acs.est.5b05073.

Liu, L.Y., Salamova, A., He, K., Hites, R.A (2015). Analysis of polybrominated diphenyl ethers and emerging halogenated and organophosphate flame retardants in human hair and nails. *J. Chromatogr. A* 2015, 1406 (0), 251−257. http://dx.doi.org/10.1016/j.chroma.2015.06.003.

Ma, Y., Venier, M., Hites, R.A. (2012b). 2-ethylhexyl tetrabromobenzoate and bis(2-ethylhexyl) tetrabromophthalate flame retardants in the Great Lakes atmosphere. *Environmental Science and Technology*, 46, 204-208. https://doi.org/10.1021/es203251f.

Mendy, A., Percy, Z., Braun, J. M., Lanphear, B., La Guardia, M. J., Hale, R., Yolton, K., Chen, A. (2023). Exposure to dust organophosphate and replacement brominated flame retardants during infancy and risk of subsequent adverse respiratory outcomes, *Environmetnal Research*, 235, 116560. https://doi.org/10.1016/j.envres.2023.116560.

Mendy, A., Percy, Z., Braun, J.M., Lanphear, B., La Guardia, M. J., Hale, R. C., Yolton, K., Chen, A. (2024). Prenatal exposure to replacement flame retardants and organophosphate esters and childhood adverse respiratory outcomes, *Environ. Res.*, 240, 117523. Epub 2023 Nov 2. https://doi.org/10.1016/j.envres.2023.117523.

Möller, A., Xie, Z., Cai, M., Sturm, R., Ebinghaus, R. (2012). Brominated flame retardants and dechlorane plus in the marine atmosphere from southeast Asia toward Antarctica. *Environ. Sci. Tech.,* 46 (6), 3141-3148. https://doi.org/10.1021/es300138q

Möller, A., Xie, Z., Cai, M., Zhong, G., Huang, P., Cai, M., Sturm, R., Ebinghaus, R. (2011b). Polybrominated diphenyl ethers vs. alternate brominated flame retardants and dechloranes from East Asia to the Arctic. *Environ. Sci. Technol*, 45(16), 6793–6799. https://doi.org/10.1021/es300138q.

Möller, A., Xie, Z., Sturm, R., Ebinghaus, R. (2011a). Polybrominated diphenyl ethers (PBDEs) and alternative brominated flame retardants in air and seawater of the European Arctic. *Environnemental Pollution*, 159, 1577-1583. https://doi.org/10.1016/j.envpol.2011.02.054.

Nacci, D., Clark, B., La Guardia, M. J., Miller, K., Champlin, D., Kirby, I., Bertrand, A., Jayaraman, S. (2018). Bioaccumulation and effects of dietary exposure to the alternative flame retardant, bis(2-ethylhexyl) tetrabromophthalate (TBPH), in the Atlantic killifish, Fundulus heteroclitus. *Environmental Toxicology and Chemistry*. 37(9), 2350-2360. https://doi.org/10.1002/etc.4180.

OECD (2017). Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation. Series on Testing & Assessment. No. 264. ENV/JM/MONO(2017)16.

OECD (2019). Guidance document on aqueous-phase aquatic toxicity testing of difficult test chemicals. Series on testing and assessment No. 23 (Second Edition). Environment Directorate, Joint meeting of the chemicals Committee and the working party on chemicals, pesticides and biotechnology. ENV/JM/MONO(2000)6/REV1. https://www.oecd.org/en/publications/guidance-document-on-aquatic-toxicity-testing-of-difficult-substances-and-mixtures_0ed2f88e-en.html.

Pakalin, S., Aschberger, K., Cosgrove, O., Lund, B., Paya Perez, A., Vegro, S. (2008). Editors. European Union Risk Assessment Report - bis (2-ethylhexyl) phthalate (DEHP). EUR 23384 EN. Luxembourg (Luxembourg): OPOCE; 2008. JRC45705. https://publications.jrc.ec.europa.eu/repository/handle/JRC45705.

Papachlimitzou, A., Barber, J.L., Losada, S., Bersuder, P., Law, R.J. (2012). A review of the analysis of novel brominated flame retardants, *Journal of Chromatography A*, Volume 1219, 2012, Pages 15-28, ISSN 0021-9673, https://doi.org/10.1016/j.chroma.2011.11.029.

Rauert, C., Schuster, J., Eng, A., Harner, T. (2018). Global atmospheric concentrations of brominated and chlorinated flame retardants and organophosphate esters. *Environ. Sci. Technol.*, 52(5), 2777–2789. https://doi.org/10.1021/acs.est.7b06239.

Roberts, S.C., Macaulay, L.J., Stapleton, H.M. (2012). *In vitro* metabolism of the brominated flame retardants 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB) and bis(2-ethylhexyl) 2,3,4,5-tetrabromophathalate (TBPH) in human and rat tissues. *Chemical Research in Toxicology,* 25, 1435-1441. dx.doi.org/10.1021/tx300086x.

Sagerup, K., Herzke, D., Harju, M., Evenset, A., Christensen, G.N., Routti, H., Fuglei, E., Aars, J., Strøm, H., Gabrielsen, G.W. (2010). New brominated flame retardants in Arctic biota. Statlig program for forurensningsovervåking. https://brage.npolar.no/npolar-xmlui/bitstream/handle/11250/173191/NewBrominatedFlameRetardants.pdf?sequence=1&isAllowed=y.

Salamova, A., Hermanson, M., Hites, R. (2014). Organophosphate and Halogenated Flame Retardants in Atmospheric Particles from a European Arctic Site. *Environmental Science & Technology,* 48, 6133-6140. https://doi.org/10.1021/es500911d.

Silva, M.J., Hilton, D., Furr, J., Gray, L.E., Preau J.L., Calafat, A.M., Ye, X. (2015): Quantification of tetrabromo benzoic acid and tetrabromo phthalic acid in rats exposed to the flame retardant Uniplex FRP-45. *Archives in Toxicology,* 90, 551-557. DOI 10.1007/s00204-015-1489-6.

Sobotka, J., Lammel, G., Slobodník, J., Schink, A., Prokeš, R., Branislav, V. (2021). Dynamic passive sampling of hydrophobic organic compounds in surface seawater along the South Atlantic Ocean east-to-west transect and across the Black Sea. *Marine Pollution Bulletin*, 168, 112375, ISSN 0025-326X. https://doi.org/10.1016/j.marpolbul.2021.112375.

Swedish Competent Authority (2022). Annex XV report, proposal for identification of a Substance of very High Concern on the basis of the criteria set out in Reach Article 57. Substances Names: bis(2-ethylhexyl) tetrabromophthalate covering any of the individual isomers and/or combinations thereof. August 2022. https://echa.europa.eu/documents/10162/b20c32ea-baac-f4b9-919f-eb2784203c24.

Swedish Chemicals Agency [KEMI] (2020). Substance evaluation conclusion as required by REACH article 48 and evaluation report for Bis(2-ethylhexyl) tetrabromophthalate, EC No 247-426-5, CAS No 26040-51-7. Dated: 9 July 2020. https://echa.europa.eu/documents/10162/eb2870ff-83c2-bd58-6e25-3f37d03a6c50.

Tao F., Abdallah M.A-E., Ashworth D.C., Douglas P., Toledano M. B., Harrad S. (2017). Emerging and legacy flame retardants in UK human milk and food suggest slow response to restrictions on use of PBDEs and HBCDD. *Environ. Int.* 105 (2017) 95–104. https://doi.org/10.1016/j.envint.2017.05.010.

Unpublished (2018). Dietary bioaccumulation in *O. mykiss*. Summary available in the public registration dossier for TBPH available from: Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.

US EPA [US Environmental Protection Agency] (2000). Test method 100.3. Methods for Measuring the Toxicity and Bioaccumulation of Sediment-associated Contaminants with Freshwater Invertebrates-Second Edition. https://archive.epa.gov/water/archive/polwaste/web/pdf/freshmanual.pdf.

US EPA (2012). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.11. United States Environmental Protection Agency, Washington, DC, USA.

US EPA (2015a). TSCA Work Plan Chemical Technical Supplement – Use and Exposure of the Brominated Phthalates Cluster (BPC) chemicals. Brominated Phthalates Cluster Flame Retardants. EPA Document# 740-Q1-4002. August 2015. Office of Chemical Safety and Pollution Prevention. https://www.epa.gov/sites/default/files/2015-09/documents/bpc_data_needs_assessment_technical_supplement_use_and_exposure_assessment.pdf.

US EPA (2015b). Flame Retardants Used in Flexible Polyurethane Foam: An Alternative Assessment Update. Sections1-6. August 2015. EPA Publication 744-R-15-002. https://www.epa.gov/sites/default/files/2015-08/documents/ffr_final_body.pdf.

US EPA (2015c). TSCA Work Plan Chemical Problem Formulation and Data Needs Assessment Brominated Phthalates Cluster Flame Retardants. EPA Document: 740-Q1-4004. August 2015.: https://www.epa.gov/sites/default/files/2015-09/documents/brominated_phthalates_cluster_data_needs_assessment.pdf.

Vorkamp, K., Bossi, R., Rigét, F., Skov, H., Sonne, C., Dietz, R. (2015). Novel brominated flame retardants and dechlorane plus in Greenland air and biota. *Environmental Pollution*, 196, 284-291. https://doi.org/10.1016/j.envpol.2014.10.007.

Xiao, H., Hung, H., Wania, F., Lao, R., Sabljic, E., Sverko, E., Lei, Y.D., Fellin, P., Barresi, E. (2012b). Field evaluation of a flow-through sampler for measuring pesticides and brominated flame retardants in the Arctic atmosphere. *Environ Sci Techol*. 46(14), 7669- 7676. dx.doi.org/10.1021/es301481w.

Xiao, H., Shen, L., Su, Y., Barresi, E., de Jong, M., Hung, H., Lei, Y-D., Wania, F., Reiner, E.J., Sverko, E., Kang, S.C. (2012a). Atmospheric concentrations of halogenated flame retardants at two remote locations: the Canadian High Arctic and the Tibetan Plateau. *Environmental Pollution,* 161, 154-161. https://doi.org/10.1016/j.envpol.2011.09.041.

Xie, J., Zhang, G., Wu, Q., Luo, M., Chen, D., Zhang, Y., He, L., Li, Y., Zhang, Q., Lin, T., Jiang, G. (2023). First evidence and potential sources of novel brominated flame retardants and BDE 209 in the deepest ocean. *Journal of Hazardous Materials*, 448, 130974. https://doi.org/10.1016/j.jhazmat.2023.130974.

Xing, B., Lan, H., Li, H. (2024). TBPH-induced lung injury is induced by mitochondrial-derived ds-DNA-mediated inflammatory response. *Ecotoxicology and Environmental Safety*, 286, 117200, https://doi.org/10.1016/j.ecoenv.2024.117200.

Xiong, S., Hao, Y., Li, Y., Yang, R., Pei, Z., Zhang, Q., Jiang, G. (2021). Accumulation and influencing factors of novel brominated flame retardants in soil and vegetation from Fildes Peninsula, Antarctica. *Science of The Total Environment*, 756, 144088. https://doi.org/10.1016/j.scitotenv.2020.144088.

Xiong, Z., Zhenhua, L., Sima, X., Zeng, Z. (2024). Astaxanthin reduces TBPH-induced neurobehavioral deficits in mice by the ROS-ERK1/2-FOS pathway. *Ecotoxicology and Environmental Safety,* 281, 116674. https://doi.org/10.1016/j.ecoenv.2024.116674.

Yi, J., Ma, Y., Ma, J., Yu, H., Zhang, K., Jin, L., Yang, Q., Sun, D., Wu, D. (2023). Rapid Assessment of Ocular Toxicity from Environmental Contaminants Based on Visually Mediated Zebrafish Behavior Studies. *Toxics*, 11, 706. https://doi.org/10.3390/toxics11080706.

Yuan, Y., Zhuang, Y., Cui, Y., Liu, Y., Zhang, Q., Xiao, Q., Meng, Q., Jiang, J., Hao, W., Wei, X. (2024). IL-10-TG/TPO-T4 axis, the target of bis (2-ethylhexyl) tetrabromophthalate on thyroid function imbalance. *Toxicology*, 501, 153713. https://doi.org/10.1016/j.tox.2023.153713.

Zhao, J., Wang, P., Wang, C., Fu, M., Li, Y., Yang, R., Fu, J., Hao, Y., Matsiko, J., Zhang, Q., Jiang, G. (2020). Novel brominated flame retardants in West Antarctic atmosphere (2011–2018): Temporal trends, sources and chiral signature. *Science of The Total Environment*, 720, 137557. https://doi.org/10.1016/j.scitotenv.2020.137557.

Zhou, S.N., Buchar, A., Siddique, S., Takser, L., Abdelouahab, N., Zhu, J. (2014). Measurements of Selected Brominated Flame Retardants in Nursing Women: Implications for Human Exposure. *Environmental Science & Technology.* 48(15), 8873-8880. dx.doi.org/10.1021/es5016839.

Zhou, Y., Guo, W., Lei, L., Sun, Y., Li, R., Guo, Y., Yang, L., Shi, X., Han, J., Zhou, B. (2021). Bis(2-ethylhexyl)-tetrabromophthalate induces zebrafish obesity by altering the brain-gut axis and intestinal microbial composition. *Environ Pollut.* 290, 118-127. https://doi.org/10.1016/j.envpol.2021.118127.

Zhou, Y., Lei, L., Chen, P., Guo, W., Guo, Y., Yang, L., Han, J., Hu, B., Zhou, B. (2022). Effects of nano-TiO2 on the bioavailability and toxicity of bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate (TBPH) in developing zebrafish. *Chemosphere*, 295, 133862. https://doi.org/10.1016/j.chemosphere.2022.133862.

Zhou, Y., Lei, L., Zhu, B., Li, R., Zuo, Y., Guo, Y., Han, J., Yang, L., Zhou, B. (2024). Aggravated visual toxicity in zebrafish larvae upon co-exposure to titanium dioxide nanoparticles and bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate. *Sci Total Environ* 921, 171133. https://doi.org/10.1016/j.scitotenv.2024.171133.

Zhu, B., Lai, N., Wai, T.C., Chan, L.L., Lam, J.C., Lam, P.K. (2014). Changes of accumulation profiles from PBDEs to brominated and chlorinated alternatives in marine mammals from the South China Sea. *Environment International* 66, 65–70. http://dx.doi.org/10.1016/j.envint.2014.01.023.

Appendix

Table A1: Monitoring data from remote areas – Air samples

Location	Year(s)	n	Nbr or % of detect	Concentration range (pg/m^3)	MDL (pg/m^3)	Remarks	Reference
Zeppelin, Svalbard, Norwegian Arctic (78° 54' N, 11° 53' E)	2022	26	17%	<0.076 – 0.128 (gas and particle phases) <0.076 (annual mean/median in the gas and particle phases)	0.076 (high value compared to other NBFRs in the study, likely due to findings of TBPH in blank values)	Method: GFF and PUF, GC/HRMS EI Halvorsen personal communication, June 2025: TBPH recovery: 35–50% (the concentrations were corrected for the recovery) Field and lab blanks were included. TBPH was found in the blanks at 0.03–0.04 pg/m^3. The field blanks were comparable with the lab blanks Concentrations in the samples have not been corrected for the blank values Clean-up of the samples performed with sulfuric acid which can break phthalates and thus lead to low recovery of the substance The results of this study are considered to be semi-quantitative considering the limited number of recovery standards and above uncertainties Benchmark (gas and particle phases): PentaBDE (BDE-47 and BDE-99): nd – 1.81 pg/m^3 (DF: 76–100%, n=52; after its inclusion to the SC in 2009) OctaBDE (BDE-196, BDE-197 and BDE-202): nd – 0.158 pg/m^3 (DF: 4–14%, n=52; after its inclusion to the SC in 2009) *Syn*DP: nd – 0.432 pg/m^3 (DF:17%, n=12; before its inclusion to the SC in 2023) *Anti*DP: nd – 1.53 pg/m^3 (DF:58%, n=12; before its inclusion to the SC in 2023)	Halvorsen *et al.,* 2023
Ny-Ålesund, Norwegian Arctic (78.907, 11.887)	2014	4	1/4	<1–74 (gas and particle phases)	1	Method: PUF-PAS, GC-MS/MS HSEI Surrogate recoveries: 96± 38% TBPH was not detected in lab and field blanks The concentration of 74 pg/m^3 is questionable considering the highest concentration observed at Paris (France) was 43 pg/m^3	Rauert *et al.*, 2018
Alert, Nunavut, Canadian Arctic (82.450, -63.504)		2	0/2	<1 (gas and particle phases)		Benchmark (gas and particle phases):	

Location	Year(s)	n	Nbr or % of detect	Concentration range (pg/m^3)	MDL (pg/m^3)	Remarks	Reference
						Ny-Ålesund: PentaBDE (BDE-47 and BDE-99): <2–4 pg/m^3 (4/8; after its inclusion to the SC in 2009) BDE-209: <1 pg/m^3 (0/4; before its inclusion to the SC in 2017) Alert: PentaBDE (BDE-47 and BDE-99): 0.031–35 pg/m^3 (4/4; after its inclusion to the SC in 2009) BDE-209: 3.2–3.5 pg/m^3 (2/2; before its inclusion to the SC in 2017)	
Alert, Nuvanut, Canada	2008 2009 2010 2011 2012	27 17 13 26 26	78% 100% 100% 100% 100%	<MDL–3.4 0.30 (mean) 0.099 (median) 0.079–0.94 0.39 (mean) 0.35 (median) 0.033–0.85 0.23 (mean) 0.21 (median) 0.14–4.3 0.51 (mean) 0.39 (median) 0.16–80 6.7 (mean) 0.89 (median)			Hung *et al.,* 2013a as cited in AMAP, 2016
Ny-Ålesund, Norwegian Arctic (78º54'N, 11º53' E)	March 2005–May 2006	4	1/4	<0.04–0.28 (gas and particle phases)	0.04	Method: PUF-PAS, GC-MS negative ion Recovery range for the BFRs: 78–111% Laboratory blanks were included. No field blanks analysed for TBPH According to the authors, the reported concentrations in air should be viewed as semi-	Lee *et al.*, 2016

Location	Year(s)	n	Nbr or % of detect	Concentration range (pg/m^3)	MDL (pg/m^3)	Remarks	Reference
Alert, Nunavut, Canadian Arctic (82º27'N, 63º30ºW)				No deployment or no analysis in this study		quantitative, due to uncertainties associated with analytical and sampling challenges Benchmark (gas and particle phases): Ny-Ålesund: HBCD: <0.1–5.1 pg/m^3 (DF: 3/4; before its inclusion to the SC in 2013) Alert: HBCD: No deployment or no analysis in this study	
Longyearbyen, Svalbard (78.22°N, 15.65°E)	September 2012 to May 2013	34	88%	0.27–14 2.7±0.49 (mean) 1.8 (median) (particle phase)	0.002-0.08 (for BFRs)	Method: a high-volume air sampler with quartz fiber filters, GC/MS ECNI Laboratory blanks, recovery spike samples and field blanks were included. The average BFR surrogate recoveries were 93%. The average BFR recoveries for the spikes recovery samples were 85% Benchmark (particle phase): PentaBDE (BDE-47/99): 0.07–6.8 pg/m^3 (DF:100%, n=34; after its inclusion to the SC in 2009) BDE-209: 0.12–6.8 pg/m^3 (DF:100%, n=34; before its inclusion to the SC in 2017) ∑DP: 0.05 – 5.03 pg/m^3 (DF:100%, n=34; before its inclusion to the SC in 2023) TBPH concentration in the Arctic air (particle phase) is higher than the concentrations of POP substances. TBB and TBPH were the dominant non-PBDE BFRs measured in these samples and TBPH comprised ~17% of ΣBFR concentrations from a total of 45 BFRs	Salamova *et al.*, 2014
Alert, Nunavut, Canadian Arctic (82° 30' N, 60° 20' W)	2006 – 2007	14	21% (3/15)	0.13–1.5 0.8 (mean) 0.69 (median) (gas and particle phases)	1.2 (gas and particle phases)	Method: super high-volume air sampler (Super-HiVol)-GFFs-PUFs, GC/MS in NCI mode Recoveries in the range of 68%–103%	Xiao *et al.,* 2012a

Location	Year(s)	n	Nbr or % of detect	Concentration range (pg/m^3)	MDL (pg/m^3)	Remarks	Reference
Nam Co Lake, Tibetan plateau (30° 46.44' N, 90° 59.31' E, 4730 m above the seal level)	October 2006 to February 2008	15	53% (8/15)	0.049–1.7 0.38 (mean) 0.27 (median) (gas and particle phases)		TBPH was detected above the blank and above the MDL so that no blank correction or recovery adjustment was made Benchmark (gas and particle phases): PentaBDE (BDE-99): 0.06–5.3 pg/m^3 (before its inclusion to the SC in 2009) Method: Flow-Through Sampler (FTS), GC/HRMS in EI positive mode TBPH was detected above the blank and above the MDL so that no blank correction or recovery adjustment was made Benchmark (gas and particle phases): PentaBDE (BDE-99): 0.21–1.2 pg/m^3, before its inclusion to the SC in 2009 OctaBDE (BDE-196/197/203/204/205): 0.00034–1.0 pg/m^3, before its inclusion to the SC in 2009 Concentrations of TBPH in air (gas and particle phases) from Alert and Nam Co Lake are in the same range as those of POP substances and before their inclusion to the SC TBPH concentrations at both sampling sites show decreasing trends during the sampling campaign	
Arctic Ocean (Samples A11 to A13 situated at ca. 690 km to 1049 km from the Coast)	June to September 2010	3	1/3	<0.16 – 0.36 (gas phase)	0.16 (air column and filter)	Method: GFF and PUF/Amberlite XAD-2 resin, GC/MS ECNCI Recoveries of the surrogates: 78 – 95 % (± 32 – 57 %) TBPH was not detected in any blanks Uncertainty on the concentration values as the actual recovery of TBPH is not reported Benchmark (gas phase): BDE-209: nd – 0.56 pg/m^3 (2/3) *Syn*DP: 0.01 – 0.17 pg/m^3 (3/3) *Anti*DP: nd – 0.25 pg/m^3 (2/3)	Möller *et al.,* 2011b

Location	Year(s)	n	Nbr or % of detect	Concentration range (pg/m^3)	MDL (pg/m^3)	Remarks	Reference
			0/3	<0.16 (particulate phase)		Concentrations of TBPH in the gas phase are in the same range as those of POP substances and before their inclusion to the SC Benchmark (particulate phase): BDE-209: 0.19 – 3.43 pg/m^3 (3/3) *Syn*DP: 0.01 – 0.02 pg/m^3 (3/3) *Anti*DP: 0.01 – 0.02 pg/m^3 (3/3)	
East Greenland Sea (69–80.5°N) Samples A1 (195 km from the Greenland Coast) and A8 (245 km from the Svalbard Coast) are the most remote ones	August and September 2009	10	0% 40%	n.d. (gas phase) n.d. – 0.08 (particulate phase)	0.009 (for both dissolved and particulate phases)	Method: GFF and PUF/Amberlite XAD-2 resin, GC/MS ECNCI TBPH was not detected in field blanks Recovery determined by spike tests with the surrogate standard ^{13}C-BDE-77: 73±12% for non-PBDE BFRs Uncertainty on the concentration values as the actual recovery of TBPH is not reported Benchmark (gas phase): PentaBDE (BDE-47/99): nd–0.82 pg/m^3 BDE-209: nd Benchmark (particulate phase): PentaBDE (BDE-47/99): 0.01–0.32 pg/m^3 BDE-209: nd–0.07 pg/m^3 Concentrations of TBPH in air (gas and particulate phases) are in the same range as those of POP substances	Möller *et al.,* 2011a
King George Island, South Shetland Islands, West Antarctic (62°13′12″S, 58°57′48″W)	2011 to 2018	94 (total samples for all 12 NBFRs)	30%	n.d. – 0.098 (gas and particle phases)	0.002–0.06 (LOD for EHTBB and TBPH)	Method: A high-volume active air sampler (HV-AAS) coupled with GFF and polyurethane foam (PUF) plug, HRGC/HRMS in positive electron impact (EI+) mode The average recoveries of BDE-77 and BDE-128 in GFF matrix blanks were 92 ±14% and 90 ± 6% and in PUF matrix blanks were 92 ±8% and 86 ± 8%, respectively TBPH relative gas/particle distribution: ca. 50/50. No field blanks, only lab and GFF and PUF matrix blanks which are considered to be ‘cleaned’. It is unlikely that there was any contamination from the	Zhao *et al.,* 2020

Location	Year(s)	n	Nbr or % of detect	Concentration range (pg/m^3)	MDL (pg/m^3)	Remarks	Reference
						field considering the results are in line with those of Möller *et al.,* 2012 study	
Oceanic Southern hemisphere (South West Australia to Antarctica: Samples A7 to A14)	November 2010 to March 2011	8	0/8 7/8	<1.2 (gas phase, non-detected due to high contamination level in the air column) <0.025 – 1.5 (particulate phase)	1.2 (air column) 0.025 (air filter)	Method: GFF and PUF/Amberlite XAD-2 resin, GC/MS ECNCI Recoveries of the target analytes of 86 ± 19% and relative recoveries corrected by the surrogates of 101 ± 16% TBPH mean blank value: 120 ±160 pg (air column) and n.d. (air filter) Benchmark (particulate phase): BDE-209: nd – 6.5 pg/m^3 (1/8), after its inclusion to the SC in 2009 *Syn*DP: 0.12 – 1.6 pg/m^3 (8/8) *Anti*DP: 0.12 – 0.56 pg/m^3 (8/8) Concentrations of TBPH in the particulate phase are in the same range as those of POP substances and before their inclusion to the SC	Möller *et al.,* 2012

