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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) (i)

技术工作：审议拟议列入《公约》附件 A、B 和/或 C 的化学品：十溴二苯乙烷（DBDPE）及其相关物质溴化 1,1'-乙烷-1,2-二基双苯

关于将十溴二苯乙烷（DBDPE）及其相关物质溴化 1,1'-乙烷-1,2-二基双苯列入《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. 挪威政府已根据《关于持久性有机污染物的斯德哥尔摩公约》第 8 条第 1 款，提交了一项关于将十溴二苯乙烷（DBDPE）及其相关物质溴化 1,1'-乙烷-1,2-二基双苯列入《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。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；

(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。

* UNEP/POPS/POPRC.22/1。

** 本文件英文原文未经正式编辑。

附件*

关于将十溴二苯乙烷（DBDPE）及其相关物质溴化 1,1'-乙烷-1,2-二基双苯列入《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. 十溴二苯乙烷（DBDPE）是一种溴化芳香族阻燃剂，由两个被五个通过中心乙烷部分连接的溴原子完全取代的苯环组成。溴化二苯乙烷，包括十溴二苯乙烷和相关的 UVCB 物质[1]（溴化 1,1'-乙烷-1,2-二基双苯），是广泛使用的非反应型溴化阻燃添加剂。其广泛用途涵盖电气和电子设备、汽车零部件、建筑和施工材料以及纺织品。过去十年，全球产量和使用量显著增长，主要是作为 2017 年列入《斯德哥尔摩公约》的十溴二苯醚的替代品（欧洲化学品管理局，2024a）。

2. 十溴二苯乙烷在欧洲联盟按照《化学品注册、评估、许可和限制条例》注册，每年进口量在 10 000 至 100 000 吨之间。根据欧洲化学品管理局（2024a）的数据，溴化二苯乙烷占欧盟市场上芳香族溴化阻燃剂估计总吨数的 43%。美国也大量生产或进口（2016–2019 年为 9 000–45 000 吨/年，美国环保局，2020）。估计加拿大每年进口 1 000–10 000 吨（加拿大环境与气候变化部和加拿大卫生部，2019），澳大利亚每年进口 120 吨（澳大利亚工业化学品引入管理署，2021）。中国是十溴二苯乙烷的主要生产国，2012 年产量占全球产量的 50%以上。2006 年至 2016 年间，中国生产了约 230 000 吨十溴二苯乙烷，其中约 20%（39 000 吨）含十溴二苯乙烷的产品形式出口。到 2026 年，出口量预计将增加到 100 000 吨/年，主要包含在出口电子设备（EEE）中（Liu 等人，2026）。溴化 1,1'-乙烷-1,2-二基双苯已在《化学品注册、评估、许可和限制条例》下注册，产量为 1–10 吨/年。

3. 国际上的监管审查有所增加。2025 年，由于具有高持久性和高生物积累性（vPvB）特性，十溴二苯乙烷在欧盟被确定为高度关注物质（SVHC）（欧洲化学品管理局，2025）。包括加拿大和澳大利亚在内的几个司法管辖区已经通过或宣布了带有豁免的禁令（加拿大环境与气候变化部和加拿大卫生部，2025；澳大利亚工业化学品引入管理署，2022）。美国继续根据美国《有毒物质控制法》评估该物质，而大多数亚洲国家尚未出台国家法规。

4. 十溴二苯乙烷没有已知的自然来源，但已在空气、地表水、沉积物、生物群和人等所有环境区间以及偏远的北极和南极区域检测到该物质（北极监测和评估方案，2016；欧洲化学品管理局，2025）。在偏远地区的空气、雪、土壤和生物群样本中广泛检测了该物质，证明发生了远距离大气迁移。已在 1989 年至 2011 年意大利马焦雷湖的测年沉积物柱样（Poma 等人，2014）以及 2011 年至 2018 年渤海软体动物（Wang 等人，2021）中观察到增加趋势。在环境样

* 本文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] 成分未知或可变的物质、复杂反应产物或生物材料。

本中，检测到的十溴二苯乙烷含量通常高于其他新型溴化阻燃剂（Wang 等人，2023a）。

5. 据报道，使用寿命期间的释放量若以室内灰尘含量衡量，在 307-540 000 纳克/克范围内；若以污水污泥衡量，在低于检测限度至 220 纳克/克干重范围内；若以生物群（鱼类和贻贝）中含量衡量，在低于检测限度至 3 300 皮克/克脂重范围内（欧洲化学品管理局，2024a，附录 G）。据报告，职业接触工人的血清含量为 87–54 400 纳克/克脂重，表明存在长期接触（Wang 等人，2019a）。

6. 根据现有数据，可以认为十溴二苯乙烷符合《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。十溴二苯乙烷还可能导致在环境中形成具有持久性、生物积累性和固有毒性的转化产物（溴化程度较低的二苯乙烷类化合物）。

7. 为了评估十溴二苯乙烷，使用了用于识别高度关注物质的辅助文件（欧洲化学品管理局，2025）中的信息，以及来自同行评审的科学期刊和灰色文献的信息。欧洲化学品管理局（2025）充分介绍了未发表的研究，作者可以在识别高度关注物质的过程中获得完整的研究报告。经合组织 TG 443（未发布，2026）未被纳入此前的评估，且仅提供了摘要。

化学特性

8. 溴化二苯乙烷包括十溴二苯乙烷，该物质在欧洲化学品管理局化学品数据库的公开注册档案中注册为单一成分。该组物质还包括溴化 1,1'-乙烷-1,2-二基双苯，注册为UVCB物质，其中含有十溴二苯乙烷，含量高于0.1%（质量分数），以及其他结构相似的同系物（欧洲化学品管理局，2024a）。

表 1. 十溴二苯乙烷（DBDPE）的化学特性

化学文摘社编号：	84852-53-9
国际化联名称：	1,1'-(乙烷-1,2-二基)双(五溴苯)
欧盟委员会编号：	284-366-9
欧盟委员会名称：	1,1'-(乙烷-1,2-二基)双(五溴苯)
分子式：	$C_{14}H_4Br_{10}$
分子量：	971.226 克/摩尔
别名：	1,1'-(乙烷-1,2-二基)双[2,3,4,5,6-五溴苯]； 1,2-双(五溴苯基)乙烷； 1,1'-(1,2-乙烷二基)双(2,3,4,5,6-五溴)-十溴二苯乙烷（DBDPE）； 1,2,3,4,5-五溴-6-[2-(2,3,4,5,6--五溴苯基）乙基]苯
商品名	十溴二苯乙烷、十溴二苯乙烷/RDT-3、Ecoflame B-971、Firemaster 2100 R、SAYTEX 4010 阻燃剂、SAYTEX 4010 ZD、SAYTEX 402 阻燃剂（不再销售）、SAYTEX 8010、SAYTEX 8010 阻燃剂、SAYTEX 8010 ZD、SLFR-2、YCFR-03

表 2. 部分物理化学性质概述

性质	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	无色或白色固体粉末	目视检查[2]
熔点/凝固点	350 °C	差示扫描量热法 [2]
蒸汽压	**20 °C 时 3.14 × 10^{-11}Pa** 20°C 时<1 × 10^{-4} 帕 3.8 × 10^{-9} 帕 20 °C 时 1.55 × 10^{-11}Pa 9.33 × 10^{-9} 帕 供比较：十溴二苯醚 21°C 时为 4.63 × 10^{-6} 帕，熔点为 300–310°C	**采用值**：经合组织 TG 104 蒸气压–逸出法：等温热重法（澳大利亚工业化学品引入管理署，2021） 经合组织 TG 104，蒸汽压–旋转转子法 [2] Wania 和 Dugani（2003）的预测 COSMOtherm 预测（Glüge 和 Scheringer，2023） 根据 AEROWIN v1.00 预测（欧盟委员会，2002）
水溶性	**20 °C 时<0.05 微克/升十溴二苯乙烷** 25 °C 时 0.72 微克/升 25 °C 时<0.05 微克/升 20°C 时 0.00000867 微克/升 供比较：十溴联苯醚为 25°C 时<0.1 微克/升	**采用值**：经合组织 TG 105 水溶解度–柱洗脱法 美国环保局 OPPTS 830.7860（水溶解度发生器柱法）[2] 经合组织 TG 105 水溶解度–柱洗脱法（澳大利亚工业化学品引入管理署，2021） COSMOtherm 预测（Glüge 和 Scheringer，2023） （欧盟委员会，2002）
正辛醇/水分配系数（log K_{OW}）	**9.23** 25°C 时 3.55 >6.50 9.89 20°C 时 9.23 供比较：十溴二苯醚为 6.27–9.19	**采用值**：COSMOtherm 预测（Glüge 和 Scheringer，2023） 发生器柱法 [2] 经合组织 TG 117 – 高效液相色谱法（澳大利亚工业化学品引入管理署，2021） 加拿大环境与气候变化部和加拿大卫生部预测，2019 COSMOtherm 预测（Glüge 和 Scheringer，2023） （欧盟委员会，2002）

[2] 84852-53-9 - ECHA CHEM 的搜索结果。

性质	数值[单位]	参考资料/信息来源
有机碳/水分配系数（log K_{OC}）	**6.86** 6.38 8.01 25 °C 时 6.54	采用值：经合组织 TG 106 [2] PCKOC v1.66 v2.00 预测 KOCWIN v2.00 预测，正辛醇/水分配系数为 9.23 COSMOtherm 预测（Glüge 和 Scheringer，2023）
正辛醇/空气分配系数（log K_{OA}）	**13.81** 20°C 时 16.66	采用值：KOAWIN v1.10 预测；使用正辛醇/水分配系数 = 9.23 和亨利常数 = 0.061 帕·立方米/摩尔（= 0.00000060 标准大气压·立方米/摩尔） COSMOtherm 预测（Glüge 和 Scheringer，2023）

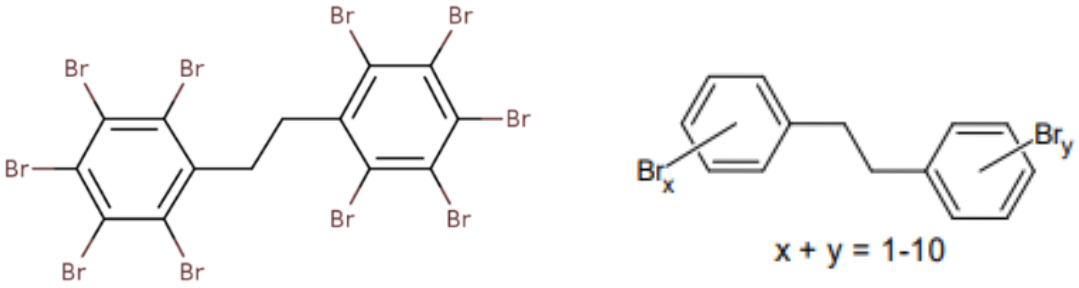

图 1. 十溴二苯乙烷（化学文摘社编号 84852-53-9）和 UVCB 物质溴化 1,1'-乙烷-1,2-二基双苯（化学文摘社编号 1092834-40-6）的结构式

2. 关于十溴二苯乙烷及其如何满足附件 D 筛选标准的信息

2.1 持久性

9. DBDPE 在环境区间中的化学性质非常稳定，并且在好氧和厌氧条件下的降解都非常有限。现有的筛选测试、模拟研究和实地观察一致表明，十溴二苯乙烷具有高度耐降解性，因此具有环境持久性。与十溴联苯醚（BDE-209）一样，在各种条件下也观察到脱溴现象，尽管 BDE-209 似乎比十溴二苯乙烷更容易脱溴。

10. 十溴二苯乙烷不含任何易于水解的官能团，因此预计降解不会是重要的非生物降解过程。其水溶解度极低（20°C 时约为 0.05 微克/升，欧洲化学品管理局，2025），有机碳/水分配系数高（6.86），进一步佐证了这一点；这会导致其强烈吸附于悬浮颗粒物和沉积物，极大限制其参与水相反应的可能性（未发表，2015a）。因此，认为水解作用对十溴二苯乙烷的环境意义不大。