Table A2: Monitoring data from remote areas – Seawater samples

Location	Year(s)	n	Nbr or % detect	Concentration range (pg/L)	MDL (pg/L)	Remark	Reference
Western Pacific to the Arctic Ocean (TBPH was detected in the Bering Sea, sample W2 located at ca. 400 km from the Russian Coast)	July to September 2010	18	1/18	<0.089 – 0.22 (dissolved phase, maximum value from sample W2)	0.089 (water column and filter)	Method: GFF (GF/C, pore size: 1.2 µm) following self-packed Serdolit PAD-3 glass column, GC/MS ECNCI Recoveries of the surrogates: 78 – 95 % (± 32 – 57 %) TBPH was not detected in any blanks Uncertainty on the concentration values as the actual recovery of TBPH is not reported Benchmark (dissolved phase): BDE-209: nd – 0.18 pg/L *Syn*DP: 0.003 – 0.22 pg/L *Anti*DP: nd – 0.14 pg/L Concentrations of TBPH in the seawater are in the same range as those of POP substances and before their inclusion to the SC	Möller *et al.,* 2011b
East Greenland Sea (69–80.5°N) Depth: ca. 11 meters Samples W7 (215 km from the Greenland Coast) and W10 (225 km from the Svalbard Coast) are the most remotes	August and September 2009	16	25% 6%	n.d. – 0.21 (dissolved phase, maximum value from sample W10) n.d. (particulate phase, n.d. in samples W7 and W10 but detected in sample W16)	0.013 (for both dissolved and particulate phases)	Method: GFF and glass column packed with Serdolit PAD-2, GC/MS ECNCI TBPH was not detected in field blanks Recovery determined by spike tests with the surrogate standard ^{13}C-BDE-77: 73±12% for non-PBDE BFRs Uncertainty on the concentration values as the actual recovery of TBPH is not reported Benchmark (dissolved phase): PentaBDE (BDE-47/99): nd–0.06 pg/L BDE-209: nd–0.37 pg/L Benchmark (particulate phase): PentaBDE (BDE-47/99): nd BDE-209: nd–0.11 pg/L Concentrations of TBPH in the seawater are in the same range as those of POP substances	Möller *et al.,* 2011a Zhiyong personal communication, May 2025

Location	Year(s)	n	Nbr or % detect	Concentration range (pg/L)	MDL (pg/L)	Remark	Reference
South Atlantic Ocean Surface seawater From Cape Town (South Africa) to Rio de Janeiro (Brazil). The cruise covered 34°S/17°E – 25°S/38°W in five stretches with approximately 3.5 days/stretch Stretch 3 sample is the most remote stretch (located in the middle of the Ocean; stretch length: 1000 km)	February to March 2016	1	1/1	14.497 (dissolved phase; Stretch 3)	0.252 (LOQ)	Method: Silicone Rubber (SR) Dynamic Passive Sampling (DPS), GC/MS TBPH recovery: 206±41% Field/control/procedural blanks were used TBPH was found in the field blanks at 42 pg/sample Blank values higher than the LOQ were subtracted from the corresponding value of the exposed sample The authors concluded that the deployment time in this study might not be long enough to capture sufficient amount of compounds in the sampler to be quantifiable The results of this study are considered to be semi-quantitative considering the high contamination in the field blanks. Benchmark (dissolved phase, Stretch 3 sample): PentaBDE (BDE-47/99): 0.593–1.545 pg/L *Syn*-DP: 1.471 pg/L *Anti*-DP: <0.083 pg/L Before the inclusion of DP to the SC in 2023 Concentration of TBPH in the Ocean is higher than those of POP substances	Sobotka *et al.,* 2021

Table A3: Monitoring data from remote areas – Sediment samples

Location	Year(s)	n	% detect	Concentration range	MDL (pg/g)	Remark	Reference
Surface sediment (1-2 cm) from western Pacific Ocean deep sea trenches (Mariana, Mussau and New Britain) MT-1 samples situated at 320 km from Guam at a water depth of 10853.2 m	December 2016 to January 2019	8	100%	Detected	5.53	Method: GC-MS/MS in electron ionisation mode Sample recoveries (mean ± standard deviation (SD)) were 92% ± 27% for NBFRs Procedural blanks included. NBFRs were not detected or below the MDL in the blanks Limited industrial activities in Papua New Guinea and Guam, the pollutant input from such sources was expected by the authors to be low	Xie et *al.,* 2023

Table A4: Monitoring data from remote areas – Soil samples

Location	Year(s)	n	% detect	Concentration range (pg/g dw)	MDL (pg/g dw)	Remark	Reference
Chinese Antarctic GreatWall Station and surrounding Fildes Peninsula area in West Antarctica	January 2014	7	71%	n.d.–20.22 7.94±7.92 (mean)	0.0042–178 for all BFRs	Method: GC/MS ECNI The sample recoveries of the internal standards were in the range of 32.8–112.8% (average 85.1%) No specific standard for TBPH was used Laboratory blanks included. TBPH was not detected in the blanks Uncertainty on the concentration values as the actual recovery of TBPH is not reported	Xiong et *al.,* 2021

Table A5: Monitoring data from remote areas – Vegetation/mushroom samples

Location	Year(s)	n	% detect	Concentration range| (pg/g dw)	MDL (pg/g dw)	Remark	Reference
Chinese Antarctic GreatWall Station and surrounding Fildes Peninsula area in West Antarctica	January 2014	9	67%	Moss (*Sanionia uncinata*): n.d.–484.1 115.4±160.2 (mean)	0.0042–178 for all BFRs	Method: GC/MS ECNI The sample recoveries of the internal standards were in the range of 42.5–126.7% (82.9%) for mosses, and 46.0–101.0% (78.4%) for lichens No specific standard for TBPH was used Laboratory blanks included. TBPH was not detected in the blanks Uncertainty on the concentration values as the actual recovery of TBPH is not reported TBHP was one of the two mains contributing NBFRs in moss among the nine NBFRs studied	Xiong et *al.,* 2021
		8	0%	Lichen (*Usnea aurantiaco-atra*): n.d.			

Table A6: Monitoring data from remote areas – Biota samples (excluding vegetation/mushroom)

Location	Year(s)	n	% detect	Concentration range	MDL	Remark	Reference
Svalbard	2012	20	95%	Polar bear (*Ursus maritimus*) plasma: 0.15±0.16 ng/mL (mean)		Method: GC/MS No recovery reported for TBPH while the extraction method uses a strong acid, to which TBPH has been	Harju *et al.,* 2013

Location	Year(s)	n	% detect	Concentration range	MDL	Remark	Reference
				Lipid content: 0.9%		reported as being unstable. Sulfuric acid can break phthalates and thus the concentrations of TBPH reported in this study can be significantly underestimated Laboratory blanks included, no field blanks MDL not specified Benchmark: Polar bear plasma: PentaBDE (PBDE-47): 0.10±0.08 ng/mL (mean; DF:100%, n=20; after its inclusion to the SC in 2009)	
Kongsfjord, Svalbard	2012	10	10%	Ringed seal (*Phoca hispida*) plasma: 0.04 ng/mL (mean) Lipid content: 0.7%		Ringed seal plasma: PentaBDE (PBDE-47): 0.08±0.02 ng/mL (mean; DF:100%, n=10)	
Kongsfjord, Svalbard	2012	12	17%	Glaucous gull (*Larus hyperboreus*) plasma: 0.026±0.001 ng/mL (mean) Lipid content: 14.4%		Glaucous gull plasma: PentaBDE (PBDE-47): 2.28±1.7 ng/mL (mean; DF:100%, n=12)	
Kongsfjord, Svalbard	2012	12	100%	Kittiwake (*Rissa Tridactyla*) egg 0.10±0.09 ng/g ww (mean) Lipid content: 8.1%		Kittiwake egg: PentaBDE (PBDE-47): 2.68±0.78 ng/g ww (mean; DF:100%, n=12)	
Kongsfjord, Svalbard	2012	12	58%	Common Eider (*Somateria mollissima*) egg: 0.06±0.07 ng/g ww (mean) Lipid content: 17.4%		Common Eider egg: PentaBDE (PBDE-47): 0.12±0.06 ng/g ww (mean; DF:100%, n=12)	
Svalbard	2012	10 or 3 (unclear from the report)	10 %	Atlantic Cod (*Gadus morhua*) liver: 0.07 ng/g ww (mean) Lipid content: 50.5%		Atlantic Cod liver: PentaBDE (PBDE-47): 0.41±0.42 ng/g ww (mean; DF:100%, n=10)	

Location	Year(s)	n	% detect	Concentration range	MDL	Remark	Reference
Svalbard	2012	1	0	Polar Cod (*Boreagadus saida*) whole fish: <MDL (mean) Lipid content: 1.7%		Polar Cod whole fish: PentaBDE (PBDE-47): 0.19 ng/g ww (mean; DF:100%, n=1)	
Kongsfjorden, Svalbard	2009	10	90% 9/10	Capelin (*Mallotus villosus*) whole fish, females and males: <0.120–1.306 ng/g ww 0.719±0.292 ng/g ww (mean) 33.65 ng/g lw (mean) Lipid content: 2.6%	For all BFRs: the detection limit varied from 0.0005 to 0.292 ng/g ww	Method: not specified Recoveries for labelled PBDEs: 67 and 120% Control samples and laboratory blanks included. No blank contamination was detected. No field blanks were used. Exact concentrations expressed as ng/g lw were communicated by the author.	Sagerup *et al.* 2010 Sagerup personal communication, May 2025
Kongsfjorden, Svalbard	2009	10	60% 6/10	Common Eider (*Somateria mollissima*) liver, female adults: <0.142–3.754 ng/g ww 1.652±1.396 ng/g ww (mean) 44.29 ng/g lw (mean) Lipid content: 3.7%			
Kongsfjorden, Svalbard Bjørnøya (or Bear Island), Norwegian Svalbard Archipelago	2008 2008	5 5	70% 7/10 (total)	Brünnich's guillemot (*Uria lomvia*) egg : <0.106–3.414 ng/g ww 1.799±1.358 ng/g ww (mean) 19.17 ng/g lw (mean) Lipid content: 11%			
Kongsfjorden, Svalbard	2009	10	50% 5/10	Black-legged Kittiwake (*Rissa Tridactyla*) liver, Adult males and females: <0.171–1.398 ng/g ww 0.800±0.356 ng/g ww (mean) 14.62 ng/g lw (mean) Lipid content: 5.5%			

Location	Year(s)	n	% detect	Concentration range	MDL	Remark	Reference
Tempelfjorden, Svalbard	2007	10	60% 6/10	Ringed seal (*Phoca hispida*) liver, adult males and females (5-19 years old): <0.138–0.876 ng/g ww 0.573±0.198 ng/g ww (mean) 16.36 ng/g lw (mean) Lipid content: 3.5%			
Van Mijenfjorden, Svalbard	2007-2008	10	0% 0/10	Arctic fox (*Vulpes lagopus*) liver adult males and females (3-14 years old): <0.142 ng/g ww Lipid content: 7.1%			
Hornsund / Storfjorden, Svalbard	2008	10	0% 0/10	Polar bear (*Ursus maritimus*) plasma, adult males (5-23 years old): <0.292 ng/g ww Lipid content: 0.9%			
Canadian Arctic:			19% (total samples)	Concentrations refer to geometric mean concentrations expressed as ng/g lw	0.006 ng/mL	Method: GC/MS ECNI Recovery of TBPH in the range of 95.6-118%. TBPH has never been detected in lab blanks (Houde personal communication, May 2025). Interlab comparison of results was performed leading to good agreement with all analytes quantified to within ±15% of certified values	Houde *et al.,* 2017
				Ringed Seal (*Phoca hispida*) blubber:		Blubber lipid content was consistently >90% 80% of sampled animals were females and juvenile males	
Arctic Bay, Lancaster Sound	2009	10		<MDL		Benchmark: PentaBDE (BDE-47 and BDE-99): 0.12–1.33 ng/g lw (n=10; PentaBDE was included to the SC in 2009))	
Resolute Bay, Lancaster Sound	2009–2013	42		<MDL–0.34		PentaBDE (BDE-47 and BDE-99): n.d.–7.43 ng/g lw (n=49)	

Location	Year(s)	n	% detect	Concentration range	MDL	Remark	Reference
Sachs Harbour, Beaufort Sea	2010–2013	34		<MDL–0.19		PentaBDE (BDE-47 and BDE-99): 0.05–11.7 ng/g lw (n=34)	
Gjoa Haven	2009	6		<MDL		PentaBDE (BDE-47 and BDE-99): 0.88–9.12 ng/g lw (n=67)	
Central East Greenland (closed to 70°N)	2012	3	24% (total samples)	Black guillemot (*Cepphus grylle*) eggs: 0.061 ng/g ww (mean) 0.050 – 0.066 ng/g ww 0.61 ng/g lw (mean) 0.48 – 0.67 ng/g lw Lipid content: 10.2%	0.024–0.025 ng/g ww	Method: GC/LRMS ECNI TBPH recovery in spikes samples: 96–137% The concentrations were corrected for those in non-spiked samples. Procedural blanks included Unclear how the MDL was derived Detection frequencies for total samples: BDE-47 (100%), *Syn*DP (95%) and *Anti*DP (100%) Benchmark: Black guillemot eggs: *Syn*DP: 0.005–0.030 ng/g ww or 0.048–0.28 ng/g lw (n=4; before its inclusion to the SC in 2023) *Anti*DP: 0.010–0.19 ng/g ww 0.096–1.78 ng/g lw (n=4; before its inclusion to the SC in 2023) Concentrations of TBPH in Black guillemot eggs are in the same range as those of POP substances before their inclusion to the SC	Vorkamp *et al.,* 2015
		4		Glaucous gull (*Larus hyperboreus*) liver: <0.025 ng/g ww <0.74 ng/g lw Lipid content: 5.28%	0.024–0.025 ng/g ww	Glaucous gull liver: *Syn*DP: 0.010–0.041 ng/g ww or 0.19–0.63 ng/g lw (n=4) *Anti*DP: 0.066–0.18 ng/g ww or 1.24–2.89 ng/g lw (n=4)	
		5		Ringed seal (*Pusa hispida*) blubber <0.14 ng/g ww <0.15 ng/g lw Lipid content: 93.1%	0.13–0.14 ng/g ww	Ringed seal blubber: PentaBDE (BDE-47): 20.1–36.3 ng/g ww or 21.7–39.1 ng/g lw (n=5; after its inclusion to the SC in 2009) *Syn*DP: <0.013–0.42 ng/g ww or <0.014–0.45 ng/g lw (n=5) *Anti*DP: 0.035–1.84 ng/g ww or 0.038–1.96 ng/g lw (n=5)	

Location	Year(s)	n	% detect	Concentration range	MDL	Remark	Reference
		5		Polar bear (*Ursus maritimus*) adipose tissue 0.26 ng/g ww (mean) <0.128 – 0.402 ng/g ww 0.39 ng/g lw (mean) <0.14 – 0.44 ng/g lw Lipid content: 86.4%	0.13 ng/g ww	Polar bear adipose tissue: *Syn*DP: 0.013–0.030 ng/g ww or 0.015–0.039 ng/g lw (n=5) *Anti*DP: 0.028–0.079 ng/g ww or 0.030–0.10 ng/g lw (n=5) Concentrations of TBPH in Polar bear adipose tissue are in the same range as those of POP substances before their inclusion to the SC	
West Greenland		4		Ringed seal (*Pusa hispida*) <0.13 ng/g ww <0.14 ng/g lw Lipid content: 94.2%	0.12–0.13 ng/g ww	Ringed seal blubber: PentaBDE (BDE-47): 2.64–10.9 ng/g ww or 2.89–11.4 ng/g lw (n=4) *Syn*DP: 0.014–0.030 ng/g ww or 0.015–0.032 ng/g lw (n=4) *Anti*DP: 0.053–0.083 ng/g ww or 0.058–0.087 ng/g lw (n=4)	
Western Pacific Ocean deep sea trenches (Mariana, New Britain) MT-2 samples situated at 310 km from Guam at a water depth of 6025 m	December 2016 to January 2019	10	19%	Amphipod (*Alicella gigantea*): Detected	5.53 pg/g	Method: GC-MS/MS in electron ionisation mode Sample recoveries (mean ± standard deviation (SD)) were 92% ± 27% for NBFRs Procedural blanks included. NBFRs were not detected or below the MDL in the blanks Limited industrial activities in Papua New Guinea and Guam, the pollutant input from such sources was expected by the authors to be low	Xie et *al.*, 2023

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Technical work: consideration of chemicals proposed for listing in Annexes A, B and/or C to the Convention: bis(2-ethylhexyl) tetrabromophthalate (TBPH), covering any of its individual isomers and/or combinations thereof

Proposal to list bis(2-ethylhexyl) tetrabromophthalate (TBPH), covering any of its individual isomers and/or combinations thereof, in Annexes A, B and/or C to the Stockholm Convention on Persistent Organic Pollutants**

Note by the Secretariat

I. Introduction

1. The European Union has submitted a proposal to list bis(2-ethylhexyl) tetrabromophthalate (TBPH), covering any of its individual isomers and/or combinations thereof, in Annexes A, B and/or C to the Stockholm Convention on Persistent Organic Pollutants, pursuant to paragraph 1 of Article 8 of the Convention (see annex to the present note). The proposal is being circulated as submitted and has not been formally edited. Additional information relating to the proposal is set out in document UNEP/POPS/POPRC.22/INF/6, as submitted by the European Union. The Secretariat's verification of whether the proposal contains the information specified in Annex D to the Convention is set out in document UNEP/POPS/POPRC.22/INF/7.

II. Proposed action

2. The Committee may wish:

(a) To consider the information provided in the present note;

(b) To decide whether it is satisfied that the proposal fulfils the requirements of Article 8 of and Annex D to the Convention;

(c) To develop and agree on, if it decides that the proposal fulfils the requirements referred to in subparagraph 2 (b) above, a workplan for preparing a draft risk profile pursuant to paragraph 6 of Article 8 of the Convention.

* UNEP/POPS/POPRC.22/1.

** The present document has not been formally edited.

Annex*

Proposal to list bis(2-ethylhexyl) tetrabromophthalate (TBPH), covering any of its individual isomers and/or combinations thereof, in Annexes A, B and/or C to the Stockholm Convention on Persistent Organic Pollutants

1. Introduction

1. Bis(2-ethylhexyl) tetrabromophthalate (TBPH) is a brominated phthalate derivative having four bromine atoms at the aromatic ring and two diester substituents. TBPH consists of three stereoisomers: two enantiomers (*R*,*R* and *S*,*S*) and the *meso* isomer (*R*,*S*). They have the same molecular formula and sequence of bonded elements and differ only in the 3D (orientations of the atoms in space) geometry of the structure. There are no available data for the individual stereoisomers and therefore properties are assumed to be similar.

2. TBPH is a novel brominated flame retardant (NBFR) with first commercial uses reported between 1987 and 1994 (Environment and Climate Change Canada (ECCC), Health Canada (HC), 2019). It is primarily used as a non-reactive flame-retardant additive and it is also used as a plasticiser (US EPA, 2015a). TBPH has been marketed as a replacement for polybrominated diphenyl ethers (PBDEs) flame retardants such as the commercial pentabromodiphenyl ether (pentaBDE) and octabromodiphenyl ether (octaBDE) formulations (Knudsen *et al*., 2017). TBPH can be used alone, or with benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester (TBB; CAS No 183658-27-7) in commercial mixtures. The latter might include also organophosphate flame retardants (ECCC and HC, 2019). Uses of TBPH include flexible polyvinyl chloride (PVC) used in wires and cable insulation, rigid polyurethane (PUR) in construction sector and flexible PUR in upholstery applications (ECCC and HC, 2019; US EPA, 2015b and Swedish Competent Authority, 2022).

3. In the European Union (EU), the substance is registered under the Registration, Evaluation and Authorisation of Chemicals (REACH) Regulation. TBPH is manufactured and/or imported to the European Economic Area (EEA) at 100−1,000 tonnes/year. In the United States of America (USA), TBPH is a High Production Volume (HPV; produced or imported into the US at volumes ≥ one million pounds (or ≥ 450 tonnes/year)) chemical (US EPA, 2015c). According to the 2020 Chemical Data Reporting (CDR) database,[1] the national aggregated production volume of TBPH in the USA was between 1,000,000 – <10,000,000 lbs (equivalent to 453.6– < 4,536 tonnes/year) between 2016 and 2019. There is evidence that TBPH is still in use in some countries. However, according to the International Bromine Council (BSEF), TBPH is no longer produced and used by most/if not all countries (BSEF, 2025). It seems that one of the main US manufacturers of the commercial mixtures Firemaster® 550 and Uniplex™ FRP 45 stopped manufacturing TBPH in 2022.[2] On the contrary, there is evidence that the manufacture of Uniplex™ FRP 45 in the US is still ongoing.[3]

4. While there are no known natural sources of TBPH, it has been detected in all compartments of the environment including air, surface water, sediment, biota (including wildlife) and humans. In addition, there is evidence of TBPH presence in remote areas without known local sources. According to AMAP (2017), levels of TBPH in Arctic air are comparable to those of PBDEs and have shown signs of increase. In combination with increasing trends observed in the Great Lakes region, this might reflect the anticipated increase in use as a replacement for pentaBDE (AMAP, 2017).

5. Modelling indicates that TBPH is mainly distributed to the soil and sediment compartments when released to the environment (ECHA, 2022). TBPH is expected to be released to the environment from industrial sources and manufactured items primarily through wastewater (ECCC and HC, 2019). Release to the soil could also occur through the application of wastewater biosolids to agricultural and pasture lands (ECCC and HC, 2019). Potential release of TBPH from products available to consumers

* The annex has not been formally edited. The studies and other information referred to in this document do not necessarily reflect the views of the Secretariat, the United Nations Environment Programme (UNEP) or the United Nations. The designations employed and the presentation of the material in such studies and references do not imply the expression of any opinion whatsoever on the part of the Secretariat, UNEP or the United Nations concerning geopolitical situations or the legal status of any country, territory, area or city or its authorities.

[1] https://www.epa.gov/chemical-data-reporting/access-chemical-data-reporting-data#2020.

[2] https://lanxess.com/en/sustainability/material-topics/sustainable-products/elimination-of-critical-substances.

[3] https://www.hallstarindustrial.com/product/uniplex-frp45/.

may also be very significant. As additive flame retardants (rather than reactive flame retardants chemically bonded to the polymer), there is a greater possibility for release of TBPH from products available to consumers to the environment (Guerra *et al.,* 2011 as cited in ECCC and HC, 2019). As summarised in Environment and Climate Change Canada, Health Canada (2019), TBPH can be released to the environment from consumer products via several ways, i.e. volatilisation and leaching from treated products, partitioning to indoor dust, as well as during the waste stage. The main sources of exposure to TBPH for the general population are expected to be from environmental media (air, dust, soil, and water), food, including breast milk, and from the use of products available to consumers such as foam-containing furniture (ECCC and HC, 2019).

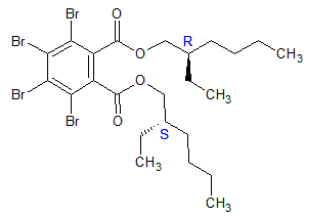
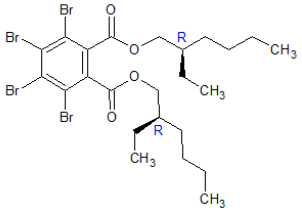
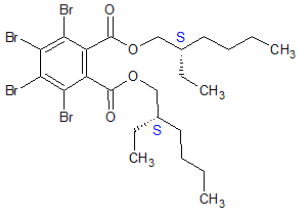
6. TBPH has been identified in the EU under REACH as a Substance of Very High Concern (SVHC) and included in the Candidate List[4] for Authorisation in November 2022 due to its very Persistent, very Bioaccumulative (vPvB) properties. TBPH is part of a group of aromatic brominated flame retardants assessed by the European Chemicals Agency (ECHA) for a possible restriction proposal under REACH (ECHA, 2024a).

7. This proposal specifically addresses the information requirements and screening criteria of Annex D in the Stockholm Convention on Persistent Organic Pollutants and summarises relevant evidence relating to the screening criteria for persistence, bioaccumulation, long-range environmental transport and adverse effects. The proposal is based on the EU SVHC dossier prepared under the REACH Regulation (ECHA, 2022), information from peer-reviewed scientific journals as well as grey literature.

2. Chemical identity

8. This proposal concerns bis(2-ethylhexyl) tetrabromophthalate, covering any of its individual stereoisomers and/or combinations thereof:

Figure 1: Structural formulae of the possible stereoisomers

		
(2*R*)-2-ethylhexyl (2*S*)-2-ethylhexyl tetrabromophthalate	bis[(2*R*)-2-ethylhexyl] tetrabromophthalate	bis[(2*S*)-2-ethylhexyl] tetrabromophthalate

9. Bis(2-ethylhexyl) tetrabromophthalate is a diastereoisomer consisting of two stereoisomers (which create three possible formations).

10. Table 1 provides the available identifiers associated to TBPH. The EC and CAS number correspond to a multi-constituent substance which comprises all possible isomer formations of bis(2-ethylhexyl) tetrabromophthalate.

Table 1: Chemical identity of bis(2-ethylhexyl) tetrabromophthalate

EC number:	247-426-5
EC name:	bis(2-ethylhexyl) tetrabromophthalate
CAS number:	26040-51-7
IUPAC name:	bis(2-ethylhexyl) 3,4,5,6-tetrabromobenzene-1,2-dicarboxylate
Molecular formula:	$C_{24}H_{34}Br_4O_4$
Molecular weight range:	706.14 g/mol

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

Synonyms or acronyms:	TBPH, BEHTP, BEHTBP, BEHTEBP and BEH-TEBP
Trade names:	BZ 45, DP 45, FRP 45, Firemaster® BZ-54, Firemaster® 550 (FM 550), Firemaster® 552, Firemaster® 600, Pyronil 45 and Uniplex™ FRP 45

11. Information on the physicochemical properties for TBPH is presented in Table 2. Values for physicochemical properties were experimentally determined for the substance and not for the three individual isomers. Considering the very similar chemical structures, namely R,R, R,S or S,S stereoisomers of the 2-ethylhexyl chain, it is reasonable to assume that the physicochemical properties for the individual isomers are similar.

Table 2: Overview of available physicochemical properties of TBPH

Property	Description of key information	Value [Unit]	Reference/source of information
Physical state at 20 °C and 101.3 kPa	Experimental	Liquid at 20 °C and 101.3 kPa	Experimental study (visual inspection)[5]
Melting/freezing point	Experimental	-27 °C at 101.3 kPa (atmospheric pressure was not reported, ambient conditions are assumed)	Guideline study (DIN ISO 3016; Pour point) without detailed documentation[6]
Boiling point	Experimental	>300 °C at 1013 hPa	Guideline study (EU Method A.2 - Boiling temperature; Differential Scanning Calorimetry) without detailed documentation[7]
Vapour pressure	(Q)SAR prediction	2.28×10^{-9} Pa at 25 °C (modified grain method) 2.12×10^{-9} Pa at 25 °C	MPBPWIN v1.43[8] COSMOtherm 2020 as cited in Glüge and Scheringer (2023)
Density	Experimental	1.541 kg/m^3 at 20 °C	Guideline study (EU Method A.3 - Relative Density; U-tube method) without detailed documentation[9]
Water solubility	Experimental	< 0.05 µg/L at 20 °C (not detectable without solubiliser) 794 µg/L at 20 °C (using 1 % acetonitrile as solubiliser)	Guideline study (EU Method A.6. – Water Solubility; Flask method), which in most parts is equivalent to OECD TG 105[10]
Partition coefficient n-octanol/water (log value) K_{OW}	Experimental	10.2 at 25 °C	Guideline study (OECD TG 117, HPLC method)[11]

[5] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.

[6] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.

[7] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.

[8] EPI Suite (http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm).

[9] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.

[10] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.

[11] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.

Property	Description of key information	Value [Unit]	Reference/source of information
Partition coefficient organic carbon/water (log value) K_{OC}	Experimental	7.3 at 25 °C	Guideline study (OECD TG 121, HPLC method)[12]
Partition coefficient organic carbon/air (log value) K_{OA}	(Q)SAR prediction	15.114 15.489 at 20°C	KOAWIN v1.10, using measured log K_{OW} (of 10.2; US EPA, 2012) COSMOtherm 2020 as cited in Glüge and Scheringer (2023)
Partition coefficient air/water (log value) K_{AW}	(Q)SAR prediction	- 4.914 - 3.525 at 25°C	HenryWin (US EPA, 2012) COSMOtherm 2020 as cited in Glüge and Scheringer (2023)

3. Information on TBPH and how it fulfils the Annex D screening criteria

12. There is experimental information available for the whole substance, but not for the single isomers. As the isomers are structurally similar, and in the absence of other evidence, the properties of the isomers are expected to be reasonably similar to the properties determined for the whole substance (ECHA, 2022).

3.1 Persistence

13. The abiotic hydrolytic transformations of TBPH was assessed in a preliminary hydrolysis test according to OECD TG 111, available in the EU registration dossier.[13] The preliminary test was performed with an aqueous solution with 1% acetonitrile of 0.4 mg TBPH/L. Only the preliminary phase of the study at pH 4, 7 and 9 at 50ºC was performed. The disappearance of the test item was > 91% after the study period at each pH. The resulting half-lives were 30.4 hours at pH 4, 44.1 hours at pH 7 and 77.5 hours at pH 9. The registrant used the van´t Hoff equation to extrapolate the half-lives to a temperature of 20°C, which gave the following values: 10.1 days at pH 4, 14.7 days at pH 7 and 25.8 days at pH 9. In a second screening experiment performed at 60°C and pH 4 one transformation product, tetrabromophthalic acid, was identified. As these results have not been followed up by a definitive study, performed with at least three different temperatures according to the guideline, the results are questionable.

14. According to Environment and Climate Change Canada, Health Canada (2019), consideration of the chemical structure of TBPH suggests that abiotic hydrolysis of the ester groups may be favourable owing to the electron withdrawing character of multiple bromine substitutions on the aromatic ring. Conversely, steric effects from the branched ester substituents and sparing solubility of TBPH in water are suggestive of slow hydrolysis reactions. Empirical data pertaining to a commercial mixture of TBB and TBPH shows that the hydrolysis reaction is in fact slow. An abiotic hydrolysis study found no measurable hydrolysis of the TBB/TBPH mixture at pH 4, 7, or 9 and 50°C. According to the criteria stated within the test method (92/69/EEC C7 equivalent to OECD TG 111), the hydrolysis half-life was concluded to be greater than 1 year at each pH value and 25°C (unpublished study by Great Lakes Chemical Corporation in 1997 as cited in ECCC and HC, 2019).

15. In addition, Bis(2-ethylhexyl) phthalate (or DEHP; the unbrominated skeleton of TBPH) has an estimated hydrolysis half-life of approximately 2000 years (Giam *et al.,* 1984 as cited in Pakalin *et al.,* 2008). This indicates that the hydrolysis of TBPH may not be rapid. Furthermore, considering its low water solubility and high K_{oc}, TBPH is highly adsorptive to organic matter in suspended solids, sediment and soils, and this adsorption may limit the rate of hydrolysis in natural waters. Furthermore,

[12] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.

[13] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.

the International Bromine Council (BSEF) mentioned that TBPH abiotic hydrolysis is extremely slow due to bulky brominated atoms and ester structure, thus TBPH does not break down under environmental conditions (BSEF, 2025).

16. BIOWIN modelling (US EPA, 2012) predicts TBPH to be not readily biodegradable, and the combination of Biowin 2 or Biowin 6 and Biowin 3 model predictions (as specified in REACH PBT[14] guidance Chapter R.11; ECHA, 2023) indicate that TBPH screens as potentially persistent or very persistent to biodegradation. The substance can be considered within the structural domain, although noting that for the parametric domain of Biowin 2 and 3, the substance is at (or just above) the upper limit of the molecular weight range. The classification model for ready biodegradation by Körner *et al.* (2024) predicts TBPH to be not readily biodegradable (predicted probability not readily biodegradable[15] = 0.991). Two ready biodegradation tests referred to by the US EPA (2015b) show that TBPH is not readily biodegradable (< 4% degradation). In addition, Li *et al.* (2025) assessed the biodegradability of TBPH among other NBFRs using OECD TG 301F at 22±1°C for 28 days. Aniline was used as a reference compound. TBPH exhibited a limited biodegradation under OECD TG 301F conditions with a biodegradation rate of 1.4% after 28 days. This is confirmed by the results of two inherent degradation tests performed according to OECD TG 302C at 25°C, which gave 7% and 12.9% degradation in 28 days and indicate that TBPH is not readily or inherently biodegradable (ECHA, 2022 and Li *et al.,* 2025). According to REACH PBT guidance Chapter R.11 (ECHA, 2023), 'Lack of degradation (<20% degradation) in an inherent biodegradability test equivalent to the OECD TG 302 series may provide sufficient information to confirm that the P-criteria (degradation half-life >120 days) are fulfilled without the need for further simulation testing for the purpose of PBT/vPvB assessment. Additionally, in specific cases it may be possible to conclude that the vP-criteria (degradation half-life >180 days) are fulfilled with this result if there is additional specific information supporting'.

17. No degradation simulation study is available for TBPH. However, a non-guideline outdoor mesocosms study completed by de Jourdan *et al.* (2013) studied the fate of four NBFRs including TBPH (ECHA, 2022). The study was performed in Ontario (Canada) during summer (July–September 2008 and July–September 2009) with an air temperature in the range 15–22°C. The mesocosms had a depth of 1.2 m, a diameter of 3.9 m and were filled with water to approximately 1 m. The water supply for the mesocosms was an irrigation pond supplied by a well located on site. Artificial sediment containing organics-rich soil (1:1:1 mixture of topsoil: manure:compost) with an organic content of 11.6% dry total C (1.6% dry inorganic C, and 10.0% dry organic C) was placed on trays that were placed on the bottom of each mesocosm so that > 50% of bottom surface was covered. The fate study took place over two years (2008 and 2009), with year 1 serving for method development purposes. The mesocosms were established in May 2008 and treated in July 2008 and again in July 2009. In year 1, Firemaster® BZ-54 (TBPH:TBB 1:4) was applied to the water phase of three mesocosms by subsurface injection. The simultaneous application of TBPH and TBB is not expected to have affected the results of this study. Five injections of 25 mL of commercial BZ-54, dissolved in dimethyl sulfoxide (DMSO; 0.001% (v/v)) were made at several locations in the mesocosms. The aim was to achieve homogeneous distribution of the compound at a nominal concentration of 0.03 mg/L to achieve a target concentration of 500 ng TBPH/g sediment in the upper 5 cm on partitioning into the sediment, which is consistent with concentrations observed in sewage sludge from the San Francisco Bay area. In Year 2 (July 16, 2009), two mesocosms from each treatment were retreated at the same concentration, but no additional water was added. The mean recovery rate of the analytical method was 77.4 % (range 60%–88%, standard deviation of 5.9 %).

18. There were large fluctuations in TBPH concentration in the particulate matter throughout the study while the concentration in the sediment did not fluctuate in the same manner with the maximum concentration being almost equal to the mean concentration during the whole sampling period. TBPH DT_{50} in the particulate matter was estimated to 25 days with a 95% confidence interval (CI) of 7–44 days. Some degradation may have occurred in the particulate matter. There was one major unknown peak in the chromatogram which agreed fairly well with the expected mass of a tribrominated anhydride. de Jourdan *et al.* (2013) mentioned that this could have been formed via hydrolysis of the ester groups to tetrabromo phthalic acid subsequently forming an anhydride. The authors speculate that this could be due to photolysis in the particulate compartment as debrominated analogues of TBPH were detected in a photolysis study by Davis and Stapleton (2009; see paragraph on photolysis in Section 3.3). For the sediment, the regression equations were not significant, suggesting no significant decline. The authors of the study report the result as DT_{50} > 200 days for the sediment phase. The actual DT_{50} estimation (regression analysis) gave a value of 9,303 days with a 95% CI of

[14] Persistent bioaccumulative and toxic.

[15] https://biodegradability-prediction-app.streamlit.app/ accessed 27.5.2025.

1,330 – 17,280 days. The concentrations of TBPH in the sediment were almost the same as the maximum concentration during the study period thus indicating that there was no dissipation/degradation of TBPH from the sediment compartment. Furthermore, no degradation products were identified in the sediment. The authors mentioned that minor brominated degradation products were detected in sediment, but because of matrix interference, they could not be accurately determined. This study strongly indicates that TBPH is persistent in sediment (DT_{50} > 200 days). Persistence of TBPH is also supported by monitoring data indicating its presence in sediment (ECHA, 2022), including in remote areas away from point sources in the Western Pacific (100% detected in hadal surface sediment samples from deep sea oceanic trenches; Xie *et al.,* 2023).

19. Furthermore, the presence of TBPH in all environmental compartments including air, surface water, groundwater, seawater, sediment, soil and in remote areas such as the Arctic, the Tibetan Plateau, the Bering sea, the East Greenland Sea, the western Pacific Ocean, the South Atlantic Ocean, the oceanic Southern hemisphere and the Antarctic, gives further support to conclude that the substance is very recalcitrant to degradation (see monitoring data in Annex I – Environmental and human monitoring data of the EU dossier (ECHA, 2022); Han *et al.,* 2022 and in Section 3.3).

3.1.1 Conclusion on persistence according to the criteria in Annex D

20. The criteria for persistence listed in paragraph 1 (b) (i) and (ii) of Annex D are considered to be met. TBPH has a degradation half-life in sediment greater than six months (or 180 days; TBPH DT_{50} >200 days in sediment). Persistence of TBPH is also supported by monitoring data indicating its presence in sediment, including in remote areas away from point sources (including detection in hadal surface sediments, see section 3.3).

3.2 Bioaccumulation

21. TBPH meets the Annex D screening criteria with an octanol-water partition coefficient (log K_{ow}) greater than 5 for bioaccumulation with a log K_{ow} of 10.2 (ECHA, 2022).

22. The bioaccumulation potential of TBPH in juvenile rainbow trout (*Oncorhynchus mykiss*) was investigated in a study according to OECD TG 305 (dietary exposure; unpublished, 2018). The growth and lipid corrected kinetic biomagnification factor (BMF_{kgL}) was 0.038 for TBPH (with a kinetic BMF of 0.0048 without correction). According to REACH PBT guidance Chapter R.11 (ECHA, 2023), even if a BMF from an OECD TG 305 dietary bioaccumulation study is found to be below 1, it cannot be considered as a good discriminator for concluding substances not to be (very) bioaccumulative. The substance was poorly absorbed with an assimilation efficiency of 0.011. In this study, the fish depuration was slow with a growth and lipid corrected depuration rate constant (k_{2gL}) of 0.018 day^{-1}, a growth corrected depuration rate constant (k_{2g}) of 0.015 day^{-1}, a depuration rate constant (k_2) of 0.044 day^{-1} and a long growth corrected half-life of 46.2 days (or 15.6 days without growth correction) for TBPH. Brooke and Crookes (2012) suggest that a lipid normalised depuration rate constant around 0.085 day^{-1} or less, would indicate a bioconcentration factor (BCF) above 5,000 L/kg. The low rate of depuration seen in the feeding study with *Oncorhynchus mykiss* (k_{2gL} of 0.018 day^{-1}) is consistent with the BCF for TBPH being > 5,000 L/kg. The predicted BCF values using method 1 and method 2 models (as referred to in the OECD TG 305 guidance; OECD, 2017) were all above a BCF of 5,000 L/kg (BCFs in the range of 5,878–167,655 L/kg) except one (method 3 model). Method 3 model gives a BCF estimates of 881 L/kg for TBPH. However, the later model was derived for carp only and thus its applicability to other fish species such as rainbow trout is unknown. Considering the low uptake seen in the bioaccumulation study these methods probably overestimate the uptake rate and thus overestimate the BCF of TBPH. It is also noted that the log K_{ow} of TBPH is above the indicative applicability domain of these models. However, the OECD TG 305 BCF estimation tool is the only recommended tool in OECD TG 305 to derive BCF values from dietary bioaccumulation studies.

23. A comparison of laboratory depuration rate constants and biomagnification factor (BMF) values in rainbow trout for TBPH against known PBT/vPvB/POP substances was performed in the support document for the identification of TBPH as an SVHC in the EU (ECHA, 2022). TBPH has a BMF_{kgL} of 0.038 and a k_{2g} of 0.015 day^{-1} in rainbow trout, which are similar to POP and bioaccumulative substances, dechlorane plus (BMF_{kgL} of 0.023 and k_{2g} of 0.010–0.013 day^{-1} for *anti*-isomer; BMF_{kgL} of 0.046–0.062 and k_{2g} of 0.017–0.023 day^{-1} for *syn*-isomer) and methoxychlor (BMF of 0.16 and k_{2g} of 0.124 day^{-1}). Dechlorane plus and methoxychlor meet the bioaccumulation criteria of Annex D (BCF > 5,000 L/kg), further indicating that TBPH is bioaccumulative.

24. Burkhard *et al.* (2023) exposed Rainbow trout (*Oncorhynchus mykiss*) through the diet to a mixture of hydrophobic substances, including TBPH, for 28 days in accordance with the OECD TG 305 method. The growth and lipid corrected kinetic biomagnification factor (BMF_{kgL}) was 0.0018 for

TBPH (with a kinetic BMF of 0.0009 without correction). The substance was poorly absorbed with an assimilation efficiency of 0.004. In this study, the fish depuration was slow with a growth and lipid corrected depuration rate constant (k_{2gL}) of 0.054 day^{-1}, a growth corrected depuration rate constant (k_{2g}) of 0.047 day^{-1}, a depuration rate constant (k_2) of 0.056 day^{-1} and a long growth corrected half-life of 14.8 days (or 12.3 days without growth correction) for TBPH. Brooke and Crookes (2012) suggest that a lipid normalised depuration rate constant around 0.085 day^{-1} or less, would indicate a bioconcentration factor (BCF) above 5,000 L/kg. The low rate of depuration seen in the feeding study with *Oncorhynchus mykiss* (k_{2gL} of 0.054 day^{-1}) is consistent with the BCF for TBPH being > 5,000 L/kg. Most of the predicted BCF values using method 1 and method 2 models (as referred to in the OECD TG 305 guidance; OECD, 2017) were above a BCF of 5,000 L/kg (9 out of 13 models predict a BCF > 5,000; BCFs in the range of 1,295–55,595 L/kg, see Table A1 in the information document (UNEP/POPS/POPRC.22/INF/6). Method 3 model gives a BCF estimate of 71.6 L/kg for TBPH. However, the later model was derived for carp only and thus its applicability to other fish species such as rainbow trout is unknown. The uncertainties of these BCFs estimates are similar to those described in unpublished (2018) study (see above).

25. A bioaccumulation study performed by Nacci *et al.* (2018) investigated the uptake and depuration of TBPH in the estuarine fish, Atlantic killifish (*Fundulus heteroclitus*) following similar design to OECD TG 305 study (dietary exposure). A polychlorinated biphenyl (PCB 153) was included as a positive control for bioaccumulation. According to Nacci *et al.* (2018), TBPH had a BMF of 0.02 at low exposure level (139 mg TBPH/kg dry weight (dw)), and a BMF of 0.005 at high exposure level (4,360 mg TBPH/kg dw) and PCB 153 had a BMF of 1.08 at 13 mg/kg dw exposure level. The growth and lipid corrected kinetic biomagnification factor (BMF_{kgL}) was 0.01625 for TBPH (with a kinetic BMF of 0.0291 without correction). There appears to be a critical uptake amount of TBPH for fish, where at high TBPH concentrations not all of the TBPH underwent uptake. At low concentrations, or slow dosing, TBPH will undergo a higher uptake rate and therefore have a higher BMF. This concentration dependence indicates reduced bioavailability with increasing exposure. The study showed that TBPH was not well metabolised with a low depuration rate constant (k_2) of 0.0696 and a long growth corrected half-life of 10.4 days (or 9.96 days without growth correction) in *F. heteroclitus*. Most of the predicted BCF values using method 1 and method 2 models were below a BCF of 5,000 L/kg (11 out of 13 models predict a BCF<5,000; BCFs in the range of 445–13,017 L/kg; see Table A2 in the information document (UNEP/POPS/POPRC.22/INF/6)). Method 3 model gives a BCF estimate of 435 L/kg for TBPH. However, the later model was derived for carp only and thus its applicability to other fish species such as Atlantic killifish is unknown. The uncertainties of these BCFs estimates are similar to those described in unpublished (2018) study (see above). It is worth noting that the depuration rate constant (k_2) was not statistically different from zero ($p = 0.1768$), thus it cannot be excluded that the substance does bioaccumulate in *F. heteroclitus.*

26. Hou *et al.* (2022) performed *in vitro* incubation of seven NBFRs in liver microsomes of the fish species *Epinephelus fasciatus* and *Plectorhynchus orientalis* to assess biotransformation clearance rates. Microsomes were incubated at 25 °C for 0, 0.5, 1, 2, 4, and 6 hours instead of the recommended 2 hours (maximum 4 hours) in OECD TG 319B thus only five time points were relevant for deriving the clearance rate instead of the recommended 6 time points. Furthermore, the liver microsomes were evaluated for the ability to catalyse phase I reactions, that are most relevant for TBPH metabolism. The incubation mixtures consisted of 3 µL of TBPH in DMSO (5 µmol/L). The test used 1 mg/mL of protein. Experiments were repeated in triplicate. The recovery for the microsomes samples was around 90%. The biotransformation followed first-order kinetics in liver microsomes of both fish species and the measured values did not differ significantly between the two species. *In vitro* biotransformation rate for TBPH was, together with hexabromobenzene (HBB), the lowest in sweetlips (0.017 ± 0.004 mL/mg protein/hr, r^2=0.803) and the single lowest in grouper (0.016 ± 0.002 mL/mg protein/hr; r^2=0.964). This study indicates that TBPH is very poorly metabolised by fish.

27. A biota-sediment accumulation factors (BSAFs) of 0.254 kg organic carbon/kg lipid for TBPH was determined in oligochaetes, *Lumbriculus variegatus* (US EPA test method 100.3 (US EPA, 2000); Burkhard *et al.,* 2021). The sediment exposure test was conducted over 56-day period: a subset of the worms was continuously exposed to TBPH, while a subset was assessed for depuration by exposure to TBPH sediment for 28 days, followed by 28 days of clean sediment. The organisms were not fed during the study in alignment with US EPA test method (US EPA, 2000). Steady-state conditions for the uptake of TBPH was not reported to be reached in 28 days thus suggesting that the BSAF would have been even higher if steady-state was reached. TBPH displayed a biphasic elimination in *L. variegatus* where 94% of the body burden was depleted within the first 12 h of elimination (i.e., half-life of 1.2 h or less) and the remaining 6% eliminated very slowly thereafter (half-life of 15 days) with a slow elimination rate constant of 0.0461 (±0.00485) day^{-1}. According to Burkhard *et al.* (2021) the mechanism for biphasic uptake and elimination kinetics of highly hydrophobic chemicals such as

TBPH in *L. variegatus* is unknown. The authors speculated that causes might be residual sediment within the organisms, chemical associated with GI tract membranes/ mucous, and possibly, by physical displacement by clean sediment. There was little evidence for biotransformation of TBPH by *L. variegatus*. These results suggest a possible accumulation of TBPH in *L. variegatus*.

28. Field studies seem to indicate that biomagnification of TBPH is possible in a benthic marine food web:

29. In October and November 2020, Hou *et al.* (2022) measured concentrations of TBPH from coral reef waters of Xisha Island, South Chinese Sea. TBPH was found in seawater (mean concentration = 0.037 pg/L, detection frequency (DF) = 12.5%, n = 8), sediment (mean concentration = 0.181 µg/kg dw, DF = 62.5%, n = 8), and in 29 different types of aquatic organisms (DF = 78.4%, n = 109 for all organisms (n = 3–6 per species)) with a concentration range of <MDL (method detection limit)[16] to 0.369 µg/kg lipid weight (lw). The highest concentrations have been reported in benthic species with a higher trophic level (the carnivore or apex predator species). Concentrations of TBPH in biota are referring to measurements in whole bodies of invertebrates and muscles of fish. From these measured concentrations, field BSAF[17] values in the range from 0.11 ± 0.01 in sea cucumbers to 0.86 ± 0.32 for seashell and 0.86 ± 0.61 for fish (grouper) have been found for TBPH. According to REACH Chapter R.11 (see Appendix R.11—3; ECHA, 2023), lipid and organic carbon normalized BSAF values of 0.5 and higher are an indication of high bioaccumulation (BCF>5,000), based on pore water concentration. The BSAF values for TBPH in seashell and fish are indicative of a high bioaccumulation potential. Furthermore, these BSAF values indicate that TBPH from sediments is transferred equally to benthic invertebrates as to benthic fish. However, as sediment is not a direct source of TBPH for fish, the observed bioaccumulation of TBPH is considered to be the result of food chain magnification.

30. Biomagnification factor (BMF)[18] estimates were calculated in fish-crabs predator-prey relationship for the fish species for which crab is indicated as a food source. The estimated BMFs indicated that TBPH was biomagnified in fish, with BMFs ranging from 4.2 to 24 (median = 6.8) in fish-crabs predator-prey relationship (Hou *et al.,* 2022). It is acknowledged that these estimated BMFs are only rough and probably over-estimates potential biomagnification of TBPH as the fish do not forage only on crabs. Adult *Cephalopholis argus* for example feed mainly on fish (75-95%) according to Fish base.[19] This species has the highest concentration of TBPH of all the sampled fish species in this study (0.369±0.066 µg TBPH/kg lipid weight) and the second highest value for Trophic Level (TL). A BMF based on the average concentration of TBPH in these species and the average concentration of TBPH in all of the sampled fish species (0.129 TBPH/kg lipid weight) results in a BMF of 2.9. This is considered a more realistic estimation of the biomagnification of TBPH in fish. It is acknowledged that there is a large uncertainty also in this BMF value as e.g., the average concentration of TBPH in *C. argus* is based only on three individuals. However, taken together the evidence from this study indicate that TBPH is biomagnified in fish. It is worth noting that the samples analysed refer to whole bodies of invertebrates and to fish muscles rather than whole body of prey and predator, and thus the levels found may not reflect the levels present in whole fish. The reliability of these BMFs is thus unknown.