11. 通过紫外/可见光吸收测量研究了空气中的光转化；测量结果表明十溴二苯乙烷在 290–295 纳米以上的波长处吸收较弱，说明在自然阳光条件下对直接光分解的敏感性较低（Dungey 和 Akintoye，2007）。使用 AOPWIN 进行的模型估计预测，与氢氧自由基反应的大气半衰期约为 4.5–6.7 天；然而，由于十溴二苯乙烷的蒸汽压非常低（20°C 时为 3.14×10^{-11}帕）并且与空气中的颗粒物强烈关联，因此认为气态光转化的环境意义有限（欧洲化学品管理局，2025）。由于十溴二苯乙烷的水溶解度低，尚未在纯净水中研究过光分解情况，预计其对十溴二苯乙烷而言的重要性有限。

12. 在实验室光分解研究中，使用人工紫外光和反应性基质（例如溶剂和腐殖酸/水体系）研究了十溴二苯乙烷在其他媒介中的光转化。研究表明，在高能辐照下，十溴二苯乙烷可以发生分步脱溴反应。例如，Wang 等人（2012）使十溴二苯乙烷在溶剂、腐殖酸/水体系和硅胶（模拟土壤区间）中接触紫外线，观察到快速转变，形成九溴至七溴二苯乙烷同系物。Kierkegaard（2004）、Granelli（2011）、Wei 等人（2012a）、Li 等人（2019）和 Klimm 等人（2019）也报告了类似的脱溴模式。Wang 等人（2010）使用紫外光产生十溴二苯乙烷脱溴产物并研究其吸收情况。接触紫外线后主要形成了脱溴产物，如九溴至七溴二苯基乙烷，尽管 Klimm 等人（2019）和 Li 等人（2019）观察到了一些含氧转化产物。此外，Zeng 等人（2025）证明了十溴二苯乙烷的光分解和脱溴，并以此来制备脱溴产物的参比标准品。相比之下，当将十溴二苯乙烷掺入塑料基质（高抗冲聚苯乙烯（HIPS））中并暴露在自然阳光下长达 224 天时，没有观察到母体化合物的可测量降解（Kajiwara 等人，2008），这表明光转化是依赖于基质的，并且在大多数环境设置下可能重要性有限，因为十溴二苯乙烷会分配到颗粒和沉积物中。总体而言，认为十溴二苯乙烷的光转化环境意义不大。

13. 十溴二苯乙烷在土壤和沉积物中具有高度持久性。在根据经合组织 TG 308 进行的水–沉积物模拟研究中，在室温下好氧或厌氧条件下六个月期间均未观察到相关降解，因此沉积物中的降解半衰期超过 180 天（未发表，2015b）。同样，根据经合组织 TG 307 在多种土壤类型中进行的两项土壤模拟研究表明，在好氧和厌氧条件下均没有显著降解，在所有情况下降解半衰期值均超过 180 天（未发表，2015c 和 2015d），从而满足附件 D 标准。此外，一项包括生长植物在内的土壤研究也表明转化没有增强，这说明植物与土壤的相互作用不会对十溴二苯乙烷的环境稳定性产生重大影响（未发表，2019）。

14. 易生物降解性与固有生物降解性研究支持了模拟研究的结果，表明十溴二苯乙烷既不易生物降解，也不具有固有生物降解性。在根据经合组织 TG 301C（未发布，1991）进行的易生物降解性测试中，根据氧消耗情况，未观察到生物降解，并且通过化学分析仅检测到极少的初级降解（~2%）。根据拟议的经合组织 TG 302D（未发布，2015e）进行的固有生物降解性测试显示，在好氧条件下 90 天后，矿化度仅为 2.2%，没有证据表明形成了降解产物（欧洲化学品管理局，2025 概述）。此外，根据经合组织 TG 314C（未发布，2011，概述于 ECHA，2025）对厌氧消化污泥的转化和矿化进行了测试，结果显示在 63 天内没有微生物介导的矿化，表明十溴二苯乙烷在厌氧废水处理条件下不会降解。

15. 生物体将十溴二苯乙烷转化为溴化程度较低同系物的情况已得到证实。Wang 等人（2010）观察了大鼠体内的生物转化。虽然观察到还原脱溴现象，但用 $MeSO_2$ 取代是主要的代谢途径。Wang 等人（2019b）观察到斑马鱼幼体中的十溴二苯乙烷转化，但未确定具体有哪些转化产物。Wang 等人（2022a）还观察到了斑马鱼幼体中的转化，并鉴定出九溴、八溴和七溴二苯乙烷脱溴产物以及其他溴化化合物。Wang 等人（2020a）表明，在蜗牛体内发生了脱溴，其中还原脱溴是主要途径，形成九溴至七溴和溴化程度更低的二苯乙烷同系物。Wang 等人（2022b）表明，白腐真菌（Pleurotus ostreatus）能够快速脱溴，在 5 至 25 毫克十溴二苯乙烷/升的浓度范围内，该菌株能够降解 48%至 38%的十溴二苯乙烷。浓度较高时，降解速度减慢，可能是因为毒性的缘故。细胞间酶（P450）和细胞外酶（例如漆酶和木质素过氧化物酶）都参与其中，其中漆酶

在降解中发挥着特别重要的作用。脱溴和羟化形成的降解产物是主要类型。Jiang 等人（2021）在蚯蚓体内和蚯蚓粪中均观察到了转化产物，对应于形成九溴至七溴和溴化程度更低的二苯乙烷同系物。其他类型的脱溴产物（如 OH 加合物）也可能已经形成，但没有对其进行鉴定。

根据附件 D 标准得出的持久性结论

16. 十溴二苯乙烷符合附件 D 的持久性标准，在沉积物和土壤中的降解半衰期超过六个月（>180 天）。该物质还在所有环境区间中均被检测到，包括北极和南极洲等偏远区域，这为其持久性提供了强有力的证据。根据高度关注物质附件十三（欧洲化学品管理局，2025），十溴二苯乙烷此前因其高持久性和高生物积累性特性而被确定为高度关注物质。

2.2 生物积累

17. 根据附件 D，在水生生物中生物浓缩系数（BCF）> 5 000 的物质符合生物积累性（B）标准，或者由于在其他物种中的高生物积累性或监测数据而符合标准。十溴二苯乙烷具有极强的疏水性（正辛醇/水分配系数 9.23；水溶解度 ~0.05 微克/升），会强烈分配到有机质，并对沉积物和土壤表现出非常高的吸附力（有机碳/水分配系数最高达 6.86），这限制了溶解接触，但使饮食和颗粒介导的吸收成为可能。

18. 多项实验室研究表明十溴二苯乙烷符合生物积累性标准。Burkhard 等人（2023）对虹鳟进行了经合组织 TG 305 饮食研究，欧洲化学品管理局（2025）后来根据这些结果对生物浓缩系数进行了建模。欧洲化学品管理局（2025）发现生物浓缩系数超过 5 000，净化缓慢，表明生物积累潜力很高。同样，当标准化为孔隙水时，用 Lumbriculus variegatus 进行的基于沉积物的测试得出的生物浓缩系数大于 5 000（Zhang 等人，2013）。

19. 监测数据显示，无脊椎动物、鱼类、两栖动物、爬行动物、鸟类、哺乳动物和人类（包括北极野生动物）体内存在十溴二苯乙烷，表明尽管其水溶性低，但仍被环境吸收（KLIF，2013；de Wit 等人，2020）。监测研究表明，通过食物发生的十溴二苯乙烷环境吸收超过了实验室环境中观察到的水平，这可能是十溴二苯乙烷的接触形式和接触持续时间造成的。欧洲化学品管理局 2025 第 3.4.3 章（监测数据和实地研究）详细描述了十溴二苯乙烷的监测和实地研究。据报道，在水生、陆地和河口食物网的一系列捕食者与猎物关系中，生物放大系数（BMF）大于 1，其数值最高达 28.5（Ding 等人，2022；Wu 等人，2024；Sun 等人，2024a），而其他研究报告的生物放大系数低于 1（Wu 等人，2023；Sun 等人，2023a）。在海洋食物网中也观察到营养放大现象，营养放大系数（TMF）高于 1（最高达 4.22–5.12；Hou 等人，2022[3]）。然而，其他研究报告了营养稀释现象（营养放大系数<1；例如 Liu 等人，2020），说明生物放大作用可能某些物种特有的，并取决于食物网结构和接触条件。

20. Burkhard 等人（2023）对接触十溴二苯乙烷以及其他几种卤代化合物（包括已确定的持久性有机污染物）28 天的虹鳟进行了一项经合组织 TG 305 饮食研究。十溴二苯乙烷的吸收率非常低且变化不定。十溴二苯乙烷等超疏水性物质往往吸收阶段非常缓慢，需要很长的时间才能达到平衡。十溴二苯乙烷

[3] Hou 等人（2022）的研究跨越了 2.14 个营养级。Kidd 等人（2018）认为，2.0 个营养级足以得出可靠的营养放大系数。

系以固体形式添加到饲料中且未溶解，这可能会降低其吸收。对吸收持续时间和通过饲料进行引入这种方式的关切得到了现有监测数据的支持，这些数据证明在广泛的生物群中存在吸收现象，而这项研究中的吸收量非常有限。消除似乎比吸收要快，消除速率常数（k_2）为 0.084，因此脂质标准化生物放大系数值低于 1。Brooke 和 Crookes（2012）提出，k_2 值< 0.085，即相当于生物浓缩系数为 5 000；这项研究得出的 k_2 值略低于该数值。由于存在这些关切，以及净化数据通常接近检测限并且没有考虑到生长稀释（测试期间鱼的重量增加了一倍），因此认为该研究不适合直接得出确定的生物放大系数值。作者得出的结论是，在实验室条件下预计不会发生生物放大作用，尽管这与几项报告十溴二苯乙烷的生物放大系数和营养放大系数大于 1 的实地研究相矛盾。

21. 欧洲化学品管理局（2025）采用与经合组织 TG 305 以及经合组织 GD 305 中描述的经合组织生物浓缩系数估算工具一致的动力学模型（其中纳入了脂质和生长校正），重新评价了 Burkhard 数据集。该模型得出的生物浓缩系数估计值大多大于 5 000，并证实净化缓慢（经生长校正的净化速率常数 $k_{2g}\approx$ 0.045/天；生物半衰期约为 15.5 天），与高度疏水、难溶物质的性质一致。尽管混合物接触设计存在固有的不确定性，但重新评估提供了强有力的支持证据，证明十溴二苯乙烷符合附件 D 的生物积累性标准。

22. Qiao 等人（2023）观察到斑马鱼中的组织特异性生物积累系数范围约为 6 500 至 12 900，并表明鱼子情况显示十溴二苯乙烷可以转移到后代。这项研究证明十溴二苯乙烷在多个组织中出现明显的浓度依赖性积累；研究是在受控实验室条件下进行的，并对接触水平进行了分析验证。研究中还观察到逐渐脱溴为九溴、八溴、七溴、六溴和五溴二苯乙烷。尽管接触水平高于环境相关水平，但内部浓度的分析结果具有一致性，并且符合高度疏水性物质的预期表现。该研究提供了生物积累的强有力证据。

23. Zhang 等人（2013）基于估算的孔隙水浓度进行校正后，计算得到 L. variegatus 从实地采集沉积物中摄取十溴二苯乙烷的生物浓缩系数值非常高。这项研究表明，尽管十溴二苯乙烷的水溶性低，从沉积物中迁移有限，但其仍能明显被组织吸收，生物浓缩系数对数值最高为 9.87，远超 5 000 的生物浓缩系数标准。接触体系没有严格遵循标准准则程序，在实现稳态方面仍然存在不确定性。由于孔隙水水平不是直接测量的（通过 SPME 纤维测量并反算），并且测试体系偏离了准则条件，因此所得到的生物浓缩系数仍然存在一些不确定性。据认为，这项研究不适合推导定量生物浓缩系数，但发现其支持关于高生物积累潜力的定性结论。