31. With a measured log K_{ow} of 10.2 and an estimated log K_{oa} of 15.1 or 15.5 (KOAWIN v1.10, US EPA, 2012; COSMOtherm 2020 as cited in Glüge and Scheringer (2023)) TBPH fulfils the REACH bioaccumulation screening criteria for air-breathing organisms (log $K_{ow} \geq 2$ and log Koa ≥ 5; Kelly *et al.,* 2007 as cited in ECHA, 2023). Metabolism of TBPH has been studied *in vitro* using human liver microsomes and intestinal subcellular fractions (Roberts *et al.,* 2012). No significant loss of TBPH was observed and no metabolites were detected in experiments with human liver microsomes. Mono(2-ethylhexyl) tetrabromophthalate (TBMEHP), a metabolite of TBPH, was slowly formed when porcine hepatic carboxylesterase was added to the assay. Roberts *et al.* (2012) mentioned that the metabolism of TBPH to form TBMEHP may have implications on the toxicity of TBPH but may not be rapid enough to affect the bioaccumulation of TBPH. The available *in vivo* toxicokinetic data in rats indicate that TBPH is poorly absorbed and poorly metabolised and is mainly excreted unchanged via faeces after oral exposure (Knudsen *et al.,* 2017, Roberts *et al.,* 2012 and Silva *et al.,* 2015). However, after IV administration TBPH was largely eliminated in the faeces as a mixture of

[16] The MDL of TBPH in biota was 0.012 µg/kg lw or ng/g lw.

[17] BSAF is a ratio of the concentration of substance in normalised lipid content and the concentration of substance in normalised carbon content.

[18] The BMFs have been calculated by dividing the lipid normalised concentration in the predator by the lipid normalised concentration in the diet of the predatory.

[19] https://www.fishbase.se/search.php.

parent (30%) and metabolite (TBMEHP 70%), with a significant proportion of the dose retained in tissues (Knudsen *et al.,* 2017). Indeed, after single exposure 20% of the orally and IV-administered TBPH (at 0.1 µmol/kg) was retained in tissues of rats, including 7% in liver, 5% in muscle, 3% in skin, 2% in fat, and 1% in the adrenal gland (Knudsen *et al*., 2017). Studies of repeated oral exposures showed similar results and indicate that while only a small amount of TBPH is absorbed, TBPH showed a significant increase in concentrations in liver and adrenal tissues. These results suggest that TBPH has the potential to accumulate in adrenal and liver tissue, largely as the parent substance. This is apparent from the available monitoring data that suggest that TBPH accumulates in air-breathing animals.

32. Monitoring data have detected TBPH in liver (concentrations range <0.75–803 µg/kg lw in 2010–2011; n=69), eggs (<0.4–31.3 µg/kg ww in 2011–2013, DF=25% (3/12), n=12) and blood plasma (nd–98.3 µg/kg ww in 2011–2013, DF=40%, n=15) from several bird species including raptors preying on terrestrial species as well as birds that feed on aquatic organisms in the Arctic (Jin *et al.,* 2016, Lazarus *et al.,* 2016 and Fernie *et al.,* 2017). TBPH reported the highest detection rate (54% for all the bird tissues; n=69 from 10 bird species) in bird livers of the assessed NBFRs 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE) and decabromodiphenyl ethane (or DBDPE; Jin *et al.* 2016). Furthermore, TBPH has been detected in the blubber from marine mammals such as dolphins (Zhu *et al.,* 2014) and finless porpoises (<0.04–3859 µg/kg lw in 2003–2008, n=33, TBPH concentration was higher than the concentration of HBCDD, Lam *et al.,* 2009) and in the plasma (0.04 µg/L (mean) in 2010, DF=10%, n=10; Harju *et al.,* 2013) and liver (<0.138–0.876 µg/kg ww in 2007, DF=60%, n=10; Sagerup *et al.,* 2010) of the Arctic ringed seal and in the adipose tissue and plasma of polar bears (0.15 ng/mL (mean in plasma) and <0.128–0.402 µg/kg ww in fat; Harju *et al.,* 2013 and Vorkamp *et al.,* 2015).

33. TBPH was detected in placenta of rats exposed to TBPH during gestation (concentration up to 31.5 mg/kg body weight (bw)/day; Baldwin *et al.* 2017). In addition, TBPH was detected in human serum (concentrations range n.d.[20]–260 µg TBPH/kg lw in adults/mothers/children; DF=16–83%), breast milk (n.d.–6.6 µg TBPH/kg lw; DF=32.4–50%), hair[21] (13–2600 ng/g, DF=94%), fingernails[21] (4.21–1120 µg TBPH/kg, DF=86–100%) and toenails[21] (18–1990 ng/g, DF=80%) from samples collected in Canada, China, the UK and the USA between 2008 and 2016 (He *et al.* 2013; Zhou *et al.,* 2014; Liu *et al.*, 2016; Tao *et al.,* 2017; Guo *et al.*, 2018 and Chen *et al.,* 2019). There was a significant positive correlation between TBPH in fingernails and indoor dust ($p < 0.001$, r=0.37) which indicates that indoor dust plays an important part in the exposure of TBPH via pathways such as dust ingestion/inhalation and dust contact (Chen *et al.,* 2019).

34. Humans can be exposed to TBPH through their diet. For instance, consumption of food containing TBPH is a potential exposure pathway for the general population. Tao *et al.* (2017) examined the presence of TBPH in 14 groups of composite food samples covering meat, liver, oily fish, eggs and cheese from two supermarkets representing national chains and one local market in Birmingham, UK during May and June 2015. TBPH was detected in 63% of the samples at concentrations in the range of 0.20–0.57 ng/g lw in meat, 0.69–5.8 ng/g lw in liver, <0.1–1.1 ng/g lw in fish and 0.22–1.8 ng/g lw in eggs and dairy products. However, Tao *et al.* (2017) concluded that dust ingestion plays a more important role in driving body burdens of TBPH in UK adults.

35. Xiong *et al.* (2021) studied the bioaccumulation potential of nine NBFRs in Antarctic terrestrial plants. The authors collected plants from the Great Wall Station, Fildes Peninsula and Ardley Island, West Antarctica in January 2014. TBPH shows with a moss/soil accumulation factor (BAF)[22] of 5.01 (mean; 12.55 (maximum value)) the second highest accumulation factor among the nine NBFRs studied, indicating a high transfer potential of TBPH from soil to Antarctic mosses (*Sanionia uncinate*). This is of concern, as the enrichment in plants might lead to an enrichment in other organisms.

36. Monitoring data in mammals (including in humans), plants and aquatic species provide supporting evidence that TBPH can be taken up by organisms in the environment.

[20] n.d. means not detected.

[21] The concentrations in hair and nails reported in Liu *et al.* (2016) are likely overestimated considering that the mean recoveries for TBPH were 120% in hair and 141% in nail in the validation method (Liu *et al.,* 2015).

[22] The bioaccumulation factors (BAFs) have been calculated by dividing the concentration in moss (pg/g dw) by the concentration at the same site in soil (pg/g dw).

3.2.1 Conclusion on bioaccumulation according to the criteria in Annex D

37. The criteria for bioaccumulation listed in paragraph 1 (c) (i) and (iii) of Annex D are considered to be met for TBPH as BCF values exceed 5,000 L/kg and its log K_{ow} is greater than 5. Laboratory experiments show that there is little evidence for biotransformation of TBPH by fish, oligochaetes, rats and humans thus suggesting its potential for bioaccumulation. Toxicokinetic data indicate that while only a small amount of TBPH is absorbed, it has the potential to accumulate in adrenal and liver tissue of rats. Field studies seem to indicate a biomagnification potential of TBPH in a benthic marine food chain. In addition, field BSAF values above 0.5 for TBPH in seashell and fish are indicative of a high bioaccumulation potential. A benchmark approach comparing laboratory depuration rate constants and BMF values for TBPH and substances having POP properties such as dechlorane plus and methoxychlor provides further evidence that TBPH is bioaccumulative. The bioaccumulation potential of TBPH is supported by biomonitoring data indicating widespread uptake by a wide range of organisms (fish and aquatic invertebrates but also birds and mammals, including humans) also in Arctic species such as ringed seal and polar bear (an endangered species) and in Antarctic mosses. TBPH can be transferred at sensitive life stages through bird eggs, human breast milk and it can pass through the placenta into offsprings.

3.3 Potential for long-range environmental transport

3.3.1 Screening of physicochemical properties

38. The estimated Henry's Law constant for TBPH is 3.02×10^{-2} Pa.m^3/mol at 25°C (bond method, HENRYWIN v3.20; US EPA, 2012) and its estimated vapour pressure is 2.28×10^{-9} Pa at 25 °C (MPBPVP v1.43; US EPA, 2012) or 2.12×10^{-9} Pa at 25 °C (COSMOtherm 2020 as cited in Glüge and Scheringer, 2023), these values suggest a low potential for volatilisation of TBPH to the atmosphere. However, concentrations of TBPH found in remote regions suggest that atmospheric transport has occurred. Vapour-phase TBPH will be degraded in the atmosphere primarily by reaction with photochemically-produced hydroxyl radicals. The rate constant for the vapour-phase reaction of TBPH with hydroxyl radicals has been estimated as 21.82×10^{-12} cm^3.molecule^{-1}.s^{-1} at 25°C (AOPWIN v1.92; US EPA, 2012). The estimated half-life of TBPH in air (gas phase) is 5.883 hours or 0.490 day based on a 12-h photoperiod with 1.5×10^6 OH/cm^3 (AOPWIN v1.92; US EPA, 2012). Because the sorbed fraction is likely to be resistant to atmospheric oxidation, the AOPWIN half-life value based on reaction with hydroxyl radicals is most probably an underestimate of the half-life in air. Modelling predicts that the major portion of TBPH in air may be sorbed to particulates (fraction of TBPH sorbed to atmospheric particles ranges from 99.7 to 100%; AEROWIN v1.00; US EPA, 2012). Based on its low vapour pressure and its high log K_{oa} (15.1), TBPH is expected to be associated with particles in the atmosphere. The sorption of TBPH to particulates in air may increase its residence time and potential for long-range transport. The atmospheric transport of airborne particulates provides a potential route for long-range transport, and this is supported by the detection of TBPH in air samples (gas and particulate phases or particulate phase only) taken in remote locations such as the Arctic and the Antarctic (Halvorsen *et al.,* 2023; Lee *et al.,* 2016; Möller *et al.,* 2011a and 2012; Rauert *et al.*, 2018; Salamova *et al.,* 2014; Xiao *et al.,* 2012a; Zhao *et al.,* 2020).

39. Davis and Stapleton (2009 as cited in ECCC and HC, 2019) reported the reductive photodebromination of both TBB and TBPH under solar radiation in a series of organic solvents. The rates of degradation were slower for TBB and TBPH than for decaBDE and the nonaDBE congeners included in the study across all solvents. Dibrominated and tribrominated degradation products were observed for both TBB and TBPH, most missing both ester branches in the case of TBPH. Although photodegradation data for TBB and TBPH in the air compartment were not identified, the observation of both particulate and gaseous phase TBB and TBPH at Alert, Nunavut suggests that photodegradation in the air compartment may be relatively slow (Xiao *et al.*, 2012b).

3.3.2 Long-range transport model predictions

40. The Characteristic Travel Distance (CTD) of TBPH was modelled using the OECD Pov and LRTP Screening Tool to be 2,850 km by Environment and Climate Change Canada, Health Canada (2019; the input parameters to the model are not reported). Xiao *et al.* (2012a) reported a CTD of 2,900 km for TBPH with a transfer efficiency of 13% (input parameters to the model: half-life in air of 5.9 hours, half-life in water of 1,400 hours (or 58 days) and half-life in soil of 2,900 hours (or 121 days); degradation half-lives were estimated using SPARC and EPI Suite, respectively). The long-range transport potential (LRTP) boundaries are 5097 km (CTD of PCB 28) and 2.248 % (TE of PCB-28). Thus, these modelling results obtained for TBPH suggest that it has a low LRTP with a transfer potential to surface media. The results from the modelling are associated with uncertainty due

to the uncertainties of the input parameters (half-lives in water and soil which are unknown). Furthermore, the OECD Tool does not contain a sediment compartment while TBPH is persistent in sediment.

41. The log K_{ow} (10.2), log K_{oa} (15.114) and log K_{aw} (-4.914) values for TBPH suggest high potential to reach the Arctic and to accumulate in the Arctic human food chain according to the criteria cited by Brown and Wania (2008). Indeed, the area of elevated Arctic Contamination and Bioaccumulation Potential (AC-BAP) selected by Brown and Wania (2008) comprises the following criteria: log $K_{ow} \geq 3.5$; log $K_{oa} \geq 6$; $0.5 \geq$ log $K_{aw} \geq -7$; log $K_{aw} \leq -1.78 \times$ log $K_{oa}+14.56$.

3.3.3 Measurements in remote areas

42. The potential for long-range transport of TBPH is shown by monitoring studies and measurements in environmental and biota samples from remote regions (see Tables A1 to A6 in the Appendix for further information). It is worth noting that the concentration values reported for TBPH in biota and environmental samples may be underestimated and as reported by Papachlimitzou *et al.* (2012). The analytical challenges of TBPH are further discussed in the information document (UNEP/POPS/POPRC.22/INF/6).

43. TBPH was detected in various media in the Arctic, including in the Arctic air at Zeppelin, Ny-Ålesund and Longyearbyen (Svalbard) and at Alert (Canada) between 2005 and 2022 (concentrations in the range of <0.025–14 pg/m^3 (gas and/or particle phases); Halvorsen *et al.,* 2023; Lee *et al.*, 2016; Salamova *et al.,* 2014; Xiao *et al.,* 2012a; Hung *et al.,* 2013a as cited in AMAP, 2016), in the air of the Arctic Ocean and the East Greenland Sea, between 2009 and 2010 (concentrations in the gas and/or particulate phases in the range of <0.16–0.36 pg/m^3; Möller *et al.,* 2011a and 2011b), in seawater from the Bering Sea and the East Greenland Sea between 2009 and 2010 (concentrations in the range of n.d. – 0.22 pg/L (dissolved fraction); Möller *et al.,* 2011a and 2011b) and in terrestrial, avian and marine biota samples from Central East Greenland, Svalbard and the Canadian Arctic, including in a top predator the polar bear (*Ursus maritimus*), a vulnerable species between 2008 and 2013 (concentrations in the range of <0.106–3.754 ng/g ww and <0.14–44.29 ng/g lw; Harju *et al.*, 2013; Houde *et al.,* 2017; Sagerup *et al.,* 2010 and Vorkamp *et al.*, 2015)).

44. AMAP (2017) mentioned that the high-volume air sampling at Alert in the Canadian High Arctic showed increasing concentrations of TBPH between 2008 and 2012. Increasing trends have also been observed in air in the Great Lakes region (Ma *et al.,* 2012b as cited in AMAP (2017)).

45. TBPH was detected in the air of the Tibetan plateau at 4,730 m above the sea level between 2006 and 2007 (concentrations in the range of 0.049–1.7 pg/m^3 (gas and particle phases); Xiao *et al.,* 2012a). According to Xiao *et al.* (2012a) the concentrations of the flame retardants, including TBPH, at Nam Co in the Tibetan plateau showed no significant seasonality, even though air masses originated from distinctly different regions during different seasons. According to the authors, this suggests that flame retardants do not have regional sources, but their concentrations in Tibet are rather reflective of truly global background contamination (Xiao *et al.,* 2012a). This supports the long-range atmospheric transport potential of TBPH.

46. TBPH was also detected in the Antarctic, including in air from King George Island, South Shetland Islands, West Antarctica between 2011 and 2018 (concentrations in the range of n.d.–0.098 pg/m^3 (gas and particle phases); Zhao *et al.*, 2020), in air from the Oceanic Southern hemisphere covering the Indian Ocean to the Southern Ocean between 2010 and 2011 (concentrations in the particle phase in the range of <0.025–1.5 pg/m^3; Möller *et al.,* 2012), in soil from the Great Wall Station, Fildes Peninsula and Ardley Island in West Antarctica in 2014 (concentrations in the range of n.d.–20.22 pg/g dw; Xiong *et al.*, 2021) and in plants from the Great Wall Station, Fildes Peninsula and Ardley Island in West Antarctica in 2014 (concentrations in the range of n.d.–484.1 pg/g dw in moss (*Sanionia uncinata*); Xiong *et al.*, 2021).

47. Monitoring data indicate that TBPH can be long-range transported in the middle of the oceans, including in the deepest parts of the oceans (hadal zone) via air and/or river/oceanic currents. TBPH was detected in the middle of the South Atlantic Ocean in 2016 (Sobotka *et al.,* 2021). Furthermore, TBPH was detected in 19% of samples of hadal amphipods (*Alicella gigantea;* n=10; carapace, muscle and visceral) and in 100% of hadal surface sediment (0–2 cm) samples (n=8) taken from deep sea oceanic trenches (Mariana, Museau and New Britain trenches at a water depth up to 10,853.2 m) in the Western Pacific Ocean between December 2016 and January 2019 (Xie *et al.,* 2023). The authors mentioned that NBFRs, including TBPH, might reach trench surface seawater through long-range atmospheric transport and oceans currents. NBFRs in the hadal sediments were generally transported via the settling of sediment particles of either marine or terrigenous origin whereas in amphipods they accumulated via feeding on animal carrion through the food web (Xie *et al.,* 2023). The authors further

mentioned the possible source of NBFRs from the hadal sediments from the adsorption of the substances on plastic surfaces. Moreover, sediments have also been suggested to undergo long-range transport with turbidity currents (Kneller *et al.,* 2016). As a consequence, it is possible that sediments containing TBPH (where it is persistent) can be transported over long distances along the sea floor via turbidity currents.

48. The measurements of TBPH in seabird and marine migratory species such as glaucus gull (*Larus hyperboreus*) plasma (0.026±0.001 ng/mL in 2012, DF=17%, n=12; Harju *et al.,* 2013), kittiwake (*Rissa Tridactyla*) liver (concentrations in the range of <0.171–1.398 ng/g ww and 14.62 ng/g lw (mean) in 2009, DF=50%, n=10; Sagerup *et al.,* 2010), Common Eider (*Somateria mollissima*) liver (concentrations in the range of <0.142–3.754 ng/g ww and 44.29 ng/g lw (mean) in 2009, DF=60%, n=10; Sagerup *et al.,* 2010), Brünnich's guillemot (*Uria lomvia*) eggs (concentrations in the range of <0.106–3.414 ng/g ww and 19.17 ng/g lw (mean) in 2008, DF=70%, n=10; Sagerup *et al.,* 2010), Capelin (*Mallotus villosus*) whole fish (concentrations in the range of <0.120–1.306 ng/g ww and 33.65 ng/g lw (mean) in 2009, DF=90%, n=10; Sagerup *et al.,* 2010) and Ringed seal (*Pusa*/*Phoca hispida*) plasma (0.04 ng/mL in 2012, DF=10%, n=10; Harju *et al.,* 2013), liver (concentrations in the range of <0.138–0.876 ng/g ww and 16.36 ng/g lw (mean) in 2007, DF=60%, n=10; Sagerup *et al.,* 2010) and blubber (<MDL–0.34 ng/g lw (geometric mean) between 2009–2013; Houde *et al.,* 2017) in locations distant from known point sources such as Kongsfjord, Tempelfjord and Bjørnøya in Svalbard, the Norwegian Svalbard Archipelago and the Canadian Arctic indicate the potential for transfer of this substance to the remote environment via migratory species.

49. Furthermore, TBPH was detected in black guillemot (C*epphus grylle*) eggs (0.05–0.066 ng/g ww or 0.024–0.025 ng/g lw; n=3) from Central East Greenland in 2012 (Vorkamp *et al.,* 2015). Migration of black guillemots (*Cepphus grylle*) is limited as they overwinter in Greenland and only make shorter movements from the breeding sites to ice free areas. Analysis of the pollutant burdens in black guillemots will thus reflect the exposure to pollutants in the Greenland environment (Vorkamp *et al.,* 2004). In addition, TBPH was detected in polar bear (*Ursus maritimus*) adipose tissue (<0.128 – 0.402 ng/g ww or <0.14 – 0.44 ng/g lw in 2012, n=5; Vorkamp *et al.,* 2015) and plasma (0.15±0.16 ng/mL in 2012, DF=95%, n=20; Harju *et al.,* 2013) which is endemic to the Arctic. The observation of TBPH in eggs of black guillemots and in adipose tissue and plasma of polar bear suggests long-range transport from sources outside of the Arctic.

50. A benchmark approach comparing concentrations in air, seawater and biota (such as Black guillemot eggs and polar bear adipose tissue) from remote locations for TBPH and substances having POP properties such as BDE-209, pentaBDE, octaBDE and dechlorane plus indicates that TBPH is found in the same range of concentrations as those of POP substances before their inclusion to the Stockholm Convention on POPs (see the benchmark exercise in Tables A1, A2 and A6 in the Appendix for further information; Möller *et al.,* 2011a; 2011b and 2012; Xiao *et al.*, 2012a; Salamova *et al.,* 2014; Vorkamp *et al.*, 2015; AMAP, 2017 and Sobotka *et al.,* 2021). This supports the long-range transport potential of TBPH. In addition, in the study of Salamova *et al.* (2014), TBB and TBPH were the dominant non-PBDE BFRs measured in the Arctic air samples and comprised ∼46% and 17% of ΣBFR concentrations, respectively, among the 45 BFRs analysed.

3.3.4 Conclusion on long-range environmental transport according to the criteria in Annex D

51. While modelling predictions indicate a low potential for long-range transport with a transfer potential to surface media, monitoring data indicate that transport of TBPH to remote areas (Arctic and Antarctic) has taken place. The physico-chemical properties of TBPH suggest it has potential to reach the Arctic and to accumulate in the Arctic human food chain. This is supported by monitoring data which indicate that TBPH has been measured in environmental and biota samples from remote regions (Arctic and Antarctic). Presence of TBPH in the Arctic, the Tibetan Plateau and the Antarctic air indicates atmospheric transport. Atmospheric transport of TBPH predominantly bound to atmospheric particles and deposition to surface media is supported by findings of TBPH in mosses and soil from Antarctica. Furthermore, the measured levels of TBPH in seawater from the Bering Sea, the East Greenland Sea and the South Atlantic Ocean suggest long-range transport through air and/or water. Detection of TBPH in deep marine sediments (up to a water depth of 10,853.2 m) from the Western Pacific Ocean away from point sources indicate the potential of TBPH for long-range transport via the adsorption onto suspended matter and subsequent transport to sediment via water in rivers and ocean currents. Additionally, the presence of TBPH in migratory species in locations distant from known point sources and in endemic species from the Arctic indicate the potential for transfer of TBPH to the remote environment via migratory species. It is therefore concluded that TBPH meets the criteria for potential long-range environmental transport listed in paragraph 1 (d) (i), (ii) and (iii) of Annex D.

3.4 Adverse effects

3.4.1 Adverse effects to human health and other organisms

52. The main adverse effects of TBPH to human health are related to its neurobehavioral effects observed in mice and its effects on the thyroid system. Other effects observed and presented in this section may contribute to the adversity of TBPH.

53. Neurobehavioral effects: Bao and Jing (2021) investigated the neurobehavioral effects of TBPH in five-week-old mice. Three groups of mice (control, 20 mg/kg bw/day and 200 mg/kg bw/day; n=8 per group) were exposed via oral gavage for 28 days to TBPH. Spatial learning and memory were assessed using the Morris water maze test. Oxidative stress in the hippocampus was assessed by measuring malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione (GSH). The study also measured endoplasmic reticulum (ER) stress related proteins (glucose-regulated protein 78-kDa (GRP78), PKR-like ER kinase (PERK), and C/EBP homologous protein (CHOP)) as well as hippocampal biomarkers involved in memory including post-synaptic density protein-95 (PSD-95), brain-derived neurotrophic factor (BDNF), and phosphorylated cAMP response element binding protein (p-CREB). The study showed no effects on spatial learning and memory.

54. However, TBPH exposure at both 20 and 200 mg/kg/day, significantly altered the oxidative stress markers ($p < 0.05$), increasing MDA and reducing SOD and GHS levels, indicating enhanced lipid peroxidation and oxidative damage in the hippocampus. At 200 mg/kg/day, ER stress markers (GRP78, PERK, and CHOP) were significantly upregulated ($p < 0.01$), suggesting involvement of ER stress involvement in TBPH-induced neurotoxicity. At the same dose, TBPH also significantly reduced BDNF and PSD-95 levels ($p < 0.05$ and $p < 0.01$, respectively) whereas p-CREB was not statistically affected. Because these biomarkers are essential for memory formation, the findings indicate that TBPH may impair cognitive-related molecular pathways despite the absence of behavioural effects.