24. Zhou 等人（2023）进行的一项实验室食物网研究考察了十溴二苯乙烷在包括大型植物、软体动物和鱼类在内的构建群落中的生物积累性。生物积累系数对数值范围为 2.94 至 4.96，而营养放大系数小于 1，表明构建食物网内出现了生物稀释而不是生物放大。中华鳑鲏（鲤鱼）的生物积累系数对数值为 3.82 ± 0.329，超过了附件 D 中的生物积累阈值。然而，简化的营养结构和缺乏随着营养水平而增加的浓度表明尚未实现稳态生物放大作用。尽管上述挑战降低了结果的可靠性，但这项研究符合基本的分析质量标准，并支持高生物积累潜力的定性结论。

25. Wang 等人（2022a）使斑马鱼幼体接触 n-TiO_2（100 微克/升）和十溴二苯乙烷（0、1、10 或 100 微克/升）的水溶液 144 小时。仅在接触 10 或 100 微克/升十溴二苯乙烷（含或不含 n-TiO_2）的幼体中检测到十溴二苯乙烷的积累高

于检测限度。然而，在接触 100 微克/升十溴二苯乙烷和 n-TiO_2 的组中，十溴二苯乙烷浓度显著高于仅接触十溴二苯乙烷的组。同时接触颗粒物是有意义的，因为这可能更接近颗粒物自然出现在水体中的自然环境。由于其表面性质，颗粒可以吸收有机和无机污染物，导致生物利用率发生变化（Wang 等人，2022a）。Lu 等人（2026）的观察支持了这一点；他们观察到，十溴二苯乙烷在红脚鲣鸟的食物（鱼和鱿鱼）中的含量较低，但在采样的鸟类和环境塑料样本中发现十溴二苯乙烷的含量较高。他们得出的结论是，摄入塑料可能增加了鸟类体内的积累，这表明还有一种额外的非营养接触途径。然而，他们指出，这项研究只获得了五只死后被冲上海滩的鸟类样本，很难用于种群水平的推断。Wang 等人（2022a）和 Lu 等人（2026）的研究在总体评价中得到的权重较低。

26. Fremlin 等人的两项研究（2025a 和 2025b）评估了十溴二苯乙烷的生物积累潜力。2025a 研究使用十溴二苯乙烷作为模型物质来研究一种新方法，即如何将附件 D 的生物积累性标准注释 ii[4]用于难以测试的物质。这项研究应用了化学活性框架，得出的结论是，十溴二苯乙烷的生物积累不会达到令人关切的水平。需要指出的是，化学活性通常与急性基线毒性（也称为非极性麻醉作用）最为相关（Mackay 等人，2020），而慢性影响仍存在高度不确定性（欧洲化学工业生态学和毒理学中心，2016）。根据化学活性法，熔点极高的化合物不可能通过非极性麻醉作用产生毒性，而十溴二苯乙烷的熔点约为 350°C。这项研究还将毒性评估范围缩小到 58 项研究中的 14 项，排除了许多项报告生物学反应但缺乏经典剂量反应终点的研究。被排除的各项研究通常调查了“酶或激素反应、生物化学变化、器官组织病理学、行为反应和基因表达变化”。这些类型的影响对于十溴二苯乙烷很重要，如关于不利影响的章节所示，并且还预计非极性麻醉作用无法很好地描述这些影响。因此，这种筛选降低了该方法对微妙或慢性影响的敏感性，而这些影响可能与高度持久、溶解度低的化学物质更为相关。此外，这种拟议的方法将定量风险评估引入生物积累评估步骤中。这与监管机构对持久性、生物积累性、毒性/持久性有机污染物识别的一般理解（欧洲化学品管理局，2023）不一致，其中生物积累潜力是独立于风险进行评估的。

27. Fremlin 等人（2025b）的研究引入了结构化评分系统，用于评估实地营养放大系数/生物放大系数研究的可靠性。虽然该方法旨在将数据质量标准化，但删除了一半以上的现有研究，然后对生态多样性食物网的生物放大指标进行平均。这项研究得出的结论是，十溴二苯乙烷在环境中不会出现放大作用。由于生态系统和物种之间的积累情况差异很大，进行平均可能会掩盖在特定环境中观察到的真正生物放大作用。一些包括在其中的实地研究确实表明某些食物网中存在积累现象，即使其他食物网中不存在。

28. 实验动物研究表明，单次和重复口服接触后，十溴二苯乙烷吸收不良（未发表，2004；2012；2025，转引自欧洲化学品管理局，2025；Wang 等人，2010；Knudsen 等人，2017）。2025 年未发表的研究发现，接触 14 天后没有吸收，而 Wang 等人（2010）发现在接触 90 天后出现了吸收现象。这两项研究都使用了玉米油来溶解十溴二苯乙烷。Knudsen 等人（2017）使用的剂量为

[4] “表明该化学品有令人关注的其他原因的证据，例如在其他物种中的生物蓄积系数值较高，或具有高度的毒性或生态毒性；或”。

100 纳摩尔/千克（~0.01 毫克/千克[5]，n=4），低于未发表（2025）研究使用的 1001 000 毫克/千克剂量。Knudsen 等人（2017）也通过经口灌胃给药，但在 1 天和 10 天后观察到吸收现象。这些研究表明，较长时间重复接触会导致吸收量更高，但接触途径和剂量配方也很重要。在 Knudsen 等人（2017）的研究中，十溴二苯乙烷主要通过粪便消除，超过 90%的给药剂量在 72 小时内以原样回收，只有极少量的尿液排泄。大鼠静脉给药后，出现缓慢的排泄和在组织中的广泛滞留，72 小时后有 70%滞留在组织中。这表明全身半衰期为 55.8 天。根据欧洲化学品管理局的 PBT 指南 R.11（欧洲化学品管理局，2023），如果大鼠全身终末消除半衰期超过 4 天，即为支持生物积累性证据权重评估中高生物积累性质的证据。相比之下，在同一项研究中，静脉给药 72 小时后，30%的 BDE-209 仍保留在组织中，表明全身半衰期为 2.12.5 天。需要指出的是，十溴二苯乙烷的清除缓慢可能是高内部浓度下代谢和消除途径饱和造成的，从而表现出其本身具有缓慢清除特性的假象。皮肤接触 5 微升溶解在甲苯中的十溴二苯乙烷（浓度为 2.7 纳摩尔/平方厘米）后，也显示了吸收现象。17±10%的给药剂量被皮肤吸收，5±2%渗透皮肤并在内部组织中出现，这表明真皮吸收可以是总吸收量的一个来源。由于代谢有限且依赖于粪便消除，十溴二苯乙烷在被人体吸收后可能具有持久性。

29. 已有记录表明，在包括鸟类、两栖动物和海洋哺乳动物在内的野生动物中会出现母源转移（Zheng 等人，2018；Sun 等人，2023a；Sala 等人，2022）。研究还表明，十溴二苯乙烷会在人体中积累并通过母体转移，引发了人们对敏感生命阶段发生接触的关切；这一阶段特别值得关注，因为胚胎和新生动物极易受到接触异生物质的影响。已在人血清、脐带血、母乳、毛发和指甲中检测到这种物质（例如，Zhou 等人，2014，Leung 等人，2020，Hammel 等人，2024；Wang 等人，2020b；Wemken 等人，2020；Mannetje 等人，2013；Rawn 等人，2024；Tao 等人，2017；Schreder 等人，2023；Zhao 等人，2020b，Salah 等人，2026），且报道称职业接触工人体内的浓度特别高（Chen 等人，2019；Wang 等人，2019a）。

30. 会通过生物和非生物脱溴形成更具生物积累性的同系物，这一点已经得到证实。已经证明十溴二苯乙烷会以生物和非生物方式脱溴形成九溴、八溴、七溴、甚至六溴二苯乙烷，例如，Qiao 等人（2023），Jiang 等人（2021），Wang 等人（2012），Wang 等人（2020a）、Wang 等人（2022a）和 Zeng 等人（2025）。Wang 等人（2019c）观察到，接触 14 天后，十溴二苯乙烷给药组中有 88.2%的溴化化合物由转化产物组成。这些脱溴产物据认为比十溴二苯乙烷更具积累性，但有关十溴二苯乙烷脱溴产物性质的信息有限。然而，可以合理地预计，十溴二苯乙烷脱溴产物的生物积累潜力会增加，与 BDE-209 的脱溴产物类似。BDE-209 是一种结构非常相似的类似物，并且是一种公认的持久性有机污染物，依据是其母体物质具有生物积累性，且可转化为生物累积性更强、已列入《斯德哥尔摩公约》的低溴化二苯醚。

31. 诸多实验室研究和实地研究表明，十溴二苯乙烷具有很高的生物积累潜力，但并非所有现有的研究都一致表明这一点。几项研究报告称，在某些实验条件下生物浓度较低，甚至似乎出现营养稀释现象。然而，这些研究结果通常来自限制了环境相关性的研究设计，例如仅限于水中的接触途径、接触持续时间短，或者测试浓度超过了水溶解度。此类条件不适合评估十溴二苯乙烷这样

[5] Knudsen 等人（2018）报告的数值为 0.02 毫克/千克，但这似乎是一个印刷错误。

的高度疏水性物质。在证据权重框架内进行解释时，大于 1 的现有营养放大系数和生物放大系数值为生物放大作用提供了强有力的支持。有多条证据表明十溴二苯乙烷具有很高的生物积累潜力，包括消除半衰期长、在生物群（包括人类）中广泛检测到，以及在几个食物网中产生明显的生物放大作用。事实上，几项研究表明，十溴二苯乙烷的生物放大程度与已知的持久性有机污染物相仿，例如 BDE-209（持久性有机污染物审查委员会，2014）、中链氯化石蜡（欧洲化学品管理局，2021；de Wit 等人，2020）、短链氯化石蜡（欧洲化学品管理局，2008；de Wit 等人，2020）和 PCB-153（斯德哥尔摩公约，2001；Ding 等人，2022）。由于这些物质也在与十溴二苯乙烷相同的实地研究中进行了采样，因此该基准测试为确定十溴二苯乙烷具有生物积累性提供了强有力的佐证。此外，根据实地数据进行的摩尔浓度比较表明，如欧洲化学品管理局（2025）所述，十溴二苯乙烷的浓度与公认的高生物积累性物质浓度相似。综合来看，这些结果涵盖具有环境相关性的实验室研究、实地观察和毒代动力学证据，形成了一致的证据权重，证明十溴二苯乙烷符合附件 D 的生物积累标准。

根据附件 D 标准得出的生物积累性结论

32. 十溴二苯乙烷的生物浓缩系数>5 000、生物放大系数和营养放大系数>1、消除半衰期长、在生物群（包括顶级捕食者和人类）中广泛检测到，以及记录显示会产生母源转移，这些情况综合表明该物质符合附件 D 的生物积累标准。这一点的进一步佐证是，已根据《化学品注册、评估、许可和限制条例》附件十三（欧洲化学品管理局，2025），由于其高持久性和高生物积累性特性，将其认定为高度关注物质。

2.3 远距离环境迁移潜力

33. 监测数据：已在偏远地区的空气、冰雪和生物群中检测到十溴二苯乙烷。尽管十溴二苯乙烷的蒸汽压较低，但多份出版物报道，在偏远地点的空气中发现了这种物质。Salamova 等人（2014）在北极斯瓦尔巴群岛上检测到十溴二苯乙烷，浓度最高为2.2 皮克十溴二苯乙烷/立方米（2012–2013，n=34，检出频率（DF）88%；颗粒浓度）；Hao 等人（2020）检测到其浓度最高为 3.5 皮克十溴二苯乙烷/立方米（2014–2015，n=5，检出率 100%；被动空气采样器）；Halvorsen 等人（2020）检测到其浓度最高为 7.27 皮克十溴二苯乙烷/立方米（2022，n=26，检出率 17%；气体+颗粒）。Vorkamp 等人（2019）在格陵兰岛北部检测到的十溴二苯乙烷平均浓度为 3.1 皮克十溴二苯乙烷/立方米（2014 年每月，n=13，检测率 100%，气体+颗粒）和 9.7 皮克十溴二苯乙烷/立方米（2016 年春季，n=13，检测率 100%，气体+颗粒）。2011 年至 2018 年，南极洲每年都会检测到十溴二苯乙烷，最大浓度为 0.44–2.1 皮克十溴二苯乙烷/立方米（Zhao 等人，2020a；n=24/年，检出率 94%；颗粒+气相）。