55. Xiong *et al.* (2024) further explored TBPH-induced neurotoxicity in mice by administrating TBPH (20 mg/kg bw/day; DMSO control; n=10 per group) via intraperitoneal injections for 60 days. Neurobehavioral performance was assessed using the Morris water maze and Step-down passive avoidance test. In addition, multiple mechanistic endpoints were evaluated, including hippocampal oxidative stress markers (reactive oxygen species (ROS) and GSH); apoptosis-related indicators (cytochrome C (Cyt C), apoptotic protease activating factor-1 (Apaf-1), caspase-3 (Casp-3), caspase-activated DNase (CAD), N-methyl-D-aspartate receptor 2B (NMDAR2B), and phosphorylated CREB (p-CREB), immunohistochemistry changes, and hippocampal protein levels phosphorylated ERK (p-ERK), FOS and JUN.

56. TBPH-exposed mice showed significantly impaired performance in both behavioural tests, with increased escape latency and error rates, indicating deficits in learning, memory and cognitive function. The Morris water maze is a widely used test for assessing learning and memory in experimental neurotoxicity studies such as the OECD TG 426 (Developmental Neurotoxicity Study). Despite limitations compared to a full (developmental) neurotoxicity study, the observed neurobehavioral effects provide biologically relevant information and may be used as evidence within a weight-of-evidence approach for establishing adversity.

57. Histopathological and immunohistochemical analyses revealed marked structural damage in the hippocampus and dorsolateral prefrontal cortex. TBPH exposure significantly increased levels of ROS, GHS, Cyt C, Apaf-1, Casp-3, CAD, p-ERK, FOS, and JUN ($p < 0.05$), while significantly decreasing NMDAR2B, and p-CREB ($p < 0.05$). These alterations indicate pronounced oxidative stress and activation of apoptotic pathways, particularly within the dentate gyrus of the hippocampus. Collectively, the results suggest that TBPH induces neurotoxicity through oxidative injury and ERK1/2–FOS pathway activation, ultimately disrupting neuronal integrity and cognitive function.

58. Available studies demonstrate that TBPH induces adverse neurobehavioral effects in mice at doses as low as 20 mg/kg bw/day after intraperitoneal exposure. These effects appear to be mediated by increased oxidative stress, activation of apoptotic pathways, and overactivation of the ERK1/2–FOS signalling cascade. The lack of neurobehavioral changes reported in Bao and Jing (2021) may be related to the shorter exposure duration (28 vs. 60 days) and differences in administration route (oral gavage vs. intraperitoneal injection). Intraperitoneal injection ensures nearly complete systemic uptake, whereas TBPH exhibits low oral bioavailability (Knudsen *et al.*, 2017). Furthermore, intraperitoneal dosing bypasses first-pass hepatic metabolism, potentially resulting in higher circulating and brain concentrations.

59. Despite these methodological differences, both studies consistently demonstrated increased oxidative stress in the hippocampus. This convergence across experimental designs strengthens the conclusion that TBPH possesses neurotoxic potential.

60. A 90-day repeated-dose oral toxicity study in rats conducted according to OECD TG 408, as reported in the REACH dossier,[23] did not identified treatment-related histopathological changes in the brain or effects on brain weight at dose levels up to 1000 mg/kg bw/day. These findings do not necessarily contradict the results of mice studies by Bao and Jing (2021) and Xiong *et al.* (2024), as the OECD TG 408 study is not designed to detect neurofunctional or mechanistic effects. Moreover, the OECD TG 408 study does not include assessments of spatial learning and memory, which were specifically investigated in the mice studies, and therefore the outcomes are not directly comparable. It should also be noted that the OECD TG 408 study does not include a specific evaluation of peripheral nerves (*e.g.* sciatic nerve) and therefore potential effects on peripheral nervous system structures were not assessed.

61. Pulmonary effects in animals: Xing *et al.* (2024) reported an association between TBPH exposure and markers of lung injury in both *in vitro* and *in vivo* models.

62. *In vitro*, mouse TC-1 and MRC-5 cells were exposed to TBPH (0–20 mg/L) for 48 hours. TBPH exposure led to elevated levels of pro-inflammatory cytokines (tumor necrosis factor (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), interleukin-17 (IL-17), interferon gamma (IFN-γ)), chemokines (eotaxin, monocyte phemoattractant protein-1 (MCP-1), monocyte chemotactic protein 2 (MIP-2), and regulated on activation, normal T-cell expressed and secreted (RANTES). Additionally, cell proliferation marker Ki67 was reduced, while p16 and p21 expression increased, indicating cell cycle arrest. TBPH also upregulated extracellular matrix (ECM) markers such as fibronectin (FN), α-smooth muscle actin (α-SMA), and transforming growth factor-beta (TGF-β), while downregulating E-cadherin and increasing collagen deposition. Oxidative stress was evident through increased ROS and MDA levels, alongside decreased antioxidant markers (GSH, SOD, CAT).

63. *In vivo*, 8-week-old C57 mice were exposed to TBPH via oral gavage (0 (vegetable oil control), 10, 30 and 60 mg/kg bw/day; n=5 per group) for 28 days. Histopathological examination revealed alveolar capillary congestion and inflammatory cell infiltration at all tested doses. Pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, interleukin-8 (IL-8), IFN-γ) were significantly elevated ($p < 0.05$) in lung tissues at 10–60 mg/kg bw/day. Oxidative stress markers (ROS, MDA) increased ($p < 0.05$), while antioxidant enzymes (GSH, SOD, CAT) decreased ($p < 0.05$), particularly at 30–60 mg/kg bw/day. TGF-β expression and collagen fiber content were also significantly elevated at 30 and 60 mg/kg bw/day ($p < 0.05$), indicating early signs of lung fibrosis.

64. There are no studies available via the inhalation route. A 90-day oral toxicity study in rats (OECD TG 408), available in the REACH dossier[23], reported no histopathological lung changes at doses up to 1000 mg/kg bw/day. The discrepancy with the study by Xing *et al.* (2024) may be due to differences in species sensitivity, and study design. The molecular changes observed by Xing *et al.* (2024) may represent early or adaptive responses that, if sustained, could progress to fibrosis. These findings suggest that TBPH may initiate pro-inflammatory signalling pathways even at relatively low doses.

65. Pulmonary effects epidemiology: Two prospective epidemiological studies conducted in the Greater Cincinnati, Ohio metropolitan area by Mendy *et al.* (2023, 2024) investigated associations between early-life exposure to brominated flame retardants (BFRs), including TBPH, and respiratory outcomes in children.

66. In the 2023 study, a birth cohort of 234 children was followed. Pregnant women were enrolled based on specific inclusion criteria (e.g., ≥18 years old, fluent in English, residing locally with no plans to relocate, <16 weeks pregnant, and without certain medical conditions). Settled dust samples were collected from the child's bedroom and main activity room at age 1 using a high-volume small surface sampler. Dust was sieved (300 µm), purified, and analyzed via HPLC-MS to quantify organophosphate flame retardants (OPFRs: TCEP, TCIPP, TDCIPP, TPHP) and replacement BFRs (RBFRs: TBB and TBPH). Geometric mean (GM) concentrations of total OPFRs were 10.27 µg/g dust and 2.82 µg/m² for dust loadings. TCIPP was the most abundant OPFR. For RBFRs, GM concentrations were 0.48 µg/g dust and 0.13 µg/m² for loadings, with TBPH levels (0.27 µg/g dust and 0.08 µg/m² for loadings) higher than TBB. Respiratory health was assessed biannually via caregiver questionnaires until age 5. At age 5, children underwent spirometry to measure forced expiratory volume in 1 second (FEV_1) and peak expiratory flow (PEF). Exposure to OPFRs and RBFRs during

[23] Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.

infancy was associated with increased risk of respiratory symptoms, and TBPH dust loadings were linked to reduced PEF ($p < 0.05$). The association between TBPH dust loadings and reduced PEF at age 5 was adjusted for key potential confounders, including child sex, race/ethnicity, birth weight, gestational age, body size (height), household income, breastfeeding duration, prenatal tobacco smoke exposure (serum cotinine), and total household dust weight; sensitivity analyses additionally accounting for housing cleanliness indicators did not affect the results.

67. The 2024 study followed a cohort of 342 pregnant women (2003–2006). Indoor dust samples were collected at 20 weeks gestation, and maternal urinary concentrations of organophosphate esters (OPEs) and RBFRs were measured at 16 and 26 weeks and at delivery. Associations between prenatal exposures and respiratory outcomes (reported biannually until age 5) and lung function at age 5 were assessed. TBPH dust concentrations were associated with increased risk of childhood wheezing (breathing difficulties in children; relative risk (RR): 1.57, 95% CI: 1.28–1.94, $p < 0.0001$)). In both studies (Mendy *et al.,* 2023 and Mendy *et al.,* 2024), although causality cannot be established due to the observational study design, the observed associations with adverse respiratory outcomes are considered relevant and supportive for establishing adversity.

68. Endocrine effects: Yuan *et al.* (2024) evaluated the endocrine-disrupting potential of TBPH in male Sprague-Dawley rats. In a 28-day repeated-dose study, 48 rats (6 weeks old) were administered TBPH via oral gavage at doses of 0 (corn oil control), 5, 50, and 500 mg/kg bw/day. Blood and thyroid glands were collected for clinical chemistry and histopathological analysis. At 500 mg/kg bw/day, thyroid glands were significantly smaller ($p < 0.05$) which was supported by the calculation of the relative organ weight ($p < 0.05$), with histological changes including flattened follicular epithelium and dilated follicular cavities. Serum levels of total thyroxine (TT4) and free thyroxine (FT4) were significantly elevated in the 50 and 500 mg/kg groups ($p < 0.05$), while thyroid-stimulating hormone (TSH) was significantly decreased, indicating disruption of the hypothalamic–pituitary–thyroid (HPT) axis. ECHA/EFSA Guidance (2018) supports the interpretation that changes in thyroid organ weight and histopathology, when associated with endocrine activity, are considered thyroid-mediated adversity. In contrast, a guideline-compliant 90-day oral toxicity study in rats (OECD TG 408), available in the REACH dossier[23], reported no changes in thyroid histopathology at doses up to 1000 mg/kg bw/day (thyroid weight was not measured). However, endocrine endpoints beyond thyroid histopathology were not assessed.

69. Genetic toxicity, reproductive toxicity and carcinogenicity: TBPH is likely not toxic to reproduction based on the available information. Due to a lack of data, no conclusion can be drawn regarding its genotoxicity and its carcinogenicity. Further information is reported in the information document (UNEP/POPS/POPRC.22/INF/6) regarding these endpoints.

3.4.2 Adverse effects to the environment

70. No long-term fish toxicity study is available in the REACH registration dossier. A short-term fish toxicity study (OECD TG 203), a long term daphnia Reproduction Test (OECD TG 211) and an algae study (OECD TG 201) are available in the REACH registration dossier[5]. All these studies indicate no toxic effects observed at tested concentrations. The OECD TG 203, 211 and 201 studies are further detailed and discussed in the information document (UNEP/POPS/POPRC.22/INF/6).

71. The REACH registration dossier[5] includes a study on the solubility of TBPH investigated using the Council Regulation A.6 methodology using the flask method, mostly equivalent to OECD TG 105. The substance could not be detected in water indicating solubility of <0.05 µg/L at 20 °C, while the limit of solubility was reported as 794 µg/L when using 1% acetonitrile as a solubiliser. However, the reliability of the above study is questionable considering that OECD TG 105 recommends using the column elution method (and not the flask method) to establish water solubility for test chemicals with solubility <10 mg/L. Furthermore, the concentrations of TBPH in the different flasks were not reported. As a consequence, it was not possible to check if the concentrations between the flasks were ≤ 15%. In addition, the pH value during the test was not reported.

72. The studies reported below by Fu *et al.* (2024 a,b), Hong *et al.* (2025), Zhou *et al.* (2024) and Guo *et al.* (2020) are conducted with concentrations above the solubility limit in pure water, but the studies use DMSO as a solvent. Zhou *et al.* (2024) indicated that the concentration tested (10 µg/L nominal) in their zebrafish study was below the solubility limit in the DMSO-water mixture using 0.01% (v/v) DMSO (Zhou personal communication, October 2025) based on previous experiments with TBPH (Guo *et al.,* 2020; Zhou *et al.,* 2021; Guo *et al.,* 2021; Zhou *et al.,*2022). In another zebrafish study (Guo *et al.,* 2020), the authors mentioned that the maximum concentration of TBPH in DMSO 0.1% (v/v) was approximately 2 µM (or ca. 1412 µg/L TBPH; Guo personal communication, October 2025). According to the authors, TBPH was fully dissolved in 0.1% (v/v) DMSO at TBPH

concentration up to 141 µg/L (Guo personal communication, October 2025). The study authors of Fu *et al.* (2024a,b) used vortex oscillation and ultrasonication to ensure complete molecular-level dissolution of TBPH in DMSO (0.005%) while preparing the stock solution. During the daily renewal of the exposure solution, the stock solution was slowly added to vigorously aerated and stirred dilution water ensuring rapid diffusion and dilution of DMSO in water to promote dispersion of TBPH in molecular form, thereby minimising the formation of colloids or microcrystals (Fu personal communication, October 2025). Visual inspection was conducted, and the solution remained clear and transparent, with no observed turbidity, precipitation, opalescence, or visible crystals/particles. Furthermore, the measured TBPH concentration in the exposure solution was consistent with the nominal concentration (Fu personal communication, October 2025).

73. In the Hong *et al.* (2025) study, the reliability of the exposure regime during their test was ensured through several measures: the swimming activity of the fish, the daily renewal of the exposure media, and the monitoring of the actual exposure concentrations (Hong personal communication, October 2025). Similarly, Zhou *et al.* (2024) ensured daily renewal of the exposure media to maintain consistent concentrations and minimise potential aggregation or settling. Based on previous work on TBPH (Zhou *et al.,* 2022; Zhou *et al.,* 2021; Guo *et al.,* 2021; Guo *et al.,* 2020), the authors confirmed that the concentration tested (10 µg/L nominal) was below the solubility limit in the DMSO-water mixture (Zhou personal communication, October 2025). To ensure that TBPH was fully dissolved in the exposure medium, the stock solution in DMSO (0.01% v/v) was sonicated and vigorously vortexed before dilution (Zhou personal communication, October 2025). During exposure, no visible precipitates, crystals, or aggregates were observed in the exposure solutions and the consistency in the measured TBPH concentrations suggest that TBPH was largely dissolved (Zhou personal communication, October 2025). The later studies did not report the presence of non-dissolved test substance in the test medium, turbidity, the formation of oil slicks or other indicators that the substance was not solubilised. The study author of Guo *et al.* (2020) indicated that a white mist appeared in the test at the highest concentration group (1412 µg/L TBPH) indicating TBPH undissolved material (Guo personal communication, October 2025). According to the author, white mist was only observed in the highest concentration group, where the TBPH was near saturation. To maintain consistent exposure, the solution was renewed daily to minimize this effect. In the lower concentration groups, no such precipitation was observed, and the exposure solution remained clear throughout the experiment. Thus, according to the author (Guo personal communication, October 2025), in the lower concentration groups (up to 0.2 µM or 141 µg/L), the embryos/larvae were only exposed to dissolved TBPH. Due to this and based on the above information on analytical monitoring, the studies are considered to be reliable. The assessment of the adverse effects focuses on the effects observed at concentrations where the test organisms were only exposed to dissolved TBPH.

74. According to OECD GD 23 on aqueous-phase aquatic toxicity testing of difficult test chemicals (OECD, 2019), solvents provide a vehicle in which some poorly soluble test chemicals can be dissolved to produce a stock solution which is more amenable to adding to, and mixing with, the test medium. While the toxicity studies on algae (OECD TG 201) and invertebrates (OECD TG 211) mentioned above are not suitable to demonstrate the saturation concentration of the substance in the test medium, the OECD GD 23 explains that it is unlikely that a solvent concentration of 100 mg/L would significantly alter the maximum dissolved concentration of the test chemical which can be achieved in the test solution. DMSO is one of the solvents that have been found to be effective for aquatic toxicity testing. Hutchinson *et al.* (2006) reviewed aquatic studies conducted with solvents and reported that studies with concentrations ranging 0.001–2% DMSO induced no effects, including gonad histology, spawning, liver vitellogenin levels and other histology and biomarkers, with the exception of induction of heat shock proteins with *Danio rerio* at 0.02% and reduction in egg production in *Pimephales promelas* with 0.001% DMSO. OECD GD 23 recommends using a maximum concentration of solvent of 20 µL/L based on recommendations from Hutchinson *et al.* (2006) which are based on effects with dimethylformamide.

75. The studies reported in this section are non-standard but the data available with the solvent controls are considered reliable. The authors of Zhou *et al.* (2024) study indicated that based on published literature and established protocols in zebrafish toxicology studies, DMSO at concentrations ≤0.1% is widely regarded as non-toxic to zebrafish embryos and larvae and is commonly used as a solvent for hydrophobic compounds like TBPH (Zhou personal communication, October 2025). In their previous work on TBPH (Guo *et al.,* 2020), the development, survival, neurotoxicity, liver transcriptomics and behavior of zebrafish embryos or larvae exposed to 0.1% DMSO were compared with those in solvent-free controls and no significant differences were found thus indicating that DMSO induced no effects. According to a personal communication (October 2025), Guo mentioned that studies under OECD TG 236 also reported no significant morphological or developmental abnormalities at concentrations up to 1% DMSO, supporting the suitability of 0.1% DMSO.

Considering the poorly solubility of TBPH and the absence of effects of DMSO on test organisms, the use of this solvent in below studies is considered acceptable.

76. The critical environmental effects of TBPH are on fish reproduction and on the fish thyroid system. In the paragraphs below a broad range of adverse effects on reproduction (sperm count and malformations, adult reproductive behaviour and effects on early larval development) are presented. These effects are supported by mechanistic evidence suggestive of adverse effects on the thyroid system (eye development, effects related to light/vision, liver steatosis and swimming speed).

77. Reproductive and endocrine effects: A study by Fu *et al.* (2024a) found that TBPH affected regulation of genes and reproductive behavior of zebrafish (*Danio rerio*). Four months old male zebrafish were exposed to 0, 1.4, 14, 140 and 1400 µg/L of TBPH (20 fish/dose group; 3 replicates/group) containing 0.005% DMSO (v/v; no solvent free control was used) for 28 days in a semi-static system based on nominal/measured concentrations. In the study, 24 exposed male adult fish were chosen and then paired to unexposed females, their behavior observed, and the resulting embryo and larvae assessed for developmental parameters. The authors mentioned that chemical assays showed that the concentration of TBPH was detected up to 0.13 µg/L in influent wastewater samples close to Barcelona, Spain (Cristale *et al.*, 2015). Therefore, the authors concluded that 1.4 µg/L is an environmentally relevant concentration. Exposure to the substance induced significant, concentration-related effects on hatching success, survival, body length, and heart rate in zebrafish larvae. The direction, consistency, and concentration dependence of these responses—particularly the reductions in survival (at ≥14 µg/L; $p < 0.05$), growth (at ≥1.4 µg/L; $p < 0.05$), and cardiac activity (at ≥1.4 µg/L; $p < 0.01$)—indicate impaired developmental and physiological performance rather than adaptive modulation. Taken together, these findings demonstrate biologically[24] relevant adverse effects during early larval development. Reduced larvae hatching, survival rate, growth and heart rate of larvae can have a direct impact on populations.

78. Regarding adult fish, there were observations of endocrine activity. Specifically, the transcription of androgen receptor (*AR*) showed the most significant reduction ($p < 0.001$) in expression in the brain at all exposure concentrations (at 1.4, 14, 140 and 1400 µg/L) in male zebrafish, followed by upregulation of aromatase (cytochrome P450, *cyp19b*) in all the exposure concentrations ($p < 0.05$). The AR is a member of the nuclear receptor family and is expressed in various organs, including the gonads and brain, where it has been shown to have a role in embryogenesis, spermatogenesis and reproductive behavior (Chang *et al.*, 2013). In addition, blood samples from adult males showed 11-ketotestosterone was statistically significantly decreased at the two highest concentrations ($p < 0.05$). Furthermore, mating behavior of the exposed male fish resulted in increased average distance and proximity to females compared to the solvent control in all but the lowest concentration (LOEC[25] at 14 µg/L) and the frequency of proximity per fish pair were reduced in all TBPH exposure concentrations ($p < 0.01$). The exposed adults had statistically significant reduced percentages of spermatogonia in the two highest dose groups (140 and 1400 µg/L; $p < 0.01$) and reduced spermatocytes (SPC) at 140 µg/L treated groups ($p < 0.05$), as shown by histopathology of the gonads. In addition, the occurrence of spermatozoa malformations (shortening of body length, pericardial cyst, yolk cyst and tail askew) showed a concentration-dependent increase following TBPH exposure. TBPH also led to a decrease of sperm motility (at ≥140 µg/L; $p < 0.01$). The findings indicate that TBPH can act as an endocrine disruptor and impair the reproduction of zebrafish with adverse effects at a LOAEC[26] of 1.4 µg/L.

79. Endocrine effects: Hong *et al.* (2025) assessed the thyroid toxicity of TBPH in a 28-days exposure toxicity study using juvenile rare minnows (*Gobiocypris rarus*; two-month-old). After 14 days of acclimation, fish were exposed to nominal/measured concentrations at 0, 0.1, 100, and 1000 µg/L TBPH (containing 0.01% DMSO (v/v); Hong personal communication, October 2025) for 28 days. The exposure solutions were renewed daily and aquariums were cleaned daily to remove food residue and feces. No fish mortality was observed in any experimental group, including the controls (Hong personal communication, October 2025). The oxygen saturation was around 80% based on information communicated by the authors. Regarding adverse effects, TBPH induced a concentration-dependent decrease in body weight of juvenile rare minnows with significant reductions at 100 µg/L and 1000 µg/L of TBPH ($p < 0.05$) compared to the control groups. The authors mentioned that the prevalent symptom observed in individuals with hyperthyroidism is weight loss.

[24] It is worth noting that the biological significance of an effect is according to EFSA (2017) a critical effect size of 5% (change in mean response) for continuous data from animal studies.

[25] LOEC means Lowest Observed Effect Concentration.

[26] LOAEC means Lowest Adverse Observed Effect Concentration.

80. At the end of the exposure period, brain, liver, thyroid glands, and gut tissues were sampled for further histopathological examination and transcriptomic analysis, and thyroid hormones levels were determined in the fish brain. The transcriptional levels of thyroid-related genes in brain of fish after 28 days of exposure to TBPH indicate that the three deiodinases (*dio1, dio2 and dio3*) exhibited similar expression patterns across all TBPH treatment groups. Deiodinase gene *dio2* showed a significant increase ($p < 0.05$) at 1000 µg/L TBPH, while *dio1* and *dio3* showed a significant down-regulation ($p < 0.05$) at 1000 µg/L and 100 µg/L TBPH, respectively. A significant increase ($p < 0.05$) expression of malic dehydrogenase (*me),* sodium-iodide symporter *(nis),* and thyroperoxidase (*tpo)* in the brain (at 0.1 µg/L TBPH) was observed, indicating a tissue-specific heterogenicity. Regarding liver tissues, thyroid-related genes such as *dio3* and thyroid receptor (*tr)* showed a significant downregulation ($p < 0.05$) at 100 µg/L TBPH and transthyretin (*ttr*) showed a significant upregulation ($p < 0.05$) at 1000 µg/L TBPH. Hong *et al.* (2025) mentioned that chemically induced changes in thyroid-related gene expression are key indicators of dysfunction. Thyroid hormone levels in the fish brain tissues indicated that exposure to 1000 µg/L TBPH caused a significant alteration in T4 levels ($p < 0.05$), but T3 levels were not different from the control in all TBPH exposure groups ($p > 0.05$). The increase in T4 concentration, together with transcriptional modulation of deiodinases and thyroid hormone pathway genes, demonstrates direct perturbation of thyroid hormone homeostasis. Histopathological results indicate a significant focal hyperplasia in the thyroid tissue at 0.1 µg/L and 1000 µg/L TBPH. At 1000 µg/L TBPH epithelial cell shedding into the follicular lumen was observed. Thyroid follicular hyperplasia and epithelial degeneration represent adverse structural alterations of endocrine tissue. According to the authors, pathological damage to thyroid tissue can disrupt its function in the synthesis, storage, and secretion of thyroid hormones, indicating that the substance has the potential to be an endocrine disruptor.

81. Avian effects: Goodchild *et al.* (2021) studied whether *in ovo* exposure to TBPH at environmentally relevant concentrations may affect growth, hatching success, oxidative stress, or thyroid function of American kestrels (*Falco sparverius*). Kestrel embryos were exposed to TBPH on embryonic day 5. Specifically, fertile eggs were injected into the air cell of each egg with nominal concentrations of TBPH (dissolved in organic safflower oil) at 0 ng/g egg weight (n=23), 10 ng/g egg weight (n=23), 50 ng/g egg weight (n=25), and 100 ng/g egg weight (n=24). The authors noted that the concentrations of TBPH in egg contents (pre-hatch) and yolk sac residue (post-hatch) were substantially lower than the injected concentration (measured concentration of 1.8–9.5 ng/g egg weight (n=10) for eggs exposed 100 ng/g). Results showed significant adverse effects regarding the reduction of hatchlings' brain mass of both sexes (at 100 ng/g TBPH; $p < 0.05$), and male hatchlings exposed to 50 and 100 ng/g TBPH had significantly heavier hearts ($p < 0.05$). The authors mentioned that the enlarged hearts may reflect thyroidal changes observed in the same male hatchlings and described below.