34. 在挪威斯瓦尔巴群岛 Holtedahlfonna 北极偏远冰川的冰芯中检测到十溴二苯乙烷，并显示自 1988 年以来的近期冰芯部分中输入量几乎持续增长，约为 3.5 皮克/平方厘米/年，这表明在北极霾期间（3 月和 4 月），与颗粒结合的十溴二苯乙烷远距离迁移到该地点（Hermanson 等人，2010）。冰芯的采样地点位于斯匹次卑尔根岛西海岸的新奥勒松东北约 40 公里处。为便于分析，将冰芯进行了分样处理，包括将冰芯上部 34 米的连续部分合并为 6 个不同的样本，每个样本的液体体积为 1115 升。估计这一深度涵盖 1953 年至 2005 年期间。对十溴二苯乙烷（以及其他 18 种溴化阻燃剂）的分析结果表示为以纳克/升为单位

的净浓度。通过将溴化阻燃剂的数量除以冰芯表面积（86.6 平方厘米）以及所分析的冰芯区段对应的年份，将结果换算为通量（皮克/平方厘米/年）。为了考虑运输、储存和其他处理（包括实验室中的处理）可能产生的背景污染，分析了两个更深的冰芯区段，其深度为 52.3 米至 59.2 米，对应的是使用溴化阻燃剂之间的时期，约为 1900 年至 1914 年。这些深层样本中的最大溴化阻燃剂浓度代表程序检出限或背景浓度，从冰芯上部 34 米的含量中减去了该浓度。在 1988–1995 年冰芯分样之前，十溴二苯乙烷的输入通量低于背景水平或未检出；在 1988–1995 年冰芯分样中，其输入通量约为 3.6 皮克/平方厘米/年，在对应 1995–2005 年冰芯表层也测得了类似水平（3.4 皮克/平方厘米/年）。

35. 在加拿大北极德文岛的雪芯样本中检测到十溴二苯乙烷，浓度最高为 0.024 纳克十溴二苯乙烷/升（Meyer 等人，2011；2005–2006；浓度以水当量表示）。2005 年在一个雪芯中检测到了十溴二苯乙烷（0.002 纳克十溴二苯乙烷/升，深度 1.1–1.75 米），2006 年在两个雪芯中检测到了十溴二苯乙烷（0.024 纳克十溴二苯乙烷/升，深度 0–0.75 米；0.00092 纳克十溴二苯乙烷/升，深度 3.2–4.2 米）。

36. Hao等人（2020）在北极斯瓦尔巴群岛的土壤中检测到十溴二苯乙烷，浓度最高为 0.147 微克/千克干重（n=10，检出频率 100%）。Xiong 等人（2021）在南极洲菲尔德斯半岛的土壤中检测到十溴二苯乙烷，浓度最高为 0.19 微克十溴二苯乙烷/千克干重，检出频率为 100%（n=7）。地衣（n=8，检测频率=100%）和苔藓（n=9，检测频率=100%）中的水平范围约为 0.10.3 微克十溴二苯乙烷/千克干重（Xiong 等人，2021）。在喜马拉雅河谷距离主要道路 500 米至 1 公里处采集的样本中，十溴二苯乙烷也是存在于土壤和苔藓中的主要溴化阻燃剂（Chen 等人，2024）。

37. 已大西洋鳕鱼（G. morhua）肝脏中（n=10，检出频率=90%）测得十溴二苯乙烷浓度最高为 15 微克十溴二苯乙烷/千克脂重，在斯瓦尔巴群岛（北极）的北极鳕（B. saida）全身（n=1，检出频率=100%）测得十溴二苯乙烷浓度为 25 微克十溴二苯乙烷/千克脂重（KLIF，2013）。在来自斯瓦尔巴群岛的样本中也发现了该物质：在欧绒鸭（S. mollissima）的卵中（n=12，检出频率=100%）浓度最高为 12 微克十溴二苯乙烷/千克脂重，在三趾鸥（Rissa tridactyla）体内（n=12，检出频率=100%）浓度最高为 72 微克十溴二苯乙烷/千克脂重，在北极鸥（L.hyperboreus）血浆中（n=12，检出频率=100%）浓度最高为 76 微克十溴二苯乙烷/千克脂重（KLIF，2013）。

38. KLIF（2013）在斯瓦尔巴群岛的环斑海豹（P. hispida）血浆中（n=10，检出频率=100%）检测到十溴二苯乙烷浓度最高为 1 293 微克/千克脂重，在该地北极熊（U. maritimus）血浆中（n=20，检出频率=95%）检测到十溴二苯乙烷浓度最高为 4 300 微克/千克脂重。Vorkamp 等人（2015）在东格陵兰岛（北极）的环斑海豹脂肪中（n=5，检出频率=20%）测得十溴二苯乙烷浓度最高为 0.17 微克十溴二苯乙烷/千克脂重，在西格陵兰岛（北极）的环斑海豹脂肪中（n=4，检出频率=25%）测得其浓度最高为 0.33 微克十溴二苯乙烷/千克脂重。

39. Vorkamp 等人（2019）报告称，在格陵兰岛（北极）一个小湖的内陆红点鲑（S. alpinus）肌肉中（n=6，检出频率=100%）的十溴二苯乙烷浓度最高为 5.9 微克/千克脂重。他们还测得北极鸥肝脏中的十溴二苯乙烷含量最高为 0.561.0 微克十溴二苯乙烷/千克脂重（n=68，检出频率=2533%，格陵兰岛西北部和东部）。检测到十溴二苯乙烷的还有：环斑海豹脂肪（n=6，检出频率

=50%），最高为 0.68 微克十溴二苯乙烷/千克脂重；格陵兰海豹（P. groenlandicus）体内（n=4，检出频率=100%），最高为 1.6 微克十溴二苯乙烷/千克脂重；髯海豹（E. barbatus）体内，最高为 0.52 微克十溴二苯乙烷/千克脂重（n=5，检出频率=80%）；虎鲸（O. orca）体内（n=11，检出频率=9.1%），最高为 0.41 微克十溴二苯乙烷/千克脂重。

40. Sala 等人（2022）测量了北大西洋长须鲸（B. physalus）体内十溴二苯乙烷经胎盘转移情况，从而提供了通过洄游物种进行远距离迁移的潜力数据：母鲸脂（n=8，检出频率=62.5%）中的浓度最高为 1.61 微克十溴二苯乙烷/千克脂重，胚胎皮肤（n=8，检出频率=87.5%）中的浓度最高为 97.1 微克十溴二苯乙烷/千克脂重。十溴二苯乙烷存在于斯瓦尔巴群岛和挪威北部的四只虎鲸样本体内（范围<1.6012.9 纳克/克脂重，n=24，检出频率=16%）和一只座头鲸（M. novaeangliae）样本体内（3.39 纳克/克脂重，n=5，检出频率=20%）（Lippold 等人，2022）。

41. 建模：Dungey 和 Akintoye（2007）使用 AOPWIN v1.91（美国环保局，2012）估计气相十溴二苯乙烷的大气半衰期为 53.6 小时（4.5 天，每天 12 小时，1.5 × 10^6OH/立方厘米）。按照欧洲化学品管理局指南 R.16 章（欧洲化学品管理局，2016b）中的建议，使用较低浓度的羟基自由基（5 × 10^5OH/立方厘米），则得出的半衰期略高，为 6.7 天。模型预测 100%将吸附于空气颗粒物（AEROWIN v1.00；美国环保局，2012），并且吸附的部分可能会抵抗大气氧化。因此，基于与气相羟基自由基反应的 AOPWIN 半衰期值很可能低估了空气中十溴二苯乙烷的半衰期，因为十溴二苯乙烷吸附于颗粒物的部分可能会增加其停留时间和大气远程迁移的潜力。远离点源的偏远地区的监测数据证实了这一点。十溴二苯乙烷的大气半衰期为 4.5–6.7 天，超过了《斯德哥尔摩公约》中>2 天的标准，表明其具有远距离大气迁移的潜力。

42. 加拿大环境和气候变化部和加拿大卫生部（2019）在其对十溴二苯乙烷的评估中，使用经合组织总体持久性和 LRTP 筛选工具估计典型迁移距离（CTD）为 2 860 千米（Wengman 等人，2009），该距离低于判定阈值（5 097 公里，多氯联苯 28 的典型迁移距离）。他们还计算出总体持久性（Pov）为 277 天，转移效率（TE）为 12.7%，高于 2.248%（PCB-28）的判定阈值。转移效率高，意味着十溴二苯乙烷可能会沉积到偏远区域的地表。关于远距离迁移的结论是，虽然可能无法预测十溴二苯乙烷的典型迁移距离较长，但具有高度预测意义的迁移效率及其在偏远地区的存在表明，与颗粒物结合发生迁移的作用可以使远距离迁移成为可能。此外，由于输入参数的不确定性，例如水中的半衰期未知，建模结果存在不确定性。此外，经合组织工具不包含沉积物区间，而十溴二苯乙烷在沉积物中具有持久性。

根据附件 D 标准得出的远距离迁移结论

43. 已在远离已知点源的地点（例如北极和南极洲）的空气中检测到十溴二苯乙烷。在北极的雪、生物群和濒危物种以及南极的土壤和生物群等其他介质中也发现了这种物质。

44. 模型预测十溴二苯乙烷在气相中（每天 12 小时）的环境半衰期为 4.5–6.7 天。然而，预计超过 99.9%的十溴二苯乙烷将吸附于空气颗粒物，这可能会增加在空气中的停留时间及其在大气中远程迁移的潜力。十溴二苯乙烷的大气半衰期超过了《斯德哥尔摩公约》中>2 天的标准，表明其具有远距离大气迁移的潜力。

45. 总之，来自北极和南极洲以及迁徙物种的研究结果提供了证据，表明十溴二苯乙烷可以迁移到远离其初始排放点源的地方，证明其具有远距离迁移潜力。

2.4 不利影响

46. 现有的实验动物急性毒性研究表明，对经口、吸入和皮肤接触的急性毒性的关切较低（欧洲化学品管理局，2024b；加拿大环境与气候变化部和加拿大卫生部，2019）。然而，对于生物积累性和持久性物质来说，慢性接触对于评估对环境和人类健康的潜在危害更为重要。十溴二苯乙烷等超疏水性物质的吸收非常慢，可能需要很长时间才能达到平衡（第 28 段）。对于能够形成胶体颗粒的物质，已经报道了 U 形剂量–反应关系（Owen 等人，2014），而十溴二苯乙烷是一种难溶大分子。因此，在最高试验剂量下观察到的效应的相关性可能会受到质疑，特别是考虑到第 28 段所述的吸收特性和高浓度下结晶的可能性。因此，可认为长期接触较低剂量更适合描述潜在危险。目前还没有针对十溴二苯乙烷的啮齿动物慢性接触研究。现有的啮齿动物研究通常使用玉米油作为媒介，而本文讨论的水生生物研究则使用二甲基亚砜来制备储备溶液。尽管一些水生生物研究的浓度超过了十溴二苯乙烷的水溶解度，但可认为溶剂的使用是合理的。结果表明，在增溶剂类物质与十溴二苯乙烷共存的环境中（例如，废水排放中的共溶作用、与溶解有机碳或表面活性剂的相互作用）或者长期接触可以形成稳态的环境中，可能发生水生毒性效应（加拿大环境与气候变化部和加拿大卫生部，2019）。

2.4.1 对人类健康和环境的不利影响

47. 由于受体和信号通路存在若干保守特征，本节包含了对斑马鱼的机制研究。在大多数测试生物体中都观察到氧化应激，这可能是观察到的甲状腺和其他内分泌系统、心血管、神经和肝脏系统以及生殖、发育和行为所受多种影响的潜在机制。

48. 致突变性和遗传毒性：欧洲化学品管理局（2024b）和加拿大环境与气候变化部和加拿大卫生部（2019）概述了两项规范开展的体外研究，其中对十溴二苯乙烷的致突变性进行了测试。在一项艾姆斯试验中，在有和没有代谢活化的情况下，没有观察到十溴二苯乙烷的影响。同样，在中国仓鼠肺细胞的染色体畸变试验中，没有明显的致染色体断裂活性。目前还没有关于十溴二苯乙烷对人类或动物致癌潜力的数据。然而，重复接触研究中缺乏致癌性的迹象（例如，增生性改变）以及现有的体外致突变数据中缺乏遗传毒性活性，表明十溴二苯乙烷不太可能具有致癌性。根据有关遗传毒性的现有信息，认为十溴二苯乙烷不具有遗传毒性（欧洲化学品管理局，2024b；加拿大环境与气候变化部和加拿大卫生部，2019）。

49. 肝脏影响：在一项准则研究中，使 Sprague-Dawley 大鼠通过灌胃接触 0、100、320、1 000 毫克/千克体重的十溴二苯乙烷 90 天，高剂量雌性组的平均绝对肝脏重量、相对于体重的肝脏重量以及相对于脑重的肝脏重量在统计学上大于对照组（$p < 0.05$）。恢复 28 天后，肝脏重量的增加与对照组相似（Hardy 等人，2002）。肝脏变化的特征为极轻微至轻微肝细胞空泡化（高剂量雄性组）和极轻微至轻微小叶中央区肝细胞肥大（高剂量组和可能中等剂量雄性组）。在任何时间点，雌性大鼠的肝脏中均未发现给药相关变化（Hardy 等人，2002）。在另一项准则研究中（经合组织 TG 443，未发表，2026），在 F0 和

F1 组给予 100、300 或 1 000 毫克十溴二苯乙烷/千克体重/天的雄性大鼠肝脏中观察到与剂量相关的极轻微或轻微的大泡性/小泡性脂肪变性。对于 F0 组而言，认为这与在 1 000 毫克/千克/天剂量组雄性大鼠中观察到平均绝对肝重及相对体重的肝重均高于对照组这一情况相关。

50. 几项同行评审的研究表明，十溴二苯乙烷有可能诱导氧化应激，改变啮齿动物和鱼类的葡萄糖和脂质代谢以及酶的表达和活性，从而损害肝脏功能。Wang 等人（2010）通过灌胃方式使 Sprague-Dawley 大鼠经口接触 0 或 100 毫克十溴二苯乙烷/千克体重/天的剂量。组织中的十溴二苯乙烷水平比对照水平高出 13 至 1 444 倍，肾脏中的十溴二苯乙烷浓度为 11.2 纳克/克脂重，肝脏中为 177 纳克/克脂重，脂肪组织中为 549 纳克/克脂重。十溴二苯乙烷组的一些血清参数发生显著变化，表明可能因十溴二苯乙烷或其代谢物的积累而产生氧化应激，包括肌酐、天冬氨酸转氨酶（AST）、碱性磷酸酶（AFP）下降和总胆汁酸（TBA）升高（$p < 0.05$），葡萄糖没有改变。在十溴二苯乙烷接触组中，肝脏细胞色素 P450（CYP）3A2 信使 RNA 表达升高。

51. 使 Balb/C 小鼠经口接触 0、5、20、100 和 200 毫克十溴二苯乙烷/千克体重/天（每组 n=16）30 天，最高剂量下肝脏重量增加，组织学变化的特征是肝细胞肥大和细胞质空泡化（Sun 等人，2018）。与对照组相比，200 毫克/千克/天给药组从第 15 天开始、100 毫克/千克/天给药组从第 20 天开始、20 毫克/千克/天给药组从第 30 天开始血糖水平显著升高，但胰岛素水平未受影响。在大鼠的几项研究中也观察到血糖升高而胰岛素水平没有改变（Sun 等人，2014；2020；Gao 等人，2022；Li 等人，2021）。接触 20 毫克和 5 毫克/千克剂量的各组中，丙氨酸氨基转移酶（ALT）和天冬氨酸转氨酶的肝脏活性分别显著增加。主要外源性化学物代谢酶（葡萄糖醛酸转移酶（UDPGT）、7-戊氧基试卤灵 O-脱戊基酶活性（PROD）和乙氧基试卤灵 O-脱烷基酶（EROD））的肝微粒体活性在较高剂量组中显著增加，表明十溴二苯乙烷会对肝脏功能和甲状腺激素水平造成一定损害（见第 60 段）（Sun 等人，2018）。在雄性河鳟和虹鳟肝细胞接触十溴二苯乙烷（0、6.3、12.5、25 和 50 微克/升）96 小时的体外实验中，也观察到 EROD 活性增加（Nakari 和 Huhtala，2010）。

52. 使 Sprague-Dawley 大鼠每天一次通过灌胃接触 0、5、50、500 毫克/千克十溴二苯乙烷，持续 28 天（Sun 等人，2020）。在十溴二苯乙烷接触组中观察到肝脏形态变化、氧化应激、血清中 γ-谷氨酰转移酶和葡萄糖水平升高，以及孕烷 x 受体（PXR）、组成型雄烷受体（CAR）CYP3A1 和 CYP3A 基因表达下调。在 50 毫克十溴二苯乙烷组中，肝脏呈羽状坏死，500 毫克/千克体重/天的剂量可引起明显的病理变化，表现为肝索排列不规则、羽状坏死和炎性细胞浸润。然而，肝脏重量未观察到变化。50 和 500 毫克十溴二苯乙烷组的肝脏丙二醛（MDA）和谷胱甘肽（GSH）水平显著增加；在 500 毫克十溴二苯乙烷剂量下，超氧化物歧化酶（SOD）活性显著增加。肝脏 CYP3A1 的信使 RNA 表达在所有剂量下均降低，而组成型雄烷受体和孕烷 x 受体在 50 和 500 毫克十溴二苯乙烷/千克体重/天剂量下降低，CYP3A2 仅在毫克十溴二苯乙烷/千克体重/天组中显著降低。50 和 500 毫克/千克体重组的血清 γ-谷氨酰转移酶显著增加，表明发生了肝脏损伤，500 毫克/千克十溴二苯乙烷组的血清葡萄糖水平增加。

53. 在雄性 Wistar 大鼠中，以 0、5、50 或 500 毫克十溴二苯乙烷/千克体重/天的剂量经口灌胃 8 周后，肝脏体重比从 5 毫克/千克开始呈剂量依赖性显著增加（Cui 等人，2025）。肝脏中的脂质积聚（油红 O 染色）从 5 毫克/千克开始呈剂量依赖性增加。在中剂量接触情况下，在肝脏中检测到脂质空泡大量积

聚，表明出现了脂肪变性。高剂量接触导致肝细胞内出现明显的脂质空泡，这也与脂肪变性一致，并伴有细胞形态的显著改变。此外，在肝脏的一些区域观察到炎性浸润和气球样变性。肝脏中总胆固醇（TC）、甘油三酯（TG）和低密度脂蛋白（LDL）的水平出现剂量依赖性增加，50 和 500 毫克十溴二苯乙烷组与对照组有显著差异，而低密度脂蛋白从 5 毫克开始即有显著差异。高密度脂蛋白（HDL）仅在 5 毫克/千克剂量组中显著降低。脂质代谢关键基因的表达发生变化，脂肪酸合酶（FASN）、过氧化物酶体增殖物激活受体（PPAR）γ和酰基辅酶 A 氧化酶 1（ACOX1）显著增加，LDLR（胆固醇合成的限速酶）减少（Cui 等人，2025）。

54. Zhou 等人（2026）利用野生型和转基因斑马鱼模型，进一步探究了受精后 2 小时至受精后 72 小时接触 0、0.25、0.5、1、5、10 毫克/升十溴二苯乙烷或 BDE-209 对斑马鱼幼体的肝脏影响。BDE-209 和十溴二苯乙烷均未导致可观察到的形态异常，但 BDE-209 以剂量依赖性方式显著降低了存活率和孵化率。为了评估十溴二苯乙烷对斑马鱼幼体的肝脏毒性影响，作者使用了转基因斑马鱼，这是一种用于研究化学品诱导肝损伤的模型。给药导致肝脏面积和荧光强度显著下降，表明肝脏发育受损。通过油红 O 染色评估了脂质稳态，结果表明接触十溴二苯乙烷导致明显的卵黄囊扩张和异位脂质积聚，特别是在卵黄囊区域内。肝脏功能受损会扰乱卵黄脂质的代谢和吸收，导致其异常滞留（Lima 等人，2026），如此处所示。此外，从 1 毫克/升开始，十溴二苯乙烷给药以剂量依赖性方式升高丙氨酸氨基转移酶（ALT）和天冬氨酸氨基转移酶（AST）活性，表明出现了肝细胞损伤。接触十溴二苯乙烷后，与肝功能相关的基因以及与解毒和氧化还原稳态相关的基因表现出强烈的上调。这种基因表达谱表明肝脏解毒和氧化还原稳态遭到了破坏。这项研究表明，BDE-209 和十溴二苯乙烷表现出不同的毒性特征，其中 BDE-209 对发育构成更大的风险，而十溴二苯乙烷表现出更明显的肝脏毒性。

55. Li 等人（2023）使成年雌性斑马鱼接触 1 或 10 纳摩尔/升的十溴二苯乙烷 28 天，导致平均肝脏负荷分别为 307 和 398 纳克十溴二苯乙烷/克干重。通过禁食一天后进行部分肝切除术（PHx）研究了对肝脏再生的影响，动物在 28 天的恢复期间未接触该物质。与对照组相比，1 和 10 纳摩尔/升十溴二苯乙烷接触组的肝体指数（HSI）在部分肝切除后 28 天分别下降了 16.9%和 17.4%，表明十溴二苯乙烷显著抑制了成年斑马鱼的肝脏再生能力。同时，转录组生物信息学分析表明，被差异表达基因（DEG）显著富集的通路包括与甘油脂代谢相关通路、ABC 转运蛋白、细胞凋亡、DNA 复制和与细胞增殖有关的铁死亡通路。上述研究结果表明，接触 1 和 10 纳摩尔/升十溴二苯乙烷会扰乱斑马鱼体内的脂质代谢和细胞增殖相关过程，从而抑制肝脏再生。水生生物的修复和再生能力受损将使其更容易受到恶劣环境的损害，从而增加其生存风险。

56. 综合来看，现有结果表明十溴二苯乙烷可能会损害啮齿动物和鱼类的肝脏功能，改变葡萄糖和脂质代谢并促进脂肪变性。用于解毒的酶活性增加也可能促进甲状腺激素（TH）的清除，而孕烷 x 受体/组成型雄烷受体的下调可能会通过甲状腺素（T4）的肝脏代谢来进一步增加发生甲状腺功能减退的可能性。

57. 对下丘脑–垂体–甲状腺（HPT）轴的影响：在针对大鼠和小鼠、体外机制、流行病学以及鱼类的多项研究中，观察到接触十溴二苯乙烷后与甲状腺激素系统相关的影响。

58. 体外机制研究表明，二溴二苯醚有可能干扰甲状腺激素受体（THR）和细胞水平上对甲状腺激素效应很重要的酶。在使用表达人源甲状腺激素受体 THRα 和 THRβ 的 HEK293 细胞构建的荧光素酶报告基因检测系统中，观察到十溴二苯乙烷的拮抗作用，THRα 和 THRβ 的半数抑制浓度（IC_{50}）分别为 0.83 毫摩尔/升和 0.40 毫摩尔/升（Coi 等人，2026）。在人肝微粒体中，测量了脱碘（DIO）活性，并分别观察到从 T4 到 T3 以及由 T4 形成 3,3′-T2 的外环和内环脱碘（O 和 IRD）受到抑制，估计的半数抑制浓度为 160 纳摩尔/升十溴二苯乙烷（Smythe 等人，2017）。

59. 在一项经合组织 TG 443 试验（未发表，2026）中，使 Sprague-Dawley 大鼠经口灌胃接触 0、100、300 和 1 000 毫克十溴二苯乙烷/千克体重/天的剂量。在最高剂量组的 F0 雄性大鼠中观察到血清 T4 水平略微但显著增加（对照组的 115%），在 100 毫克/千克体重/天剂量组的 F0 雌性大鼠中观察到促甲状腺激素（TSH）水平降低。在 F1 雄性大鼠中，接受 300 或 1 000 毫克/千克体重/天剂量的动物的 T4 略有增加（分别为 119%和 108%）。甲状腺未观察到形态学改变。然而，在其他未按测试指南进行的小鼠和大鼠研究中，观察到对甲状腺系统的影响更明显（Wang 等人，2010；2019b；Sun 等人，2018）。