82. Additionally, exposure to TBPH showed a significant increase ($p < 0.05$) in different oxidative stress biomarkers in the liver such as thiol, glutathione disulfide (GSSG), total glutathione (total GSH) and reduced glutathione (GSH), and total thiols and protein bound sulfhydryls (PBSH) in both sexes at 100 ng/g TBPH. Histopathological examination of thyroid gland of hatchlings showed a significant reduction of the colloid diameter (CD) in both sexes at 100 ng/g TBPH ($p < 0.05$). As the colloid represents the storage compartment for thyroid hormones, this structural change suggests an alteration in thyroid follicle activity and may indicate disturbance of thyroid hormone homeostasis. In the study, endocrine activity was also observed in both sexes, with the ratio of plasma T3:T4 to be significantly decreased in hatchlings exposed *in ovo* to 10 ng/g TBPH ($p < 0.05$), while glandular T3:T4 ratio showed a significant increase in hatchlings exposed to 100 ng/g TBPH ($p < 0.05$). The latter suggests that exposure to TBPH disrupts thyroid hormone balance. This study showed that bird's exposure to TBPH exhibited several signs of oxidative stress in addition to potential developmental effects (such as increased heart mass (in males only at 50 ng/g egg weight) and decreased brain mass of hatchlings (at 100 ng/g TBPH)). The study further indicates that TBPH can affect thyroid development and activity in birds.

83. Effects on eye development: In a study by Zhou *et al.* (2024) zebrafish embryos (0.75 hpf; hours post fertilization) were exposed to 10 µg/L nominal concentrations of TBPH, equivalent to 7 µg/L mean measured exposure concentrations for 144 hours. Each control and treatment group had three replicates and contained 0.01% of DMSO (v/v) as solvent. No solvent-free control was used concurrently as ≤0.1% DMSO is widely accepted as non-toxic in zebrafish studies, and prior work (Guo *et al.,* 2020) showed no significant differences between DMSO and solvent-free controls, allowing clear isolation of TBPH effects (Zhou personal communication, October 2025). The transcriptomic analysis found that in embryos exposed until 144 hpf a total of 5,781 genes were significantly changed (fold change >2, $p < 0.05$), with 2,734 up-regulated genes and 3,047 down-regulated genes. Immunofluorescent staining of βB1-crystallin, a marker protein in lens, was

significantly attenuated after exposure to TBPH. Exposure also significantly decreased expression of crystallin-related genes, key proteins for lens fibre cells, which are needed for the development and normal function of lens, and the opsin gene (*opn*1*mw*4) responsible for encoding a protein essential for normal color vision. Histopathology of the eyes showed that TBPH exposure led to significant changes in the areas of the ganglion cell layer (GCL) ($p < 0.001$), inner nuclear layer (INL) ($p < 0.05$), and retinal pigment epithelium (RPE) ($p < 0.001$) areas. This study shows that exposure to TBPH can have a detrimental effect on the development of zebrafish eyes at a concentration of 7 µg/L. According to Zhou *et al.* (2024), the normal function of the vision system, especially the photoreceptor, is essential for movement, predation, or avoidance of predators in fish, and disruptions on the visual system can create a serious hazard for their survival and population stability.

84. Zhou *et al.* (2024) study suggests that these eye effects are likely persistent. The authors suggest that disruption during early development, when the lens and retina rapidly form, can lead to permanent deficits (Harding *et al*., 2008 and Yi *et al*., 2023). Downregulation of genes involved in lens differentiation (e.g. crystallins, mipa, lgsn) and photoreceptor function (e.g. rhodopsin, opsins) supports this. Prior research indicates early visual system damage often does not recover, resulting in lifelong impairment (Chen, 2020). In summary, TBPH causes lasting visual damage in zebrafish, with serious implications for individual fitness and population stability in contaminated environments.

85. Liver effects: Fu *et al.* (2024b) investigated the toxicity of TBPH in wild-type zebrafish. Sexually mature fish (20/sex/group; each group in 3 replicates; 4 months old fish) were exposed for 2 months to TBPH at nominal concentrations of 0, 0.14, 1.41, 14.1, and 141 µg/L in 20-L glass tanks each. Both the control and exposure groups received 0.005% DMSO, and the exposure solution was completely replaced daily. According to Fu *et al.* (2024b), the lowest concentration of TBPH (0.14 µg/L) was consistent with levels reported in wastewater in Barcelona, Spain (0.13 µg/L; Cristale *et al.*, 2015), indicating the environmental relevance of the exposure concentrations in this study. The highest concentration (141 µg/L) was selected based on results from pre-experiment in the authors' previous studies (Guo *et al.* 2021), which evoked toxic effects in zebrafish upon 28 days exposure. During this experiment, transcriptome, biochemical and histopathological analyses were performed.

86. Transcriptome analysis of the liver tissues from the control and 141 µg/L TBPH exposure group was performed. Statistically significant ($p < 0.05$) sex-specific metabolic disruption was observed at 141 µg/L TBPH: females showed downregulation of lipid biosynthesis genes, indicating impaired lipid metabolism, while in males upregulation of insulin signalling and glycolysis genes was observed, suggesting enhanced glycolytic activity and disturbed glucose-lipid homeostasis. Biochemical analysis revealed sex-specific hepatic biochemical alterations. In females, elevated liver glycogen was observed at 14.1 and 141 µg/L ($p <0.05$) and in males, decreased blood insulin levels at ≥0.14 µg/L ($p <0.05$) and decreased hepatic lactic acid levels at ≥1.41 µg/L ($p <0.05$) were observed. These effects reflect significant dysregulation of glucose metabolism. Fu *et al.* (2024b) suggested that changes in these indicators are considered signals of certain liver diseases. A significant increase in superoxide dismutase and reactive oxygen species (ROS) at ≥1.41 µg/L TBPH ($p < 0.05$) and catalase at 141 µg/L ($p < 0.05$) was observed in male zebrafish liver, which suggests oxidative stress. The significant increase in tumor necrosis factor α at 141 µg/L TBPH ($p < 0.05$) and interleukin 6 at ≥14.1 µg/L TBPHs ($p < 0.05$) in male zebrafish liver indicates an inflammatory response. In female zebrafish livers, significant elevated ROS levels were observed in the ≥14.1 µg/L TBPH exposure groups ($p < 0.05$).

87. When considered in combination the following described effects are considered to be adverse. Fu *et al.* (2024b) found that female zebrafish showed a significantly higher body weight and hepatosomatic index at concentrations of ≥14.1 µg/L TBPH ($p < 0.05$) compared to the solvent control, while male zebrafish showed no significant changes. Increased hepatosomatic index is commonly used to indicate metabolic stress or detoxication activity. Moreover, histopathological examination showed liver steatosis at ≥1.41 µg/L exposure groups in females ($p < 0.001$) and at 141 µg/L exposure groups in males ($p < 0.001$) where significant hepatocyte ballooning effect was shown. Hepatocyte ballooning is a key characteristic of liver lipid accumulation, ultimately leading to hepatocyte steatosis. Similarly, oil red O staining revealed a dose-dependent increase in intracellular lipid droplets in TBPH-treated hepatocytes. Alterations in inflammatory factors indicated more serious effects in the liver of male zebrafish. The study of Fu *et al.* (2024b) shows that zebrafish exposure to TBPH at environmentally relevant concentrations led to an increase visceral fat accumulation, indicating a potential abnormal liver function. Fu *et al.* (2024b) found that TBPH accumulates most in the liver of zebrafish, with slower clearance from brain (half-life up to 15.67 days in males) and muscle (half-life up to 14.52 days in females), suggesting persistent effects. Histopathology revealed dose-dependent liver damage, worse in males. Inflammatory markers were elevated, especially in males. These effects occurred at environmentally relevant concentrations (Cristale *et al.*, 2015), posing risks to wild populations.

88. Effects on energy homeostasis: Guo *et al.* (2020) investigated the effects of TBPH on peroxisome proliferator-activated receptor γ (PPARγ), lipid metabolism and swimming behavior in zebrafish embryos (0.75 hours post fertilization (hpf) ; n =~ 250) and larvae exposed to 0, 0.14, 1.4, 14, 141 and 1412 µg/L TBPH until 72 hpf (semi-static conditions, based on nominal/measured concentrations), with 0.1% (v/v) DMSO. There were four replicates for each solvent control and exposure group. According to the authors, no solvent-free control was used concurrently as 0.1% DMSO was well-established as an acceptable solvent concentration for zebrafish embryo/larvae studies (Guo personal communication, October 2025). The study includes rosiglitazone (0.1 µM), a PPARγ agonist, as a positive control and GW9662, a PPARγ antagonist, as a negative control. With continual exposure, the ATP content and locomotor behavior was measured in the 120 hpf larvae to evaluate the possible alteration of energy homeostasis.

89. Guo *et al.* (2020) found that embryos exposed to TBPH for 24 hours developed significant DNA demethylation of the PPARγ-mediated lipid promoter at ≥141 µg/L concentrations ($p < 0.05$) accompanied by upregulation of several genes in the 72 hpf larvae: the PPARrγ (at ≥141 µg/L) was significantly ($p < 0.05$) upregulated in TBPH treatment groups, while the tet methylcytosine dioxygenase 2 (*tet2*) gene transcription was significantly ($p < 0.05$) upregulated at the two highest exposure concentrations (≥141 µg/L). Among the downstream genes related to lipid metabolism, fatty acid-binding proteins (*fabp11a*) gene transcription was significantly ($p < 0.05$) upregulated in a concentration-dependent manner at ≥141 µg/L. Cytochrome P450 (*cyp11a1*) gene transcription significantly ($p < 0.05$) increased at ≥141 µg/L. The triglyceride ($p < 0.05$) concentrations and the total cholesterol ($p < 0.05$) in the 72 hpf larvae were significantly reduced in all but the lowest exposure concentration (at ≥1.4 µg/L). The total neutral lipid contents in the 72 hpf larvae were significantly ($p < 0.05$) reduced in the ≥14 µg/L TBPH. In 120 hpf larvae, adenosine triphosphate (ATP) concentration was measured. It was significantly ($p < 0.05$) increased in the two highest exposure concentrations (at ≥141 µg/L), while the mean swimming speed of 120 hpf zebrafish larvae increased significantly ($p < 0.05$) in all but the lowest treatment group (at ≥1.4 µg/L) during 15 minutes of continuous dark stimulation. According to ECHA Guidance on the Application of the CLP Criteria (ECHA, 2024b), behavioural effects that are considered to be population relevant, must be considered in the assessment of adversity. The findings indicate that TBPH affects the methylation of the PPARγ promoter (at ≥141 µg/L) and TBPH acts as a PPARγ agonist. This alteration subsequently affects lipid metabolism in larvae through the PPARγ signaling pathway, leading to disruptions in energy homeostasis (as observed in changes to ATP (at ≥141 µg/L) and swimming speed (at ≥1.4 µg/L)) which is critical for survival.

3.4.3 Conclusion on adverse effects

90. The criteria for adverse effects listed in paragraph 1 (e) (i) and (ii) of Annex D are considered to be met for TBPH.

91. For adverse effects to human health, experimental studies show that TBPH has the potential to cause adverse effects such as neurobehavioral effects in mice (20 mg/kg bw/day) and changes in the brain of mice and birds. Effects on the rat thyroid system (at 500 mg/kg bw/day) consistent with thyroid atrophy with changes of thyroid hormones (at 50 mg/kg bw/day) in one animal study indicate a potential for endocrine disruption. Other effects have been observed which may contribute to the adversity of TBPH such as effects on markers of lung injury like inflammation and fibrosis in mice (at 30–60 mg/kg bw/day). Linked to the lung effects, epidemiological evidence also suggests a possible association between early-life TBPH exposure and respiratory effects in children.

92. As regards adverse effects to the environment, data on aquatic organisms indicate that TBPH can cause environmental adverse effects on reproduction such as effects on early larval development (LOAEC at 1.4 µg/L), reduced percentages of spermatogonia and spermatocytes of fish (including sperm malformation and a decrease of sperm motility; LOAEC at 140 µg/L). Other effects have been observed which are suggestive of adverse effects on the thyroid system such as effects on eye development in fish larvae (LOAEC at 7 µg/L), thyroid hyperplasia of juvenile fish (at 0.1 µg/L), fish liver effects (steatosis at 1.41 µg/L in females and at 141 µg/L in males), and disruption in energy homeostasis of the fish larvae with effects on the swimming behavior (at 1.4 µg/L). These adversities can result in impairment of normal functions and negative impacts on prey behavior, both of which ultimately effect the population maintenance.

4. Statement of the reasons for concern and need for global action

93. Based on the existing data, the screening criteria in Annex D of the Stockholm Convention for persistence, bioaccumulation, long-range transport and adverse effects are considered to be met for TBPH.

94. Due to the ongoing use of TBPH in many applications, TBPH is directly and indirectly emitted into the environment from human activities.

95. TBPH is persistent, bioaccumulative, has evidence of adverse effects to human health and to the environment, and has the potential to undergo long-range environmental transport in air and water, making emissions of this substance a transboundary pollution problem. Globally, the occurrence and distribution of TBPH is demonstrated for wildlife, and environmental matrices (air, soil, sediment, water), including measurements in remote areas such as the Arctic and Antarctic. Furthermore, TBPH has been detected in freshwater, groundwater and seawater, as well as in wastewater treatment plant (WWTP) sludge which spreading on agricultural land can lead to contamination of soils and consecutively to plants intended for food consumption (see Annex I in ECHA, 2022). In humans, TBPH has been found in nails, hair and in (maternal) blood serum (including in the serum of school age children). TBPH can be transferred through bird eggs, human breast milk and placenta to sensitive life stages. TBPH has also been detected in food intended for human consumption and in indoor dust. Thus, humans can be exposed to TBPH through their diet and via dust ingestion/inhalation and dust contact.

96. In humans, a possible association between exposure to TBPH and adverse respiratory outcomes (especially wheezing and reduced PEF) during childhood was found.

97. Effects in animal studies, relevant for wildlife and humans, include neurotoxicity and effects on reproduction. Other effects have been observed which contribute to the adversity of TBPH that target the thyroid system such as effects on eye development in fish, thyroid atrophy and hyperplasia, pulmonary function, effects on liver, lipid metabolism and energy homeostasis. These effects can result in impairment of reproduction functions, and they can have impact on prey behaviour, both of which ultimately lead to negative effects on organisms' population numbers.

98. Other concerns include TBPH persistence which increases the probability, magnitude and duration of exposure to wildlife. TBPH is subject to long-range transport via air and/or water, and it can result in regional or global contamination. As such, releases of this substance can lead to organisms' exposure over wide areas over a long period of time. TBPH bioaccumulates and biomagnifies through the food chain, resulting in increased internal concentrations for top predator species.

99. A benchmark exercise indicated that the concentrations of TBPH found in air, seawater and biota from remote locations are in the same range of concentrations as those of POP substances such as BDE-209, pentaBDE, octaBDE and dechlorane plus before their inclusion to the Stockholm Convention on POPs.

100. The signs of increase of its concentration in Arctic air and in the Great Lakes region reflecting a possible increase in use as a replacement for PBDEs flame retardants is of concern. Indeed, TBPH is already found in remote areas which should be protected from further contamination by hazardous substances resulting from human activity because the intrinsic value of pristine environments should be protected.

101. Based on the persistence, bioaccumulation, toxicity to aquatic organisms and in terrestrial organisms (including humans) and the widespread occurrence in environmental compartments including remote regions, it is concluded that the use of TBPH is likely to lead to adverse human health and environmental effects such that global action is warranted.

5. References

AMAP [Arctic Monitoring and Assessment Programme] (2017). AMAP Assessment 2016: Chemicals of Emerging Arctic Concern. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway. xvi+353pp. https://www.amap.no/documents/download/3003/inline.

Baldwin, K.R., Phillips, A.L., Horman B., Arambula, S.E., Rebuli, M.E., Stapleton, H.M., Patisaul, H.B. (2017): Sex specific accumulation and behavioral effects of developmental Firemaster 550 exposure in Wistar rats. Scientific Reports 7, 7118. DOI:10.1038/s41598-017-07216-6.

Bao, Z. and Jing, Y. (2021). Brominated flame retardant TBPH induced oxidative damage and reduced the expression of memory-related proteins in mice, with no discernable impairment of learning and memory. *Human and Experimental Toxicology* 2021, Vol. 40(12S) S684–S692. https://doi.org/10.1177/09603271211058876.

Brooke, D. and Crookes, M. (2012). Depuration rate constant: growth correction and use as an indicator of bioaccumulation potential. Environment Agency, Horizon House, Deanery Road, Bristol, BS1 5AH. https://assets.publishing.service.gov.uk/media/5a7c778de5274a559005a103/LIT_7371_44228a.pdf.

Brown, T. and Wania, F. (2008): Screening chemicals for the potential to be persistent organic pollutants: a case study of Arctic contaminants. *Environmental Science & Technology*, 42, 5202–5209. https://doi.org/10.1021/es8004514.

BSEF [The international Bromine Council] (2025). BSEF's comments received during the stakeholder consultation on TBPH draft scientific dossier (Annex D) for an EU proposal. Consultation period: 18 June 2025 – 13 August 2025. The compilation of comments is available at: https://echa.europa.eu/list-of-substances-proposed-as-pops/-/dislist/details/0b0236e18bafb66b.

Burkhard, L.P., Lahren, T.J., Hanson, K.B., Kasparek, A.J., Mount, D.R. (2023). Dietary Uptake of Highly Hydrophobic Chemicals by Rainbow Trout (Oncorhynchus Mykiss). *Arch Environ Contam Toxicol.* 2023 Nov; 85(4):390-403. https://doi.org/10.1007/s00244-023-01038-6.

Burkhard, L.P., Lahren, T. J., Highland, T. L., Hockett, J. R., Mount, D. R., Norberg-King, T. J. (2021). Bioaccumulation of Bis-(2-ethylhexyl)-3,4,5,6-tetrabromophthalate and Mono-(2-ethylhexyl)-3,4,5,6-tetrabromophthalate by *Lumbriculus variegatus*. *Archives of Environmental Contamination and Toxicology*. 80, 579-585. https://doi.org/10.1007/s00244-021-00824-4.

Chang, C., Lee, S.O., Wang, R.S., Yeh, S., Chang, T.M. (2013). Androgen receptor (AR) physiological roles in male and female reproductive systems: lessons learned from AR-knockout mice lacking AR in selective cells. *Biol. Reprod*., 89, 1−16. https://doi.org/10.1095/biolreprod.113.109132.

Chen L. (2020). Visual system: An understudied target of aquatic toxicology. *Aquatic Toxicology*. 225: 105542. https://doi.org/10.1016/j.aquatox.2020.105542.

Chen, Y., Cao Z., Covaci, A., Li, C., Cui, X. (2019): Novel and legacy flame retardants in paired human fingernails and indoor dust samples. *Environment International* 133, 105227. https://doi.org/10.1016/j.envint.2019.105227.

Cristale, J. and Lacorte, S. (2015). PBDEs versus NBFR in wastewater treatment plants: occurrence and partitioning in water and sludge. *AIMS Environmental Science*. 2, 533−546. DOI: 10.3934/environsci.2015.3.533.

Davis, E.F. and Stapleton, H.M. (2009). Photodegradation pathways of nonabrominated diphenyl ethers, 2-ethylhexyltetrabromobenzoate and di(2- ethylhexyl)tetrabromophthalate: identifying potential markers of photodegradation. *Environ Sci Technol.* 43(15), 5739-5746. https://doi.org/10.1021/es901019w.

de Jourdan, B.P., Hanson, M.L., Muir, D.C., Solomon, K.R. (2013). Environmental fate of three novel brominated flame retardants in aquatic mesocosms. *Environmental Toxicology and Chemistry* 32(5):1060-1068. DOI: 10.1002/etc.2165.

ECHA [European Chemicals Agency] and EFSA [European Food Safety Authority] with the technical support of the Joint Research Centre (JRC), Andersson N., Arena M., Auteri D., Barmaz S., Grignard E., Kienzler A., Lepper P., Lostia AM., Munn S., Parra Morte J.M., Pellizzato F., Tarazona J., Terron A. and Van der Linden S. (2018). Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009. EFSA Journal 2018;16(6):5311, 135 pp. . https://doi.org/10.2903/j.efsa.2018.5311.

ECHA (2022). Member State Committee support document for identification of bis(2-ethylhexyl) tetrabromophthlate covering any of the individual isomers and/or combinations thereof as a substance of very high concern because of its vPvB (Article 57E) properties. https://echa.europa.eu/documents/10162/170b9b2f-a1d0-9661-d36d-faf0846f6763.

ECHA (2023). Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.11: PBT/vPvB assessment. Version 4.0. December 2023. https://echa.europa.eu/documents/10162/17224/information_requirements_r11_en.pdf/a8cce23f-a65a-46d2-ac68-92fee1f9e54f.

ECHA (2024a). Investigation report on aromatic brominated flame retardants. European Chemicals Agency, December 2024.

https://echa.europa.eu/documents/10162/17233/rest_aromatic_brominated_flame_retardants_investigation_report_en.pdf.

ECHA (2024b). Guidance on the Application of the CLP Criteria. Part 4: Environmental hazards and Part 5: Additional Hazards. Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures. Version 4.0. November 2024. https://echa.europa.eu/documents/10162/2324906/clp_parts4-5_en.pdf/56ed0738-f7e9-6a6f-e9ca-c13af265ec6b?t=1730718888268.

ECCC and HC [Environment and Climate Change Canada, Health Canada] (2019). State of Science Report: Certain Organic Flame Retardants Substance Grouping Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester (TBB) and 1,2-Benzenedicarboxylic acid, 3,4,5,6-tetrabromo-, bis(2-ethylhexyl) ester (TBPH) (2019). https://www.canada.ca/content/dam/eccc/documents/pdf/pded/ofr-tbb-tbph/State-science-report-certain-organic-flame-retardants-substance-grouping-tbb-tbph.pdf.

EFSA [European Food Safety Authority] (2017). Guidance on the assessment of biological relevance of data in scientific assessments. EFSA Journal, 154(8):4970. https://doi.org/10.2903/j.efsa.2017.4970.

Fernie, K.J., Chabot, D., Champoux, L., Brimble, S., Alaee, M., Marteinson, S., Chen, D., Palace, V., Bird, D.M., Letcher, R.J. (2017). Spatiotemporal patterns and relationships among the diet, biochemistry, and exposure to flame retardants in an apex avian predator, the peregrine falcon. *Environmental research* 158, 43-53. http://dx.doi.org/10.1016/j.envres.2017.05.035.

Fu, K., Hua, J., Zhang, Y., Du, M., Han, J., Li, N., Wang, Q., Yang, L., Li, R., Zhou, B. (2024a). Integrated studies on male reproductive toxicity of bis (2-ethylhexyl)-tetrabromophthalate: *in silico, in vitro, ex vivo,* and *in vivo*. *Environmental Science & Technology*, 58(1), 194-206. https://pubmed.ncbi.nlm.nih.gov/38113192/.

Fu, K., Zhu, B., Sun, Y., Zhou, Y., Pang, H., Ren, X., Guo, Y., Shi, X., Han, J., Yang, L., Zhou, B. (2024b). Bis(2-ethylhexyl)-tetrabromophthalate poses a higher exposure risk and induces gender-specific metabolic disruptions in Zebrafish Liver. *Environ Sci Technol*. 58(11), 4937-4947. https://doi.org/10.1021/acs.est.4c00234.

Giam, C.S. *et al.* (1984). The handbook of the environmental Chem. 3:67-142. Hutzinger O ed. Berlin, Springer-Verlag.

Glüge, J. and Scheringer, M. (2023). Evaluation of physicochemical properties data in the ECHA database. *J. Phys. Chem. Ref. Data* 52, 043101 (2023). https://doi.org/10.1063/5.0153030.

Goodchild, C., Karouna-Renier, N.K., Henry, P.F.P., Letcher, R.J., Schultz, S.L., Maddox, C.M., Bean, T.G., Peters, L.E., Palace, V., Fernie, K.J. (2021). Thyroid disruption and oxidative stress in American kestrels following embryonic exposure to the alternative flame retardants, EHTBB and TBPH. Environment International, 157, 106826. https://doi.org/10.1016/j.envint.2021.106826.https://doi.org/10.1016/j.envint.2021.106826.

Great Lakes Chemical Corporation (1997). CN-2065: Abiotic degradation: hydrolysis as a function of pH. 1997 Sep 3. Huntingdon Life Sciences Ltd. Unpublished Study # GLC 042/970941.

Guerra, P., Alaee, M., Eljarrat, E., Barcelo, D. (2011). Introduction to Brominated Flame Retardants: Commercially Products, Applications, and Physicochemical Properties. In Eljarrat E, Barceló D. editors. 2011. Brominated Flame Retardants. Series: The Handbook of Environmental Chemistry. Volume 16. Heidelberg Berlin:Springer. 290 pp.

Guo W., Han J., Wu S., Shi X., Wang Q., Zhou B. (2020). Bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate Affects Lipid Metabolism in Zebrafish Larvae via DNA Methylation Modification. *Environ. Sci. Technol*. 54(1), 355-363. doi: 10.1021/acs.est.9b05796.

Guo, W., Lei, L., Shi, X., Li, R., Wang, Q., Han, J., Yang, L., Chen, L., Zhou, B (2021). Nonalcoholic Fatty Liver Disease Development in Zebrafish upon Exposure to Bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate, a Novel Brominated Flame Retardant. *Environ. Sci. Technol*. 55, 6926−6935. https://doi.org/10.1021/acs.est.1c01476.

Guo, L.C., Xiao, J., Zhang, Y., Yu, S., Lin, H., Su, G., Liu, T., Li, X., Lv, S., Rutherford, S., Ma, W. (2018). Association between serum polybrominated diphenyl ethers, new flame retardants and thyroid hormone levels for school student near a petrochemical complex, South China. *Chemosphere*, 202 (2018), pp. 476-482. https://doi.org/10.1016/j.chemosphere.2018.03.120.

Halvorsen, H., Pfaffhuber, K., Nipen, M., Bohlin-Nizzetto, P., Berglen, T., Nikiforov, V., Hartz, W. (2023). Monitoring of environmental contaminants in air and precipitation. Annual report 2022. (Norwegian Environment Agency, M-2543|2023) (NILU report, 18/2023). Kjeller:NILU. https://nilu.brage.unit.no/nilu-xmlui/bitstream/handle/11250/3100929/NILU-report-18-2023.pdf?sequence=1&isAllowed=y.

Han, F., Chen, G., Tao, G., Xu, J., Zhang, H., Zhang, L., Li, H., Zhao, Y., Tian, D., Kimura, S.Y., Wei, X., Ruan, Y., Wu, C., Xiao, S., Zhan, M., Zheng, W. (2022).Thyroid-disrupting effects caused by exposure to alternative flame retardants from groundwater contamination in rural central China, *Science of The Total Environment*, 839, 156300, ISSN 0048-9697, https://doi.org/10.1016/j.scitotenv.2022.156300.

Harding, R.L., Howley, S., Baker, L.J., Murphy, T.R., Archer, W.E., Wistow, G., Hyde, D.R., Vihtelic, T.S. (2008). Lengsin expression and function during zebrafish lens formation. *Exp Eye Res*. 86(5), 807-18. doi: 10.1016/j.exer.2008.02.009.

Harju, M., Herzke, D., Kaasa, H. (2013). Perfluorinated alkylated substances (PFAS), brominated flame retardants (BFR) and chlorinated paraffins (CP) in the Norwegian Environment Screening 2013. NILU OR 31/2013. https://www.miljodirektoratet.no/globalassets/publikasjoner/m40/m40.pdf.

He S., Li M., Jin J., Wang Y., Bu Y., Xu M., Yang X. & Liu A. (2013): Concentrations and trends of halogenated flame retardants in the pooled serum of residents of Laizhou Bay, China. *Environmental Toxicology and Chemistry,* 32, 1242–1247. https://doi.org/10.1002/etc.2172.

Hong X-S, Yan L., Sang W., Liu W., Li Z-T., Wang J., Yan S-H., Xin J-J., Zhao G-F., Ma X-F., Zha J-M. (2025). Environmental levels of bis(2-ethylhexyl)-tetrabromophthalate (TBPH) cause thyroid toxicity and early carcinogenic signals in juvenile fish, *Environmental Pollution,* 380, 126568. https://doi.org/10.1016/j.envpol.2025.126568.

Hou, R., Huang, Q., Pan, Y., Lin, L., Liu, S., Li, H., Xu, X. (2022). Novel brominated flame retardants (NFBRs) in a tropical marine food web from the South China Sea: the influence of hydrophobicity and biotransformation on structure-related trophodynamics. *Environmental Science & Technology,* 56(5), 3147–3158. https://doi.org/10.1021/acs.est.1c08104.

Houde, M., Wang, X., Ferguson, S., Gagnon, P., Brown, T., Tanabe, S., Kunito, T., Kwan, M., Muir, D. (2017). Spatial and temporal trends of alternative flame retardants and polybrominated diphenyl ethers in ringed seals (P*hoca hispida*) across the Canadian Arctic. *Environmental Pollution*, 223, 266-276. https://doi.org/10.1016/j.envpol.2017.01.023.

Hung, H., Kurt-Karakus, P., Ahrens, L., Bidleman, T., Evans, M., Halsall, C., Harner, T., Jantunen, L., Lee, S.C., Muir, D., Shoeib, M., Stern, G., Sverko, E., Su, Y., Vlahos, P., Xiao, H. (2013a). Occurrence and trends in the physical environment. In: Muir, D.C.G., P. Kurt-Karakas and J.E. Stow (eds.), Canadian Arctic Contaminants Assessment Report on Persistent Organic Pollutants III. pp. 147-272. Aboriginal Affairs and Northern Development, Canada.

Hutchinson TH, Shillabeer N, Winter MJ, Pickford DB. (2006). Acute and chronic effects of carrier solvents in aquatic organisms: a critical review. *Aquat Toxicol.*, 76(1):69-92. doi:10.1016/j.aquatox.2005.09.008.

Jin, X., Lee, S., Jeong, Y., Yu, J., Baek W.K., Shin, K-H., Kannan, K., Moon, H-B. (2016). Species-specific accumulation of polybrominated diphenyl ethers (PBDEs) and other emerging flame retardants in several species of birds from Korea. *Environmental Pollution.* 219, 191-200. http://dx.doi.org/10.1016/j.envpol.2016.10.040.

Kelly, B.C., Ikonomou, M.G., Blair, J.D., Morin, A.E., Gobas, F.A.P.C. (2007). Food web-specific biomagnification of persistent organic pollutants. *Science*, 317: 236-239. DOI: 10.1126/science.1138275.

Kneller, B., Nasr-Azadani, M.M., Radhakrishnan, S., Meiburg, E. (2016). Long-range sediment transport in the world's oceans by stably stratified turbidity currents. *JRG Oceans*, 121(12), 8608-8620. https://doi.org/10.1002/2016JC011978.

Knudsen, G.A., Sanders, M.J., Birnbaum, L.S. (2017). Disposition of the emerging brominated flame retardant, bis(2-ethylhexyl) tetrabromophthalate, in female Sprague Dawley rats: effects of dose, route, and repeated administration. *Xenobiotica*. 47(3), 245-254. doi: 10.1080/00498254.2016.1174793.

Körner, P., Glüge, J., Glüge, S., Sheringer, M. (2024). Critical insights into data curation and label noise for accurate prediction of aerobic biodegradability of organic chemicals. *Environ. Sci.: Processes Impacts*, 2024, 26, 1780. DOI: 10.1039/d4em00431k.

Lam, J.C., Lau, R.K., Murphy, M.B., Lam, P.K.S. (2009). Temporal trends of hexabromocyclododecanes (HBCDs) and polybrominated diphenyl ethers (PBDEs) and detection of two novel flame retardants in marine mammals from Hong Kong, South China. *Environmental Science and Technology*, 43, 6944-6949.

Lazarus, R.S., Rattner, B.A., McGowan, P.C., Hale, R.C., Karouna-Renier, N.K., Erickson, R.A., Ottinger, M.A. (2016). Chesapeake Bay Fish-osprey (Pandion Haliaetus) food chain: Evaluation of contaminant exposure and genetic damage. *Environmental Toxicology and Chemistry* 35, 1560-1575. https://doi.org/10.1002/etc.3386.

Lee, S.C., Sverko, E., Harner, T., Pozo, K., Schachtschneider, J., Zaruk, D., DeJong, M., Barresi, E., Narayan, J. (2016). Retrospective analysis of "new" flame retardants in the global atmosphere under the GAPS network. *Environmental Pollution*, 217, 62-69. http://dx.doi.org/10.1016/j.envpol.2016.01.080.

Li, H., Yang, H., Sun, S., Wang, Z., Bu, J., Liu, J., Xing, W., Wang, L. (2025). Aerobic simulated biodegradation of novel brominated flame retardants: Systems and mechanisms, *Biochemical Engineering Journal*, Volume 221, 2025, 109808, ISSN 1369-703X, https://doi.org/10.1016/j.bej.2025.109808.

Liu, L., He, K., Hites, R., Salamova A. (2016). Hair and nails as noninvasive biomarkers of human exposure to brominated and organophosphate flame retardants. *Environ. Sci. Technol*., 50 (6) (2016), pp. 3065-3073. DOI: 10.1021/acs.est.5b05073.

Liu, L.Y., Salamova, A., He, K., Hites, R.A (2015). Analysis of polybrominated diphenyl ethers and emerging halogenated and organophosphate flame retardants in human hair and nails. *J. Chromatogr. A* 2015, 1406 (0), 251−257. http://dx.doi.org/10.1016/j.chroma.2015.06.003.

Ma, Y., Venier, M., Hites, R.A. (2012b). 2-ethylhexyl tetrabromobenzoate and bis(2-ethylhexyl) tetrabromophthalate flame retardants in the Great Lakes atmosphere. *Environmental Science and Technology*, 46, 204-208. https://doi.org/10.1021/es203251f.

Mendy, A., Percy, Z., Braun, J. M., Lanphear, B., La Guardia, M. J., Hale, R., Yolton, K., Chen, A. (2023). Exposure to dust organophosphate and replacement brominated flame retardants during infancy and risk of subsequent adverse respiratory outcomes, *Environmetnal Research*, 235, 116560. https://doi.org/10.1016/j.envres.2023.116560.

Mendy, A., Percy, Z., Braun, J.M., Lanphear, B., La Guardia, M. J., Hale, R. C., Yolton, K., Chen, A. (2024). Prenatal exposure to replacement flame retardants and organophosphate esters and childhood adverse respiratory outcomes, *Environ. Res.*, 240, 117523. Epub 2023 Nov 2. https://doi.org/10.1016/j.envres.2023.117523.

Möller, A., Xie, Z., Cai, M., Sturm, R., Ebinghaus, R. (2012). Brominated flame retardants and dechlorane plus in the marine atmosphere from southeast Asia toward Antarctica. *Environ. Sci. Tech.,* 46 (6), 3141-3148. https://doi.org/10.1021/es300138q

Möller, A., Xie, Z., Cai, M., Zhong, G., Huang, P., Cai, M., Sturm, R., Ebinghaus, R. (2011b). Polybrominated diphenyl ethers vs. alternate brominated flame retardants and dechloranes from East Asia to the Arctic. *Environ. Sci. Technol*, 45(16), 6793–6799. https://doi.org/10.1021/es300138q.

Möller, A., Xie, Z., Sturm, R., Ebinghaus, R. (2011a). Polybrominated diphenyl ethers (PBDEs) and alternative brominated flame retardants in air and seawater of the European Arctic. *Environnemental Pollution*, 159, 1577-1583. https://doi.org/10.1016/j.envpol.2011.02.054.

Nacci, D., Clark, B., La Guardia, M. J., Miller, K., Champlin, D., Kirby, I., Bertrand, A., Jayaraman, S. (2018). Bioaccumulation and effects of dietary exposure to the alternative flame retardant, bis(2-ethylhexyl) tetrabromophthalate (TBPH), in the Atlantic killifish, Fundulus heteroclitus. *Environmental Toxicology and Chemistry*. 37(9), 2350-2360. https://doi.org/10.1002/etc.4180.

OECD (2017). Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation. Series on Testing & Assessment. No. 264. ENV/JM/MONO(2017)16.

OECD (2019). Guidance document on aqueous-phase aquatic toxicity testing of difficult test chemicals. Series on testing and assessment No. 23 (Second Edition). Environment Directorate, Joint meeting of the chemicals Committee and the working party on chemicals, pesticides and biotechnology. ENV/JM/MONO(2000)6/REV1. https://www.oecd.org/en/publications/guidance-document-on-aquatic-toxicity-testing-of-difficult-substances-and-mixtures_0ed2f88e-en.html.

Pakalin, S., Aschberger, K., Cosgrove, O., Lund, B., Paya Perez, A., Vegro, S. (2008). Editors. European Union Risk Assessment Report - bis (2-ethylhexyl) phthalate (DEHP). EUR 23384 EN. Luxembourg (Luxembourg): OPOCE; 2008. JRC45705. https://publications.jrc.ec.europa.eu/repository/handle/JRC45705.

Papachlimitzou, A., Barber, J.L., Losada, S., Bersuder, P., Law, R.J. (2012). A review of the analysis of novel brominated flame retardants, *Journal of Chromatography A*, Volume 1219, 2012, Pages 15-28, ISSN 0021-9673, https://doi.org/10.1016/j.chroma.2011.11.029.

Rauert, C., Schuster, J., Eng, A., Harner, T. (2018). Global atmospheric concentrations of brominated and chlorinated flame retardants and organophosphate esters. *Environ. Sci. Technol.*, 52(5), 2777–2789. https://doi.org/10.1021/acs.est.7b06239.

Roberts, S.C., Macaulay, L.J., Stapleton, H.M. (2012). *In vitro* metabolism of the brominated flame retardants 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB) and bis(2-ethylhexyl) 2,3,4,5-tetrabromophathalate (TBPH) in human and rat tissues. *Chemical Research in Toxicology,* 25, 1435-1441. dx.doi.org/10.1021/tx300086x.

Sagerup, K., Herzke, D., Harju, M., Evenset, A., Christensen, G.N., Routti, H., Fuglei, E., Aars, J., Strøm, H., Gabrielsen, G.W. (2010). New brominated flame retardants in Arctic biota. Statlig program for forurensningsovervåking. https://brage.npolar.no/npolar-xmlui/bitstream/handle/11250/173191/NewBrominatedFlameRetardants.pdf?sequence=1&isAllowed=y.

Salamova, A., Hermanson, M., Hites, R. (2014). Organophosphate and Halogenated Flame Retardants in Atmospheric Particles from a European Arctic Site. *Environmental Science & Technology,* 48, 6133-6140. https://doi.org/10.1021/es500911d.

Silva, M.J., Hilton, D., Furr, J., Gray, L.E., Preau J.L., Calafat, A.M., Ye, X. (2015): Quantification of tetrabromo benzoic acid and tetrabromo phthalic acid in rats exposed to the flame retardant Uniplex FRP-45. *Archives in Toxicology,* 90, 551-557. DOI 10.1007/s00204-015-1489-6.

Sobotka, J., Lammel, G., Slobodník, J., Schink, A., Prokeš, R., Branislav, V. (2021). Dynamic passive sampling of hydrophobic organic compounds in surface seawater along the South Atlantic Ocean east-to-west transect and across the Black Sea. *Marine Pollution Bulletin*, 168, 112375, ISSN 0025-326X. https://doi.org/10.1016/j.marpolbul.2021.112375.

Swedish Competent Authority (2022). Annex XV report, proposal for identification of a Substance of very High Concern on the basis of the criteria set out in Reach Article 57. Substances Names: bis(2-ethylhexyl) tetrabromophthalate covering any of the individual isomers and/or combinations thereof. August 2022. https://echa.europa.eu/documents/10162/b20c32ea-baac-f4b9-919f-eb2784203c24.

Swedish Chemicals Agency [KEMI] (2020). Substance evaluation conclusion as required by REACH article 48 and evaluation report for Bis(2-ethylhexyl) tetrabromophthalate, EC No 247-426-5, CAS No 26040-51-7. Dated: 9 July 2020. https://echa.europa.eu/documents/10162/eb2870ff-83c2-bd58-6e25-3f37d03a6c50.

Tao F., Abdallah M.A-E., Ashworth D.C., Douglas P., Toledano M. B., Harrad S. (2017). Emerging and legacy flame retardants in UK human milk and food suggest slow response to restrictions on use of PBDEs and HBCDD. *Environ. Int.* 105 (2017) 95–104. https://doi.org/10.1016/j.envint.2017.05.010.

Unpublished (2018). Dietary bioaccumulation in *O. mykiss*. Summary available in the public registration dossier for TBPH available from: Bis(2-ethylhexyl) tetrabromophthalate 100.043.099 | 60930694-3eb6-400e-b8ab-6fc23de9ddda - ECHA CHEM.

US EPA [US Environmental Protection Agency] (2000). Test method 100.3. Methods for Measuring the Toxicity and Bioaccumulation of Sediment-associated Contaminants with Freshwater Invertebrates-Second Edition. https://archive.epa.gov/water/archive/polwaste/web/pdf/freshmanual.pdf.

US EPA (2012). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.11. United States Environmental Protection Agency, Washington, DC, USA.

US EPA (2015a). TSCA Work Plan Chemical Technical Supplement – Use and Exposure of the Brominated Phthalates Cluster (BPC) chemicals. Brominated Phthalates Cluster Flame Retardants. EPA Document# 740-Q1-4002. August 2015. Office of Chemical Safety and Pollution Prevention. https://www.epa.gov/sites/default/files/2015-09/documents/bpc_data_needs_assessment_technical_supplement_use_and_exposure_assessment.pdf.

US EPA (2015b). Flame Retardants Used in Flexible Polyurethane Foam: An Alternative Assessment Update. Sections1-6. August 2015. EPA Publication 744-R-15-002. https://www.epa.gov/sites/default/files/2015-08/documents/ffr_final_body.pdf.

US EPA (2015c). TSCA Work Plan Chemical Problem Formulation and Data Needs Assessment Brominated Phthalates Cluster Flame Retardants. EPA Document: 740-Q1-4004. August 2015.: https://www.epa.gov/sites/default/files/2015-09/documents/brominated_phthalates_cluster_data_needs_assessment.pdf.

Vorkamp, K., Bossi, R., Rigét, F., Skov, H., Sonne, C., Dietz, R. (2015). Novel brominated flame retardants and dechlorane plus in Greenland air and biota. *Environmental Pollution*, 196, 284-291. https://doi.org/10.1016/j.envpol.2014.10.007.

Xiao, H., Hung, H., Wania, F., Lao, R., Sabljic, E., Sverko, E., Lei, Y.D., Fellin, P., Barresi, E. (2012b). Field evaluation of a flow-through sampler for measuring pesticides and brominated flame retardants in the Arctic atmosphere. *Environ Sci Techol*. 46(14), 7669- 7676. dx.doi.org/10.1021/es301481w.

Xiao, H., Shen, L., Su, Y., Barresi, E., de Jong, M., Hung, H., Lei, Y-D., Wania, F., Reiner, E.J., Sverko, E., Kang, S.C. (2012a). Atmospheric concentrations of halogenated flame retardants at two remote locations: the Canadian High Arctic and the Tibetan Plateau. *Environmental Pollution,* 161, 154-161. https://doi.org/10.1016/j.envpol.2011.09.041.

Xie, J., Zhang, G., Wu, Q., Luo, M., Chen, D., Zhang, Y., He, L., Li, Y., Zhang, Q., Lin, T., Jiang, G. (2023). First evidence and potential sources of novel brominated flame retardants and BDE 209 in the deepest ocean. *Journal of Hazardous Materials*, 448, 130974. https://doi.org/10.1016/j.jhazmat.2023.130974.

Xing, B., Lan, H., Li, H. (2024). TBPH-induced lung injury is induced by mitochondrial-derived ds-DNA-mediated inflammatory response. *Ecotoxicology and Environmental Safety*, 286, 117200, https://doi.org/10.1016/j.ecoenv.2024.117200.

Xiong, S., Hao, Y., Li, Y., Yang, R., Pei, Z., Zhang, Q., Jiang, G. (2021). Accumulation and influencing factors of novel brominated flame retardants in soil and vegetation from Fildes Peninsula, Antarctica. *Science of The Total Environment*, 756, 144088. https://doi.org/10.1016/j.scitotenv.2020.144088.

Xiong, Z., Zhenhua, L., Sima, X., Zeng, Z. (2024). Astaxanthin reduces TBPH-induced neurobehavioral deficits in mice by the ROS-ERK1/2-FOS pathway. *Ecotoxicology and Environmental Safety,* 281, 116674. https://doi.org/10.1016/j.ecoenv.2024.116674.

Yi, J., Ma, Y., Ma, J., Yu, H., Zhang, K., Jin, L., Yang, Q., Sun, D., Wu, D. (2023). Rapid Assessment of Ocular Toxicity from Environmental Contaminants Based on Visually Mediated Zebrafish Behavior Studies. *Toxics*, 11, 706. https://doi.org/10.3390/toxics11080706.

Yuan, Y., Zhuang, Y., Cui, Y., Liu, Y., Zhang, Q., Xiao, Q., Meng, Q., Jiang, J., Hao, W., Wei, X. (2024). IL-10-TG/TPO-T4 axis, the target of bis (2-ethylhexyl) tetrabromophthalate on thyroid function imbalance. *Toxicology*, 501, 153713. https://doi.org/10.1016/j.tox.2023.153713.

Zhao, J., Wang, P., Wang, C., Fu, M., Li, Y., Yang, R., Fu, J., Hao, Y., Matsiko, J., Zhang, Q., Jiang, G. (2020). Novel brominated flame retardants in West Antarctic atmosphere (2011–2018): Temporal trends, sources and chiral signature. *Science of The Total Environment*, 720, 137557. https://doi.org/10.1016/j.scitotenv.2020.137557.

Zhou, S.N., Buchar, A., Siddique, S., Takser, L., Abdelouahab, N., Zhu, J. (2014). Measurements of Selected Brominated Flame Retardants in Nursing Women: Implications for Human Exposure. *Environmental Science & Technology.* 48(15), 8873-8880. dx.doi.org/10.1021/es5016839.

Zhou, Y., Guo, W., Lei, L., Sun, Y., Li, R., Guo, Y., Yang, L., Shi, X., Han, J., Zhou, B. (2021). Bis(2-ethylhexyl)-tetrabromophthalate induces zebrafish obesity by altering the brain-gut axis and intestinal microbial composition. *Environ Pollut.* 290, 118-127. https://doi.org/10.1016/j.envpol.2021.118127.

Zhou, Y., Lei, L., Chen, P., Guo, W., Guo, Y., Yang, L., Han, J., Hu, B., Zhou, B. (2022). Effects of nano-TiO2 on the bioavailability and toxicity of bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate (TBPH) in developing zebrafish. *Chemosphere*, 295, 133862. https://doi.org/10.1016/j.chemosphere.2022.133862.

Zhou, Y., Lei, L., Zhu, B., Li, R., Zuo, Y., Guo, Y., Han, J., Yang, L., Zhou, B. (2024). Aggravated visual toxicity in zebrafish larvae upon co-exposure to titanium dioxide nanoparticles and bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate. *Sci Total Environ* 921, 171133. https://doi.org/10.1016/j.scitotenv.2024.171133.

Zhu, B., Lai, N., Wai, T.C., Chan, L.L., Lam, J.C., Lam, P.K. (2014). Changes of accumulation profiles from PBDEs to brominated and chlorinated alternatives in marine mammals from the South China Sea. *Environment International* 66, 65–70. http://dx.doi.org/10.1016/j.envint.2014.01.023.