60. Sun 等人（2018）使 Balb/C 小鼠经口接触 0、5、20、100 和 200 毫克十溴二苯乙烷/千克体重/天剂量，持续 30 天（每组 n=16，每种性别 8 只），观察到 100 和 200 毫克剂量下血清中游离三碘甲状腺原氨酸（fT3）的含量降低，在 200 毫克剂量下促甲状腺激素增加，T4 呈剂量依赖性减少，尽管减少幅度不显著。甲状腺未观察到组织病理学变化。Wang 等人（2019b）使雄性 Sprague-Dawley 大鼠经口接触 0、5、50 和 500 毫克/千克体重剂量的十溴二苯乙烷或 BDE-209，持续 28 天（每组 n=12），观察到了对血清甲状腺激素的类似影响。观察结果包括，对十溴二苯乙烷和 BDE-209 而言，在 50 和 500 毫克剂量下血清游离三碘甲状腺原氨酸水平降低（$p<0.01$），在 500 毫克剂量下促甲状腺激素和促甲状腺激素释放激素（TRH）增加（$p<0.05$）。同时，甲状腺和脑下垂体中与甲状腺激素稳态相关的基因的信使 RNA 水平呈显著剂量依赖性改变。在 5 毫克/千克体重/天剂量组中，观察到甲状腺组织病理学改变，甲状腺结构紊乱；在 500 毫克/千克剂量组中，观察到上皮细胞空泡化肿胀并脱落，肥大细胞数量增加。平均胶质面积显著减少。在超微结构方面，与对照组相比，接触 5 和 50 毫克/千克体重/天的 BDE-209 或十溴二苯乙烷导致粗面面内质网扩张、线粒体肿胀和线粒体嵴消失。以 500 毫克/千克体重/天 BDE-209 或十溴二苯乙烷剂量给药的大鼠体内出现了粗面内质网萎缩和线粒体空泡化。对于甲状腺中的氧化应激标志物，丙二醛（脂质氧化降解的标志物）水平出现明显的剂量依赖性增加，并出现超氧化物歧化酶活性降低（Wang 等人，2019b）。与上述接触 28 天和 30 天研究中观察到的的血清 T3 水平降低相反，Wang 等人（2010）观察到血清 T3 水平显著增加（$p<0.05$）；雄性 Sprague-Dawley 大鼠口服接触 0 或 100 毫克十溴二苯乙烷/千克体重/天剂量 90 天后，与对照组相比，也观察到 T4 出现不显著的增加。下丘脑–垂体–甲状腺（HPT）轴受反馈机制调节，接触的剂量和持续时间都会影响观察到的反应。

61. 在一项两代斑马鱼研究中（Sun 等人，2024b），终生接触环境相关浓度的十溴二苯乙烷会扰乱所有世代的甲状腺稳态，并在未接触的 F1 和 F2 后代中诱导第 82 段进一步描述的焦虑样行为。在 F0 代中，在 0.1 和 10 纳摩尔/升浓度下观察到雌鱼血浆 T4 显著增加，在 1 和 10 纳摩尔/升浓度下观察到雄鱼血浆 T4 显著增加，而 T3 无变化。在 F1 卵中，在 10 纳摩尔/升浓度下注意到 T3 和 T4

显著升高，而在 F1 幼体中没有发现甲状腺激素显著变化。成年 F1 雌性的血浆 T3 和 T4 在 10 纳摩尔/升浓度下显著升高，而成年 F1 雄性的血浆 T3 在 0.1 纳摩尔/升浓度下显著降低。在 F2 卵中，甲状腺激素水平没有表现出显著变化，而 F2 幼体的 T4 水平显著增加。成年斑马鱼和受精后 5 天幼体的脑和肝脏中与下丘脑–垂体–甲状腺轴相关的基因转录出现剂量和世代依赖性变化，与观察到的激素水平一致。研究结果表明，F1 幼体的甲状腺干扰主要是由过量的母性甲状腺激素转移造成的，而 F2 幼体所受影响主要与相关基因的低甲基化和高甲基化的跨代表观遗传有关。

62. Wang 等人（2019c）还发现，从受精后 2 小时到受精后 6 天和 14 天（n=4）接触 0、3、10、30、100 和 300 纳摩尔/升十溴二苯乙烷的斑马鱼胚胎中的甲状腺激素水平发生了变化。对于全身甲状腺激素含量而言，在 6 天和 14 天之后，十溴二苯乙烷使 30、100 和 300 纳摩尔/升给药组的 T3 和 T4 水平出现了有统计学意义的上升。与对照组相比，从 10 纳摩尔/升开始，转甲状腺素（TTR）蛋白显著增加，且呈剂量依赖性。十溴二苯乙烷还对与下丘脑–垂体–甲状腺轴相关的基因表达模式产生了具有统计学显著性影响。Wang 等人（2022a）观察到了对甲状腺激素水平和基因表达的类似影响；他们研究了 10 微克/升 n-TiO2 是否影响十溴二苯乙烷（0、1、10 或 100 微克/升）对斑马鱼幼体的潜在毒性，接触时间为受精后 2 至 144 小时（n=3；每次重复包含 300 条幼体）。单独接触十溴二苯乙烷显著升高了总 T4（结合和未结合）和总 T3；同时接触 n-TiO2 后，反应进一步减弱。与对照组相比，单独接触 100 微克/升十溴二苯乙烷后，与下丘脑–垂体–甲状腺轴相关的基因的转录水平显著升高，与 Wang 等人（2019）和 Sun 等人（2024）一致。神经发育相关基因（syn2a 和 α1 微管蛋白）的转录水平在同时接触 100 纳摩尔/升十溴二苯乙烷和 n-TiO2 时显著升高。分子对接结果表明，十溴二苯乙烷可以与促肾上腺皮质激素释放激素受体 1（CRHR1）和 THRβ 结合，其相互作用模式可能与 T4 相似。单独接触十溴二苯乙烷和与 n-TiO_2 联合接触均引起斑马鱼幼体活动过度，神经递质含量增加。这些结果与 Sun 等人（2024b）和 Wang 等人（2019c）证明的模式一致。

63. 甲状腺影响的流行病学研究：人体测量发现，十溴二苯乙烷血清浓度增加主要但不专门导致 T3、T4 和甲状腺抗体（TG-Ab、TPO-Ab）水平增加，（Chen，2019；Zhao 等人，2020b）。Chen 等人（2019）测得十溴二苯乙烷血清浓度范围为 3.148 至 54 360 纳克/克脂重，几何平均值为 332.6 纳克/克脂重。Zhao 等人（2020b）在 100%的血清和毛发样本中检测到十溴二苯乙烷，几何平均值分别为 3.69 微克/克脂重和 672 微克/克干重。大量且持续接触十溴二苯乙烷的工人的流行病学结果为下丘脑–垂体–甲状腺轴可能受到的影响提供了一些表征。

64. 此外，在一项病例对照研究中，从中国东部山东省的甲状腺癌患者（n=242）和健康对照者（n=239）中收集了 481 份血清样本。病例组和对照组中十溴二苯乙烷的中位浓度分别为 47 和 45 纳克/克脂重，比其他新型溴化阻燃剂的浓度高出至少一个数量级。在按性别分层的 Logistic 回归中，与其他替代阻燃剂不同的是，十溴二苯乙烷在男性和女性中均表现出甲状腺癌发生优势比（OR）显著升高，且这种关联出现在第三和第四个四分位组（Liu 等人，2022）。

65. 心血管影响：现有研究表明，十溴二苯乙烷会增加氧化应激、炎症并在雄性 Sprague-Dawley 大鼠的主动脉和心脏组织中产生损伤（Jing 等人，2019；Gao 等人，2022；Zheng 等人，2021）。在这些研究中，使 Sprague-Dawley 大

鼠接触玉米油中 0、5、50 或 500 毫克/千克体重的十溴二苯乙烷 28 天（每组 n=12）。心脏组织学显示，50 和 500 毫克十溴二苯乙烷/千克体重/天接触导致内皮细胞核肿胀、内皮下间隙扩大、内皮细胞脱落和内弹力层变薄。超微结构显示 50 和 500 毫克/千克体重组线粒体肿胀和线粒体嵴排列紊乱（Jing 等人，2019；Gao 等人，2022）。Jing 等人（2019）观察到，在接触 500 毫克/千克十溴二苯乙烷的动物中，血清低密度脂蛋白（LDH）水平显著增加，同时丙二醛和超氧化物歧化酶、GHS-OX 活性增加。关键炎症因子白细胞介素（IL）1-b、白细胞介素-6 和肿瘤坏死因子-a 显著上调，表明出现了氧化应激和激活的炎症反应。Gao 等人（2022）观察到，解偶联蛋白（UCP，线粒体内膜上参与能量代谢的关键转运蛋白）的水平在 5、50 和 500 毫克/千克/天十溴二苯乙烷组中呈剂量依赖性减少（$p<0.05$），大鼠心脏组织三磷酸腺苷水平在 500 毫克/千克/天十溴二苯乙烷组中与对照组相比显著降低（$p<0.05$）。在 50 和 500 毫克/千克体重的十溴二苯乙烷组中，细胞凋亡（TUNEL 阳性细胞）也呈剂量依赖性增加，MYH6 和 SERCA2 的蛋白质表达也发生了改变，表明心肌收缩和舒张功能受到了影响。500 毫克十溴二苯乙烷组的血糖明显升高，50 和 500 毫克组 HDL-C 明显降低，总胆固醇和甘油三酯无变化。与对照组相比，与葡萄糖代谢相关的基因表达（IRS-1、PI3K、p-AKT）显著减少，GLUT2 和 RXR-a 显著增加（Gao 等人，2022）。

66. Zheng 等人（2021）观察到，在接触 50 和 500 毫克/千克体重十溴二苯乙烷的各组中，腹主动脉形态和超微结构受损，同时伴有白细胞介素 1β 和白细胞介素 18 的蛋白水平升高。对经十溴二苯乙烷（0、6.25、12.5、25、50 和 100 毫摩尔/升）处理 24 小时的人血管内皮细胞（HAEC）的进一步体外研究表明，十溴二苯乙烷不仅诱导细胞毒性和活性氧（ROS），而且还引起人血管内皮细胞的焦亡（其证据为 NOD 样受体蛋白 3（NLRP3）的表达升高），并使十溴二苯乙烷处理组出现经典炎症小体组分（ASC 和半胱天冬酶-1）（Zheng 等人，2021）。

67. 还已证明十溴二苯乙烷可以促进动脉粥样硬化的发生发展（Li 等人，2025）。使 ApoE 基因敲除小鼠（8 周龄雄性）单次经口接触玉米油中 0 或 100 毫克/千克体重的十溴二苯乙烷、BDE-47 或 BDE-209，为期 6 周。与对照组相比，所有测试溴化阻燃剂的单次接触均显著增加了小鼠主动脉根部的斑块面积和脂质含量。溴化阻燃剂显著增加斑块中的活性氧水平，并提高黏附分子 ICAM-1 的表达水平，从而促进巨噬细胞的聚集。十溴二苯乙烷转录组分析表明，差异表达基因（DEG）在与氧化应激和脂质代谢相关的信号通路中显著富集。结果表明，接触溴化阻燃剂可以通过增加巨噬细胞的聚集和泡沫细胞的形成来促进动脉粥样硬化的发生发展。接触溴化阻燃剂会对血管内皮细胞造成损害，诱导活性氧的产生和 ICAM-1 的表达，从而促进巨噬细胞的聚集。另一方面，接触溴化阻燃剂会导致脂质代谢紊乱，增加巨噬细胞中 Ox-LDL 的含量，从而促进泡沫细胞的形成（Li 等人，2025）。

68. 生殖毒性（对生育力的影响和发育毒性）：在一项为期 90 天、剂量最高为 1 000 毫克/千克/天的大鼠研究中，未观察到对生殖器官产生重量或组织学影响（Hardy 等人，2002）。研究作者称，一项经合组织 TG 443 大鼠研究表明，在最高为 1 000 毫克/千克/天的剂量下，未观察到 F0 或 F1 代的发情周期、精子测量数据或繁殖表现受到给药的影响（未发表，2026）。然而，有其他研究表明十溴二苯乙烷对大鼠、小鼠和鱼的精子和卵母细胞发育均有影响。研究表明，接触十溴二苯乙烷可以通过诱导氧化应激、激活细胞死亡信号通路并改变促性腺激素信号（GHS）来影响雄性生殖。在大鼠和小鼠研究（Li 等人，

2021；Xue等人，2022；Qi等人，2025；Shi等人，2026）以及鱼类研究中均观察到睾丸结构受损和精子质量下降。

69. 啮齿动物的睾丸毒性：Li 等人（2021）通过灌胃方式使雄性 Sprague-Dawley大鼠接触 0、5、50 和 500 毫克/千克体重剂量的十溴二苯乙烷，持续 28 天（每组 n=12）。未观察到给药对睾丸重量的影响；然而，与对照组动物相比，接触 50 和 500 毫克/千克体重十溴二苯乙烷剂量的大鼠出现了生精上皮的显著缺失。在相同剂量下，还观察到精子数量显著减少和精子活力下降，以及端粒酶活性下降和端粒缩短，表明生殖细胞出现衰老。还观察到 DNA 链断裂（TUNEL 阳性细胞）和细胞凋亡增加。Xue 等人（2022）使用了与 Li 等人（2021）相同的剂量和接触方案，观察到 50 和 500 毫克/千克体重/天剂量组的精子浓度显著降低。此外，所有剂量组的精子活力均降低，50 和 500 毫克/千克体重/天剂量组的精子畸形率增加。在睾丸的组织学检查中，在 50 和 500 毫克/千克体重组中观察到生精上皮发生变化，并观察到由线粒体扩张和空泡化形成的超微结构变化。此外，出现了线粒体损伤和功能障碍以及血清葡萄糖和 LDL-C 水平显著升高。另外，十溴二苯乙烷通过睾丸 DNA 损伤导致了染色体分裂失败，减少了减数分裂调控因子（Sohlh1、MILI、CDK2 和 CyclinA）和联会复合体蛋白（SYCP1 和 SYCP3）的表达。十溴二苯乙烷诱导了糖脂代谢紊乱，并通过线粒体介导的细胞凋亡途径促进生精细胞的凋亡，通过降低精子数量和质量来导致生殖毒性（Xue 等人，2022）。

70. Qi 等人（2025）通过口服灌胃使 C57BL/6 J 雄性小鼠连续 7 周接触玉米油中 0、5 或 50 毫克/千克体重的十溴二苯乙烷，每周给药 5 天（每组 n = 6）。与对照组相比，5 和 50 毫克/千克体重剂量组的精子计数分别减少 34%和 73%（p=0.01），精子畸形率呈剂量依赖性增加（p=0.01）。血清和睾丸内睾酮（T）水平与十溴二苯乙烷剂量的增加呈强负相关（分别为 $p < 0.05$ 和 $p < 0.01$）。与对照组相比，50 毫克/千克十溴二苯乙烷组的血清促黄体生成素（LH）下降了 50%，促卵泡激素（FSH）水平下降了 29%（$p < 0.01$）。与对照组相比，十溴二苯乙烷给药组中类固醇生成急性调节蛋白（StAR）（睾丸间质细胞产生类固醇激素的关键酶）显著降低（$p < 0.01$）。这可能会阻止睾丸间质细胞对促性腺激素信号做出适当反应。精子计数减少和精子畸形增加以及睾丸中生殖细胞层减少和睾酮减少的最低观测效应浓度（LOEC）为 5 毫克/千克体重，血清中的促黄体生成素和促卵泡激素减少的最低观测效应浓度为 50 毫克/千克（Qi 等人，2025）。

71. Shi 等人（2026）观察到，C57BL/6J 小鼠经口接触 0 和 0.5 毫克十溴二苯乙烷/千克体重/天 12 周后，精子质量和睾丸结构显著下降。睾丸生殖细胞组织混乱或缺失，精母细胞和精子细胞大幅减少。十溴二苯乙烷接触组中，参与间隙连接和细胞氧稳态的关键蛋白质显著减少。

72. 对雌性生殖器官的毒性：还研究了十溴二苯乙烷对卵母细胞和胚胎发育的影响。Shi 等人（2021）使青春期（37 周大）雌性 Kumming 小鼠接触十溴二苯乙烷（玉米油中 0、0.05、0.5、5、50 微克/千克体重/天）30 天，并通过激素处理诱导超排卵。注射人绒毛膜促性腺激素后的特定时间点分离卵巢，以采集处于减数分裂启动阶段、减数第一次分裂后期以及已发生极体排出（PBE）的卵母细胞。接触十溴二苯乙烷会损害囊胚的发育，导致囊胚细胞凋亡。在 5 和 50 微克/千克体重/天十溴二苯乙烷接触组中，卵母细胞的不对称分裂明显受损，导致卵母细胞具有更大的极体（PB）。因此，异常的不对称减数体分裂产生的大极体会带走大量的母源物质，导致胚胎发育异常、不孕或流产。

73. 在另一项研究中，Shi 等人（2022）使青春期（37 周大）雌性 Kumming 小鼠接触十溴二苯乙烷（玉米油中 0 或 50 微克/千克体重/天）30 天，并将动物分为两组。使第一组超排卵，雌性进行交配。次日上午，收集经过激素处理且出现阴道栓的雌鼠（E 0.5 天），并对 1、2 和 8 期胚胎进行采样，96 小时后收集囊胚。接触十溴二苯乙烷不会影响受精后纺锤体旋转，但导致受精卵原核（PN）大小减少。十溴二苯乙烷干扰了原核中丝状肌动蛋白的自组装，导致原核减小、DNA 损伤、合子基因组激活相关基因表达减少，最终导致胚胎发育异常。在受精卵的雌原核和雄原核中均观察到 DNA 损伤（以 γ-H2AX 增加来衡量），并且与丝状肌动蛋白水平呈负相关。在第 2 组中，雌性与雄性直接配对，并在接触 30 天后交配，并在 E11.5、E14.5 和 E18.5 通过剖宫取出胚胎。与对照组相比，接触十溴二苯乙烷的小鼠的每窝产仔数明显减少，E14.5 和 E18.5 的胚胎长度明显降低。将对照组和接触十溴二苯乙烷的母鼠所生的 F1 幼鼠饲养至 6 周大，然后使其接受行为测试。接触十溴二苯乙烷会导致雌性 F1 小鼠的运动活动增加并出现社交行为缺陷，但对雄性 F1 小鼠的运动活动和社交行为没有影响。

74. 哺乳动物的发育/畸形：根据经合组织 TG 414（1981 年采用）进行了两项符合良好实验室规范和经合组织测试指南的研究，评估了十溴二苯乙烷对大鼠和兔子的致畸作用，Hardy 等人（2010）对此做了总结。这些研究未观察到与给药相关的胚胎重量、性别比例、窝仔数、早期胚胎吸收或晚期胚胎吸收方面的影响。在大鼠研究中，未观察到外部异常或内脏异常。在骨骼异常方面，在 400 毫克/千克/天剂量下，出现舌骨未骨化和颅骨骨化减少的窝数在统计学上显著增加。这一观察结果被认为是偶然的，因为在最高剂量下没有观察到类似的增加情况。在兔子研究中，在母兔中没有观察到与给药相关的死亡或毒性的临床表征。125 和 400 毫克/千克/天剂量组各有一只动物发生流产，1 250 毫克/千克/天剂量组有两只动物发生流产。然而，鉴于该观察结果的发生率较低，并且已知兔子的自然流产率很高，因此认为这一发现是偶然的。唯一具有统计学意义的差异是 1 250 毫克/千克/天剂量下出现第 27 节骶前椎骨的窝数增加（9 窝，而对照组为 4 窝）。鉴于这种增加（56.3%）在实验室历史对照范围（12.593.8%）内，研究负责人认为其不是不良反应。中剂量和高剂量组中观察到血管异常的发生率较低。在 400 毫克/千克/天剂量组的 1 只胚胎中观察到主动脉瓣增大、球状主动脉弓和右心室发育不良。在 1 250 毫克/公斤/天组中一窝的两个胚胎中观察到主动脉弓畸形和右心室发育不全。鉴于以上发生率较低，认为所报告的畸形并不表明给药相关影响（Hardy 等人，2010）。

75. 在现有的一项经合组织 TG 443 大鼠研究（未发表，2026）摘要中，使 Sprague-Dawley 大鼠经口灌胃接触 0、100、300 和 1 000 毫克/千克/体重的十溴二苯乙烷。在 F1 中，未观察到与给药相关的不利影响。在无剂量反应的雄性中观察到一些与给药相关的血液学结果，还指出了与给药相关的生化和尿液分析结果。在 1 000 毫克/千克组的雄性和雌性中均观察到肛门生殖器距离略微增加，并且在围产期第 13 天进行评价时发现乳头滞留，100 毫克/千克组的发生率最高。肝脏组织病理学显示雄性存在极轻微或轻微的大血管/微血管脂肪变化，无明显的剂量反应。仅在 300 和 1 000 毫克十溴二苯乙烷/千克体重组的 F1 雄性中，测得血清 T4 水平略高（与对照组相比，分别为 119%和 108%）。关于发育免疫毒性，与对照组相比，观察到所有十溴二苯乙烷组粒细胞的绝对和相对出现频率显著增加，并且 300 和 100 毫克十溴二苯乙烷组雄性中单核细胞的相对出现频率增加。其他临床终点和脑形态参数的差异被认为是偶然的，因为其

在性别之间不一致，在组群之间不一致，幅度可认为很小，没有组织病理学相关性，并且（或者）没有显著的平均脑重量差异。研究作者得出的结论是，本研究中全身毒性和生殖/发育毒性的无观测不良效应水平（NOAEL）为 1 000 毫克/千克/天。

76. 对鱼类繁殖的毒性：斑马鱼在整个生命周期中产生与人类相似的关键生殖激素，包括促性腺激素释放激素（GnRH）、促卵泡激素、促黄体生成素，以及睾酮（T）、雌激素和孕酮这几种性类固醇（Hara 等人，2016；Lima 等人，2026）。多项研究报告十溴二苯乙烷会引起生殖毒性。在使用成年斑马鱼的研究中发现血清中的雌二醇（E2）和睾酮水平改变（Sun 等人，2022；Yu 等人，2026；Choi 等人，2021）。类固醇生成中断导致雌性血浆中雌二醇和睾酮水平降低，与下丘脑-垂体-性腺（HPG）轴基因表达的变化有关（Sun 等人，2022；Yu 等人，2026）。生育能力和性腺体指数（GSI）也受到接触十溴二苯乙烷的负面影响（Yu 等人，2026），接触十溴二苯乙烷的斑马鱼精子质量和精子生成受损（Yang 等人，2024；Choi 等人，2021）。

77. Yu 等人（2026）通过评估生育能力、性腺发育、性激素水平、下丘脑-垂体-性腺轴基因表达和卵巢代谢组特征来研究十溴二苯乙烷的生殖毒性。使成年斑马鱼（4 月龄）接触 0、1、10 和 100 微克/升十溴二苯乙烷，为期 21 天（n = 3；每次重复包含 15 条雄鱼+15 条雌鱼）。性腺表现出十溴二苯乙烷的浓度依赖性积累。雌鱼的生育能力（以累积产卵量衡量）、血清雌二醇水平和性腺体指数从 1 微克/升开始呈剂量依赖性下降，在 100 微克/升时显著下降。此外，该接触组的核周卵母细胞（PO）比例增加，而卵黄形成后期卵母细胞（LVO）则显著减少。雄性的性腺体指数和血浆性激素没有改变。这些结果表明十溴二苯乙烷对雌性斑马鱼表现出生殖毒性。在接触十溴二苯乙烷的鱼中观察到的滤泡细胞发育异常，原因可能是雌二醇水平显著降低。100 微克/升十溴二苯乙烷通过干扰下丘脑-垂体-性腺轴来扰乱雌激素的合成和分泌，从而显著损害雌性斑马鱼的生殖能力。大脑、性腺和肝脏中与下丘脑-垂体-性腺轴相关的几种基因的表达显著减少。此外，参与类固醇激素调节的基因在雌性性腺中发生了显著变化。对雌性性腺的代谢组和脂质组分析表明，卵巢内的脂质代谢、牛磺酸和亚牛磺酸代谢以及谷胱甘肽代谢发生了改变。综合来看，这些因素导致卵巢中成熟卵母细胞的比例降低，最终导致累积产卵量显著下降。