Appendix

Table A1: Monitoring data from remote areas – Air samples

Location	Year(s)	n	Nbr or % of detect	Concentration range (pg/m^3)	MDL (pg/m^3)	Remarks	Reference
Zeppelin, Svalbard, Norwegian Arctic (78° 54' N, 11° 53' E)	2022	26	17%	<0.076 – 0.128 (gas and particle phases) <0.076 (annual mean/median in the gas and particle phases)	0.076 (high value compared to other NBFRs in the study, likely due to findings of TBPH in blank values)	Method: GFF and PUF, GC/HRMS EI Halvorsen personal communication, June 2025: TBPH recovery: 35–50% (the concentrations were corrected for the recovery) Field and lab blanks were included. TBPH was found in the blanks at 0.03–0.04 pg/m^3. The field blanks were comparable with the lab blanks Concentrations in the samples have not been corrected for the blank values Clean-up of the samples performed with sulfuric acid which can break phthalates and thus lead to low recovery of the substance The results of this study are considered to be semi-quantitative considering the limited number of recovery standards and above uncertainties Benchmark (gas and particle phases): PentaBDE (BDE-47 and BDE-99): nd – 1.81 pg/m^3 (DF: 76–100%, n=52; after its inclusion to the SC in 2009) OctaBDE (BDE-196, BDE-197 and BDE-202): nd – 0.158 pg/m^3 (DF: 4–14%, n=52; after its inclusion to the SC in 2009) *Syn*DP: nd – 0.432 pg/m^3 (DF:17%, n=12; before its inclusion to the SC in 2023) *Anti*DP: nd – 1.53 pg/m^3 (DF:58%, n=12; before its inclusion to the SC in 2023)	Halvorsen *et al.,* 2023
Ny-Ålesund, Norwegian Arctic (78.907, 11.887) Alert, Nunavut, Canadian Arctic (82.450, -63.504)	2014	4 2	1/4 0/2	<1–74 (gas and particle phases) <1 (gas and particle phases)	1	Method: PUF-PAS, GC-MS/MS HSEI Surrogate recoveries: 96± 38% TBPH was not detected in lab and field blanks The concentration of 74 pg/m^3 is questionable considering the highest concentration observed at Paris (France) was 43 pg/m^3 Benchmark (gas and particle phases):	Rauert *et al.*, 2018

Location	Year(s)	n	Nbr or % of detect	Concentration range (pg/m^3)	MDL (pg/m^3)	Remarks	Reference
						Ny-Ålesund: PentaBDE (BDE-47 and BDE-99): <2–4 pg/m^3 (4/8; after its inclusion to the SC in 2009) BDE-209: <1 pg/m^3 (0/4; before its inclusion to the SC in 2017) Alert: PentaBDE (BDE-47 and BDE-99): 0.031–35 pg/m^3 (4/4; after its inclusion to the SC in 2009) BDE-209: 3.2–3.5 pg/m^3 (2/2; before its inclusion to the SC in 2017)	
Alert, Nuvanut, Canada	2008 2009 2010 2011 2012	27 17 13 26 26	78% 100% 100% 100% 100%	<MDL–3.4 0.30 (mean) 0.099 (median) 0.079–0.94 0.39 (mean) 0.35 (median) 0.033–0.85 0.23 (mean) 0.21 (median) 0.14–4.3 0.51 (mean) 0.39 (median) 0.16–80 6.7 (mean) 0.89 (median)			Hung *et al.,* 2013a as cited in AMAP, 2016
Ny-Ålesund, Norwegian Arctic (78º54'N, 11º53' E)	March 2005–May 2006	4	1/4	<0.04–0.28 (gas and particle phases)	0.04	Method: PUF-PAS, GC-MS negative ion Recovery range for the BFRs: 78–111% Laboratory blanks were included. No field blanks analysed for TBPH According to the authors, the reported concentrations in air should be viewed as semi-	Lee *et al.*, 2016

Location	Year(s)	n	Nbr or % of detect	Concentration range (pg/m^3)	MDL (pg/m^3)	Remarks	Reference
Alert, Nunavut, Canadian Arctic (82º27'N, 63º30ºW)				No deployment or no analysis in this study		quantitative, due to uncertainties associated with analytical and sampling challenges Benchmark (gas and particle phases): Ny-Ålesund: HBCD: <0.1–5.1 pg/m^3 (DF: 3/4; before its inclusion to the SC in 2013) Alert: HBCD: No deployment or no analysis in this study	
Longyearbyen, Svalbard (78.22°N, 15.65°E)	September 2012 to May 2013	34	88%	0.27–14 2.7±0.49 (mean) 1.8 (median) (particle phase)	0.002-0.08 (for BFRs)	Method: a high-volume air sampler with quartz fiber filters, GC/MS ECNI Laboratory blanks, recovery spike samples and field blanks were included. The average BFR surrogate recoveries were 93%. The average BFR recoveries for the spikes recovery samples were 85% Benchmark (particle phase): PentaBDE (BDE-47/99): 0.07–6.8 pg/m^3 (DF:100%, n=34; after its inclusion to the SC in 2009) BDE-209: 0.12–6.8 pg/m^3 (DF:100%, n=34; before its inclusion to the SC in 2017) ∑DP: 0.05 – 5.03 pg/m^3 (DF:100%, n=34; before its inclusion to the SC in 2023) TBPH concentration in the Arctic air (particle phase) is higher than the concentrations of POP substances. TBB and TBPH were the dominant non-PBDE BFRs measured in these samples and TBPH comprised ~17% of ΣBFR concentrations from a total of 45 BFRs	Salamova *et al.*, 2014
Alert, Nunavut, Canadian Arctic (82° 30' N, 60° 20' W)	2006 – 2007	14	21% (3/15)	0.13–1.5 0.8 (mean) 0.69 (median) (gas and particle phases)	1.2 (gas and particle phases)	Method: super high-volume air sampler (Super-HiVol)-GFFs-PUFs, GC/MS in NCI mode Recoveries in the range of 68%–103% TBPH was detected above the blank and above the MDL so that no blank correction or recovery adjustment was made	Xiao *et al.,* 2012a

Location	Year(s)	n	Nbr or % of detect	Concentration range (pg/m^3)	MDL (pg/m^3)	Remarks	Reference
Nam Co Lake, Tibetan plateau (30° 46.44' N, 90° 59.31' E, 4730 m above the seal level)	October 2006 to February 2008	15	53% (8/15)	0.049–1.7 0.38 (mean) 0.27 (median) (gas and particle phases)		Benchmark (gas and particle phases): PentaBDE (BDE-99): 0.06–5.3 pg/m^3 (before its inclusion to the SC in 2009) Method: Flow-Through Sampler (FTS), GC/HRMS in EI positive mode TBPH was detected above the blank and above the MDL so that no blank correction or recovery adjustment was made Benchmark (gas and particle phases): PentaBDE (BDE-99): 0.21–1.2 pg/m^3, before its inclusion to the SC in 2009 OctaBDE (BDE-196/197/203/204/205): 0.00034–1.0 pg/m^3, before its inclusion to the SC in 2009 Concentrations of TBPH in air (gas and particle phases) from Alert and Nam Co Lake are in the same range as those of POP substances and before their inclusion to the SC TBPH concentrations at both sampling sites show decreasing trends during the sampling campaign	
Arctic Ocean (Samples A11 to A13 situated at ca. 690 km to 1049 km from the Coast)	June to September 2010	3	1/3	<0.16 – 0.36 (gas phase)	0.16 (air column and filter)	Method: GFF and PUF/Amberlite XAD-2 resin, GC/MS ECNCI Recoveries of the surrogates: 78 – 95 % (± 32 – 57 %) TBPH was not detected in any blanks Uncertainty on the concentration values as the actual recovery of TBPH is not reported Benchmark (gas phase): BDE-209: nd – 0.56 pg/m^3 (2/3) *Syn*DP: 0.01 – 0.17 pg/m^3 (3/3) *Anti*DP: nd – 0.25 pg/m^3 (2/3) Concentrations of TBPH in the gas phase are in the same range as those of POP substances and before their inclusion to the SC	Möller *et al.,* 2011b

Location	Year(s)	n	Nbr or % of detect	Concentration range (pg/m^3)	MDL (pg/m^3)	Remarks	Reference
			0/3	<0.16 (particulate phase)		Benchmark (particulate phase): BDE-209: 0.19 – 3.43 pg/m^3 (3/3) *Syn*DP: 0.01 – 0.02 pg/m^3 (3/3) *Anti*DP: 0.01 – 0.02 pg/m^3 (3/3)	
East Greenland Sea (69–80.5°N) Samples A1 (195 km from the Greenland Coast) and A8 (245 km from the Svalbard Coast) are the most remote ones	August and September 2009	10	0% 40%	n.d. (gas phase) n.d. – 0.08 (particulate phase)	0.009 (for both dissolved and particulate phases)	Method: GFF and PUF/Amberlite XAD-2 resin, GC/MS ECNCI TBPH was not detected in field blanks Recovery determined by spike tests with the surrogate standard ^{13}C-BDE-77: 73±12% for non-PBDE BFRs Uncertainty on the concentration values as the actual recovery of TBPH is not reported Benchmark (gas phase): PentaBDE (BDE-47/99): nd–0.82 pg/m^3 BDE-209: nd Benchmark (particulate phase): PentaBDE (BDE-47/99): 0.01–0.32 pg/m^3 BDE-209: nd–0.07 pg/m^3 Concentrations of TBPH in air (gas and particulate phases) are in the same range as those of POP substances	Möller *et al.,* 2011a
King George Island, South Shetland Islands, West Antarctic (62°13′12″S, 58°57′48″W)	2011 to 2018	94 (total samples for all 12 NBFRs)	30%	n.d. – 0.098 (gas and particle phases)	0.002–0.06 (LOD for EHTBB and TBPH)	Method: A high-volume active air sampler (HV-AAS) coupled with GFF and polyurethane foam (PUF) plug, HRGC/HRMS in positive electron impact (EI+) mode The average recoveries of BDE-77 and BDE-128 in GFF matrix blanks were 92 ±14% and 90 ± 6% and in PUF matrix blanks were 92 ±8% and 86 ± 8%, respectively TBPH relative gas/particle distribution: ca. 50/50. No field blanks, only lab and GFF and PUF matrix blanks which are considered to be ‘cleaned’. It is unlikely that there was any contamination from the field considering the results are in line with those of Möller *et al.,* 2012 study	Zhao *et al.,* 2020

Location	Year(s)	n	Nbr or % of detect	Concentration range (pg/m^3)	MDL (pg/m^3)	Remarks	Reference
Oceanic Southern hemisphere	November 2010 to March 2011	8	0/8	<1.2 (gas phase, non-detected due to high contamination level in the air column)	1.2 (air column)	Method: GFF and PUF/Amberlite XAD-2 resin, GC/MS ECNCI Recoveries of the target analytes of 86 ± 19% and relative recoveries corrected by the surrogates of 101 ± 16% TBPH mean blank value: 120 ±160 pg (air column) and n.d. (air filter)	Möller *et al.,* 2012
(South West Australia to Antarctica: Samples A7 to A14)			7/8	<0.025 – 1.5 (particulate phase)	0.025 (air filter)	Benchmark (particulate phase): BDE-209: nd – 6.5 pg/m^3 (1/8), after its inclusion to the SC in 2009 *Syn*DP: 0.12 – 1.6 pg/m^3 (8/8) *Anti*DP: 0.12 – 0.56 pg/m^3 (8/8) Concentrations of TBPH in the particulate phase are in the same range as those of POP substances and before their inclusion to the SC	

Table A2: Monitoring data from remote areas – Seawater samples

Location	Year(s)	n	Nbr or % detect	Concentration range (pg/L)	MDL (pg/L)	Remark	Reference
Western Pacific to the Arctic Ocean (TBPH was detected in the Bering Sea, sample W2 located at ca. 400 km from the Russian Coast)	July to September 2010	18	1/18	<0.089 – 0.22 (dissolved phase, maximum value from sample W2)	0.089 (water column and filter)	Method: GFF (GF/C, pore size: 1.2 µm) following self-packed Serdolit PAD-3 glass column, GC/MS ECNCI Recoveries of the surrogates: 78 – 95 % (± 32 – 57 %) TBPH was not detected in any blanks Uncertainty on the concentration values as the actual recovery of TBPH is not reported Benchmark (dissolved phase): BDE-209: nd – 0.18 pg/L *Syn*DP: 0.003 – 0.22 pg/L *Anti*DP: nd – 0.14 pg/L Concentrations of TBPH in the seawater are in the same range as those of POP substances and before their inclusion to the SC	Möller *et al.,* 2011b
East Greenland Sea (69–80.5°N) Depth: ca. 11 meters Samples W7 (215 km from the Greenland Coast) and W10 (225 km from the Svalbard Coast) are the most remotes	August and September 2009	16	25% 6%	n.d. – 0.21 (dissolved phase, maximum value from sample W10) n.d. (particulate phase, n.d. in samples W7 and W10 but detected in sample W16)	0.013 (for both dissolved and particulate phases)	Method: GFF and glass column packed with Serdolit PAD-2, GC/MS ECNCI TBPH was not detected in field blanks Recovery determined by spike tests with the surrogate standard ^{13}C-BDE-77: 73±12% for non-PBDE BFRs Uncertainty on the concentration values as the actual recovery of TBPH is not reported Benchmark (dissolved phase): PentaBDE (BDE-47/99): nd–0.06 pg/L BDE-209: nd–0.37 pg/L Benchmark (particulate phase): PentaBDE (BDE-47/99): nd BDE-209: nd–0.11 pg/L Concentrations of TBPH in the seawater are in the same range as those of POP substances	Möller *et al.,* 2011a Zhiyong personal communication, May 2025

Location	Year(s)	n	Nbr or % detect	Concentration range (pg/L)	MDL (pg/L)	Remark	Reference
South Atlantic Ocean Surface seawater From Cape Town (South Africa) to Rio de Janeiro (Brazil). The cruise covered 34°S/17°E – 25°S/38°W in five stretches with approximately 3.5 days/stretch Stretch 3 sample is the most remote stretch (located in the middle of the Ocean; stretch length: 1000 km)	February to March 2016	1	1/1	14.497 (dissolved phase; Stretch 3)	0.252 (LOQ)	Method: Silicone Rubber (SR) Dynamic Passive Sampling (DPS), GC/MS TBPH recovery: 206±41% Field/control/procedural blanks were used TBPH was found in the field blanks at 42 pg/sample Blank values higher than the LOQ were subtracted from the corresponding value of the exposed sample The authors concluded that the deployment time in this study might not be long enough to capture sufficient amount of compounds in the sampler to be quantifiable The results of this study are considered to be semi-quantitative considering the high contamination in the field blanks. Benchmark (dissolved phase, Stretch 3 sample): PentaBDE (BDE-47/99): 0.593–1.545 pg/L *Syn*-DP: 1.471 pg/L *Anti*-DP: <0.083 pg/L Before the inclusion of DP to the SC in 2023 Concentration of TBPH in the Ocean is higher than those of POP substances	Sobotka *et al.,* 2021

Table A3: Monitoring data from remote areas – Sediment samples

Location	Year(s)	n	% detect	Concentration range	MDL (pg/g)	Remark	Reference
Surface sediment (1-2 cm) from western Pacific Ocean deep sea trenches (Mariana, Mussau and New Britain) MT-1 samples situated at 320 km from Guam at a water depth of 10853.2 m	December 2016 to January 2019	8	100%	Detected	5.53	Method: GC-MS/MS in electron ionisation mode Sample recoveries (mean ± standard deviation (SD)) were 92% ± 27% for NBFRs Procedural blanks included. NBFRs were not detected or below the MDL in the blanks Limited industrial activities in Papua New Guinea and Guam, the pollutant input from such sources was expected by the authors to be low	Xie et *al.,* 2023

Table A4: Monitoring data from remote areas – Soil samples

Location	Year(s)	n	% detect	Concentration range (pg/g dw)	MDL (pg/g dw)	Remark	Reference
Chinese Antarctic GreatWall Station and surrounding Fildes Peninsula area in West Antarctica	January 2014	7	71%	n.d.–20.22 7.94±7.92 (mean)	0.0042–178 for all BFRs	Method: GC/MS ECNI The sample recoveries of the internal standards were in the range of 32.8–112.8% (average 85.1%) No specific standard for TBPH was used Laboratory blanks included. TBPH was not detected in the blanks Uncertainty on the concentration values as the actual recovery of TBPH is not reported	Xiong et *al.,* 2021

Table A5: Monitoring data from remote areas – Vegetation/mushroom samples

Location	Year(s)	n	% detect	Concentration range| (pg/g dw)	MDL (pg/g dw)	Remark	Reference
Chinese Antarctic GreatWall Station and surrounding Fildes Peninsula area in West Antarctica	January 2014	9	67%	Moss (*Sanionia uncinata*): n.d.–484.1 115.4±160.2 (mean)	0.0042–178 for all BFRs	Method: GC/MS ECNI The sample recoveries of the internal standards were in the range of 42.5–126.7% (82.9%) for mosses, and 46.0–101.0% (78.4%) for lichens No specific standard for TBPH was used Laboratory blanks included. TBPH was not detected in the blanks Uncertainty on the concentration values as the actual recovery of TBPH is not reported TBHP was one of the two mains contributing NBFRs in moss among the nine NBFRs studied	Xiong et *al.,* 2021
		8	0%	Lichen (*Usnea aurantiaco-atra*): n.d.			

Table A6: Monitoring data from remote areas – Biota samples (excluding vegetation/mushroom)

Location	Year(s)	n	% detect	Concentration range	MDL	Remark	Reference
Svalbard	2012	20	95%	Polar bear (*Ursus maritimus*) plasma: 0.15±0.16 ng/mL (mean)		Method: GC/MS No recovery reported for TBPH while the extraction method uses a strong acid, to which TBPH has been	Harju *et al.,* 2013

Location	Year(s)	n	% detect	Concentration range	MDL	Remark	Reference
				Lipid content: 0.9%		reported as being unstable. Sulfuric acid can break phthalates and thus the concentrations of TBPH reported in this study can be significantly underestimated Laboratory blanks included, no field blanks MDL not specified Benchmark: Polar bear plasma: PentaBDE (PBDE-47): 0.10±0.08 ng/mL (mean; DF:100%, n=20; after its inclusion to the SC in 2009)	
Kongsfjord, Svalbard	2012	10	10%	Ringed seal (*Phoca hispida*) plasma: 0.04 ng/mL (mean) Lipid content: 0.7%		Ringed seal plasma: PentaBDE (PBDE-47): 0.08±0.02 ng/mL (mean; DF:100%, n=10)	
Kongsfjord, Svalbard	2012	12	17%	Glaucous gull (*Larus hyperboreus*) plasma: 0.026±0.001 ng/mL (mean) Lipid content: 14.4%		Glaucous gull plasma: PentaBDE (PBDE-47): 2.28±1.7 ng/mL (mean; DF:100%, n=12)	
Kongsfjord, Svalbard	2012	12	100%	Kittiwake (*Rissa Tridactyla*) egg 0.10±0.09 ng/g ww (mean) Lipid content: 8.1%		Kittiwake egg: PentaBDE (PBDE-47): 2.68±0.78 ng/g ww (mean; DF:100%, n=12)	
Kongsfjord, Svalbard	2012	12	58%	Common Eider (*Somateria mollissima*) egg: 0.06±0.07 ng/g ww (mean) Lipid content: 17.4%		Common Eider egg: PentaBDE (PBDE-47): 0.12±0.06 ng/g ww (mean; DF:100%, n=12)	
Svalbard	2012	10 or 3 (unclear from the report)	10 %	Atlantic Cod (*Gadus morhua*) liver: 0.07 ng/g ww (mean) Lipid content: 50.5%		Atlantic Cod liver: PentaBDE (PBDE-47): 0.41±0.42 ng/g ww (mean; DF:100%, n=10)	

Location	Year(s)	n	% detect	Concentration range	MDL	Remark	Reference
Svalbard	2012	1	0	Polar Cod (*Boreagadus saida*) whole fish: <MDL (mean) Lipid content: 1.7%		Polar Cod whole fish: PentaBDE (PBDE-47): 0.19 ng/g ww (mean; DF:100%, n=1)	
Kongsfjorden, Svalbard	2009	10	90% 9/10	Capelin (*Mallotus villosus*) whole fish, females and males: <0.120–1.306 ng/g ww 0.719±0.292 ng/g ww (mean) 33.65 ng/g lw (mean) Lipid content: 2.6%	For all BFRs: the detection limit varied from 0.0005 to 0.292 ng/g ww	Method: not specified Recoveries for labelled PBDEs: 67 and 120% Control samples and laboratory blanks included. No blank contamination was detected. No field blanks were used. Exact concentrations expressed as ng/g lw were communicated by the author.	Sagerup *et al.* 2010 Sagerup personal communication, May 2025
Kongsfjorden, Svalbard	2009	10	60% 6/10	Common Eider (*Somateria mollissima*) liver, female adults: <0.142–3.754 ng/g ww 1.652±1.396 ng/g ww (mean) 44.29 ng/g lw (mean) Lipid content: 3.7%			
Kongsfjorden, Svalbard Bjørnøya (or Bear Island), Norwegian Svalbard Archipelago	2008 2008	5 5	70% 7/10 (total)	Brünnich's guillemot (*Uria lomvia*) egg : <0.106–3.414 ng/g ww 1.799±1.358 ng/g ww (mean) 19.17 ng/g lw (mean) Lipid content: 11%			
Kongsfjorden, Svalbard	2009	10	50% 5/10	Black-legged Kittiwake (*Rissa Tridactyla*) liver, Adult males and females: <0.171–1.398 ng/g ww 0.800±0.356 ng/g ww (mean) 14.62 ng/g lw (mean) Lipid content: 5.5%			

Location	Year(s)	n	% detect	Concentration range	MDL	Remark	Reference
Tempelfjorden, Svalbard	2007	10	60% 6/10	Ringed seal (*Phoca hispida*) liver, adult males and females (5-19 years old): <0.138–0.876 ng/g ww 0.573±0.198 ng/g ww (mean) 16.36 ng/g lw (mean) Lipid content: 3.5%			
Van Mijenfjorden, Svalbard	2007-2008	10	0% 0/10	Arctic fox (*Vulpes lagopus*) liver adult males and females (3-14 years old): <0.142 ng/g ww Lipid content: 7.1%			
Hornsund / Storfjorden, Svalbard	2008	10	0% 0/10	Polar bear (*Ursus maritimus*) plasma, adult males (5-23 years old): <0.292 ng/g ww Lipid content: 0.9%			
Canadian Arctic:			19% (total samples)	Concentrations refer to geometric mean concentrations expressed as ng/g lw	0.006 ng/mL	Method: GC/MS ECNI Recovery of TBPH in the range of 95.6-118%. TBPH has never been detected in lab blanks (Houde personal communication, May 2025). Interlab comparison of results was performed leading to good agreement with all analytes quantified to within ±15% of certified values Blubber lipid content was consistently >90% 80% of sampled animals were females and juvenile males	Houde *et al.,* 2017
Arctic Bay, Lancaster Sound	2009	10		Ringed Seal (*Phoca hispida*) blubber: <MDL		Benchmark: PentaBDE (BDE-47 and BDE-99): 0.12–1.33 ng/g lw (n=10; PentaBDE was included to the SC in 2009))	
Resolute Bay, Lancaster Sound	2009–2013	42		<MDL–0.34		PentaBDE (BDE-47 and BDE-99): n.d.–7.43 ng/g lw (n=49)	

Location	Year(s)	n	% detect	Concentration range	MDL	Remark	Reference
Sachs Harbour, Beaufort Sea	2010–2013	34		<MDL–0.19		PentaBDE (BDE-47 and BDE-99): 0.05–11.7 ng/g lw (n=34)	
Gjoa Haven	2009	6		<MDL		PentaBDE (BDE-47 and BDE-99): 0.88–9.12 ng/g lw (n=67)	
Central East Greenland (closed to 70°N)	2012	3	24% (total samples)	Black guillemot (*Cepphus grylle*) eggs: 0.061 ng/g ww (mean) 0.050 – 0.066 ng/g ww 0.61 ng/g lw (mean) 0.48 – 0.67 ng/g lw Lipid content: 10.2%	0.024–0.025 ng/g ww	Method: GC/LRMS ECNI TBPH recovery in spikes samples: 96–137% The concentrations were corrected for those in non-spiked samples. Procedural blanks included Unclear how the MDL was derived Detection frequencies for total samples: BDE-47 (100%), *Syn*DP (95%) and *Anti*DP (100%) Benchmark: Black guillemot eggs: *Syn*DP: 0.005–0.030 ng/g ww or 0.048–0.28 ng/g lw (n=4; before its inclusion to the SC in 2023) *Anti*DP: 0.010–0.19 ng/g ww 0.096–1.78 ng/g lw (n=4; before its inclusion to the SC in 2023) Concentrations of TBPH in Black guillemot eggs are in the same range as those of POP substances before their inclusion to the SC	Vorkamp *et al.,* 2015
		4		Glaucous gull (*Larus hyperboreus*) liver: <0.025 ng/g ww <0.74 ng/g lw Lipid content: 5.28%	0.024–0.025 ng/g ww	Glaucous gull liver: *Syn*DP: 0.010–0.041 ng/g ww or 0.19–0.63 ng/g lw (n=4) *Anti*DP: 0.066–0.18 ng/g ww or 1.24–2.89 ng/g lw (n=4)	
		5		Ringed seal (*Pusa hispida*) blubber <0.14 ng/g ww <0.15 ng/g lw Lipid content: 93.1%	0.13–0.14 ng/g ww	Ringed seal blubber: PentaBDE (BDE-47): 20.1–36.3 ng/g ww or 21.7–39.1 ng/g lw (n=5; after its inclusion to the SC in 2009) *Syn*DP: <0.013–0.42 ng/g ww or <0.014–0.45 ng/g lw (n=5) *Anti*DP: 0.035–1.84 ng/g ww or 0.038–1.96 ng/g lw (n=5)	

Location	Year(s)	n	% detect	Concentration range	MDL	Remark	Reference
		5		Polar bear (*Ursus maritimus*) adipose tissue 0.26 ng/g ww (mean) <0.128 – 0.402 ng/g ww 0.39 ng/g lw (mean) <0.14 – 0.44 ng/g lw Lipid content: 86.4%	0.13 ng/g ww	Polar bear adipose tissue: *Syn*DP: 0.013–0.030 ng/g ww or 0.015–0.039 ng/g lw (n=5) *Anti*DP: 0.028–0.079 ng/g ww or 0.030–0.10 ng/g lw (n=5) Concentrations of TBPH in Polar bear adipose tissue are in the same range as those of POP substances before their inclusion to the SC	
West Greenland		4		Ringed seal (*Pusa hispida*) <0.13 ng/g ww <0.14 ng/g lw Lipid content: 94.2%	0.12–0.13 ng/g ww	Ringed seal blubber: PentaBDE (BDE-47): 2.64–10.9 ng/g ww or 2.89–11.4 ng/g lw (n=4) *Syn*DP: 0.014–0.030 ng/g ww or 0.015–0.032 ng/g lw (n=4) *Anti*DP: 0.053–0.083 ng/g ww or 0.058–0.087 ng/g lw (n=4)	
Western Pacific Ocean deep sea trenches (Mariana, New Britain) MT-2 samples situated at 310 km from Guam at a water depth of 6025 m	December 2016 to January 2019	10	19%	Amphipod (*Alicella gigantea*): Detected	5.53 pg/g	Method: GC-MS/MS in electron ionisation mode Sample recoveries (mean ± standard deviation (SD)) were 92% ± 27% for NBFRs Procedural blanks included. NBFRs were not detected or below the MDL in the blanks Limited industrial activities in Papua New Guinea and Guam, the pollutant input from such sources was expected by the authors to be low	Xie et *al.*, 2023