78. Sun 等人（2022）使雌性斑马鱼接触标称浓度 1 和 100 纳摩尔/升十溴二苯乙烷（体积分数 0.01%的二甲基亚砜），为期 28 天。在雌性斑马鱼大脑中检测到的十溴二苯乙烷浓度（2 411± 190 和 4 127 ± 547 纳克/克干重）与在电子废物回收地点的鲤鱼和罗非鱼中测量的大脑中该物质水平相当（Tao 等人，2019）。在 1 和 100 纳摩尔/升十溴二苯乙烷给药组中，血浆雌二醇和睾酮浓度均显著降低。与下丘脑-垂体-性腺相关的基因表达发生了改变。作者推测，十溴二苯乙烷接触通过抑制大脑中相关基因的转录来抑制类固醇生成的过程。然而，基因表达改变以及雌二醇和睾酮水平降低并没有导致有统计学意义的卵泡发育不良，尽管观察到核周卵母细胞呈弱下降趋势和卵黄形成期卵母细胞（VO）呈弱上升趋势，与 Yu 等人（2026）一致。十溴二苯乙烷接触组（1 和 10 纳摩尔/升）中闭锁卵母细胞普遍存在，表明十溴二苯乙烷可能导致雌性斑马鱼卵泡发育不良。

79. Choi 等人（2021）使雄性斑马鱼（n = 4，每次重复包含四条雄鱼）接触 0、0.031、0.31 和 3.1 微摩尔/升十溴二苯乙烷（体积分数 0.1%的二甲基亚砜），为期 14 天（经合组织 204，有微小修改）。此外，还采用两种人体组织细胞系（即 H295R（人肾上腺皮质癌）和 MVLN（人乳腺癌）细胞）研究对性激素合成及其相关机制的影响。接触 0.31 和 3.1 微摩尔/升十溴二苯乙烷的雄性斑马鱼中，血浆雌二醇浓度显著增加，所有给药组均呈明显增加趋势（尽管 0.031 微摩尔/升组不显著）。11-KT（鱼类体内的主要睾酮）浓度及雌二醇/11-KT 比没有显著变化。肝脏中相关基因转录水平（vtg、erα 和 erβ）水平与对照组相比没有显著差异。在接触十溴二苯乙烷的 H295R 细胞中，雌二醇/睾酮比率呈增加趋势（$p < 0.05$），而与类固醇生成相关的基因没有统计学显著变化。在人乳腺癌细胞系试验中，观察到与雌激素受体的结合亲和力低于 0%，表明十溴二苯乙烷不具有直接的雌激素受体激动作用。结果表明，接触十溴二苯乙烷会增加雄性斑马鱼的雌二醇水平和 H295R 细胞中的雌二醇/睾酮比率。然而，对与类固醇生成和雌激素受体结合亲和力相关的基因进行分析后，并未发现任何显著结果。作者认为，结果表明性激素水平可能是由类固醇生成途径改变以外的机制介导的。然而，在雄性河鳟和虹鳟肝细胞接触十溴二苯乙烷（0、6.3、12.5、25 和 50 微克/升）96 小时的体外实验中，也观察到诱导产生卵黄蛋白原的现象，在 6.3 微克/升浓度下表现显著（Nakari 和 Huhtala，2010）。

80. Yang 等人（2024）使成年雄性斑马鱼接触标称浓度为 0、0.1、1、10 和 100 纳摩尔/升十溴二苯乙烷，为期 2 个月。接触 2 个月后，十溴二苯乙烷接触组睾丸中该物质含量分别为 871、1 284、1 411 和 3 252 纳克/克脂重。在所有测试浓度下，观察到斑马鱼精子的总活力和前向活力显著降低，并且精子的头部宽度增加。然而，当接触十溴二苯乙烷的雄性与未接触的雌性配对时，繁殖行为不受影响，而 100 纳摩尔/升组的 F1 后代幼体的孵化率显著降低（从 99.81%到 83.78%）。其他参数，例如受精率、畸形率和存活率，与对照组没有差异。在睾丸的组织学研究中观察到对生殖细胞有影响，生殖细胞类型出现了一些差异。接触 1 和 100 纳摩尔/升十溴二苯乙烷的鱼体内的精原细胞比例显著升高，接触 100 纳摩尔/升十溴二苯乙烷的鱼体内的精子比例显著降低，接触 0.1–10 纳摩尔/升十溴二苯乙烷的鱼体内的精子比例出现下降趋势，这可能表明接触十溴二苯乙烷后精子生成受到抑制。使用 g-H2AX 检测时，从 1 纳摩尔/升开始观察到 DNA 链断裂增加；使用 TUNEL 染色检测时，在 100 纳摩尔/升时观察到该现象。与细胞凋亡相关的蛋白质从 1 纳摩尔/升开始呈现显著的剂量依赖性增加。接触该物质的斑马鱼睾丸呈现 DNA 损伤反应和能量代谢障碍，差异表达蛋白富集于程序性坏死和磷脂酰肌醇信号通路，并且参与丝状肌动蛋白组装的蛋白质显著下调，这可能是观察到的 DNA 损伤的根本原因。目前尚不清楚这些影响是直接源于十溴二苯乙烷还是相关的细胞死亡。使斑马鱼精子在体外接触 0.01、0.1、1 和 10 微摩尔/升十溴二苯乙烷 3 小时，然后用未接触该物质的雌性的卵进行人工受精。斑马鱼精子的总活力（0.1 和 1 微摩尔/升）和前进活力（0.1 微摩尔/升）显著低于对照组，但精子运动线性度无显著差异。尽管精子速度参数没有观察到显著差异，但在 0.1 微摩尔/升十溴二苯乙烷接触组中观察到受精率呈显著剂量依赖性降低。存活率、畸形率和孵化率与对照组没有差异（从受精后 24120 小时开始）。综合来看，结果表明，接触十溴二苯乙烷的斑马鱼可能出现精子质量和精子生成受损，其基本机制可能与睾丸生殖细胞的 DNA 损伤和能量代谢重编程有关。

81. 鱼类的发育、神经和行为毒性：如上所述，在几项鱼类研究中观察到甲状腺激素相关影响，其中观察到接触环境相关浓度的十溴二苯乙烷会导致下丘脑–垂体–甲状腺轴和血浆甲状腺激素水平紊乱（Sun 等人，2024b，Wang 等人，2019c；2022b）。发育影响已经得到证明，包括甲状腺系统、神经递质、线粒体功能、形态畸形和行为方面（例如活动过度）的变化。活动过度可能属于不利影响，因为其会增加能量消耗、疲劳以及通过异常游动和社会行为改变而增加被捕食的风险。

82. 在一项两代斑马鱼研究中（Sun 等人，2024b），终生接触环境相关浓度的十溴二苯乙烷会导致未接触该物质的 F1 和 F2 后代出现焦虑样行为和甲状腺干扰（见第 61 段）。使斑马鱼胚胎接触环境相关浓度的十溴二苯乙烷（0.1、1、10 纳摩尔/升）直至 8 月龄（每组 400 个胚胎，n=3）。水样中十溴二苯乙烷的含量测量值为 0.15、0.68 和 7.60 纳摩尔/升（146、660 和 7 381 纳克/升）。更高级的行为（例如焦虑样反应）可以在较年长（例如受精后 5 天）的幼体中通过测量趋边行为进行量化；趋边行为是停留在在试验场地边缘附近的倾向，这是一种脊椎动物中保守存在的行为，与啮齿动物开放场测试行为类似（Han 等人，2021，Lima等人，2026）。在测试趋边行为时，Sun等人（2024b）发现，祖代接触 10 纳摩尔/升十溴二苯乙烷，会显著增加 F1 幼体（受精后 5 天）在光明和黑暗条件下以及 F2 幼体在光明和黑暗条件下在外部区停留的时间比例。趋边行为（也称为“贴墙”或“跟墙”行为）是防御/反捕食行为的一部分，表明存在焦虑或压力相关行为（Champagne 等人，2010）。研究结果表明，F1 幼体的甲状腺干扰主要是由过量的母体甲状腺激素转移造成的，而 F2 幼体所受影响主要与甲状腺激素相关基因的低甲基化和高甲基化的跨代表观遗传有关。目前的研究表明，甲状腺干扰与多代和跨代焦虑样行为之间存在潜在关系。

83. Sun 等人（2023b）使 F0 代斑马鱼从受精后 2 小时到 8 月龄接触 0.1、1 和 10 纳摩尔/升十溴二苯乙烷（每次重复包含 100 只幼体，n = 3），并在不进一步接触的情况下饲养 F1 和 F2 代。F0 幼体的总身体负荷分别为 160、237 和 876 纳克/克干重，F1 和 F2 幼体的十溴二苯乙烷总身体负荷低于检测限度。F0 急性接触十溴二苯乙烷并未引起发育参数的显著变化，仅在最高剂量时出现心率增加。然而，在 F2 幼体中观察到畸形增加，其中心包和卵黄囊水肿（$p<0.01$）、脊柱和尾部弯曲（$p < 0.01$）和无眼症（$p < 0.05$）是祖代接触十溴二苯乙烷（1 和 10 纳摩尔/升）后出现的主要畸形。F0 和 F1 幼体的心率增加，而 F2 幼体的心率下降。这与神经递质水平和运动活动特征变化的结果一致。在 0.1 和 10 纳摩尔/升给药组中，F1 代的 GABA、胆碱、乙酰胆碱、NE、5-HT、Epi 和 5-HIAA 出现显著增加，而 F2 代的相同递质和 Glu 出现显著减少。鉴于神经递质在调节心血管功能中的作用，神经递质的稳态失衡可能是导致斑马鱼幼体心率异常的原因。关于由暗到明行为的论文显示，斑马鱼幼体的正常运动模式呈现一个独特的表现型：在黑暗时期立即出现强烈的活动过度，随后在光照时期活动水平显著降低。如果偏离这种模式。则表明出现了神经毒性或精神活性影响（Lima 等人，2026）。在 F0 中通过多代接触经历直接接触的 F1 幼体（受精后 5 天）中，在 10 纳摩尔/升给药组的光照和黑暗周期中都观察到活动过度。然而，在 F2 幼体（受精后 5 天）中，如果没有直接接触十溴二苯乙烷，则明暗刺激的运动活动显著降低。对转录组和 DNA 甲基化组的分析表明，从 F0 到 F1 和 F2 幼体，显著受影响的通路数量逐渐增加。总体而言，与 F0 幼体相比，在转录和 DNA 甲基化水平上，在 F2 幼体中观察到了更广泛的反应。综合来看，结果表明神经递质的多代失衡导致 F0 和 F1 幼体产生兴奋效应，但 F2 幼体在祖代

接触十溴二苯乙烷后产生跨代抑制效应。此外，通过甘油三酯、葡萄糖、肝脂肪酶、琥珀酸脱氢酶、细胞色素 c 氧化酶和三磷酸腺苷水平的变化，观察到糖脂和能量代谢紊乱方面的多代和跨代失衡。研究发现接触十溴二苯乙烷会引起氧化应激，这可能是该物质毒性作用的基本机制之一。F0 幼体中的活性氧含量升高，F1 幼体中的谷胱甘肽过氧化物酶（GSH-px）和谷胱甘肽含量明显升高，而 F2 幼体中仅谷胱甘肽过氧化物酶含量明显降低。Sun 等人（2024）描述的甲状腺激素和甲状腺激素调控轴的改变，可能部分解释了 Sun 等人（2023b）观察到的现象。甲状腺激素对于早期神经发育、神经传递，特别是焦虑样行为控制至关重要（Leach 和 Gould，2015）。

84. Hua 等人（2022）使受精后 2 小时至受精后 120 小时的胚胎接触 T0 时测量浓度为 1.9、7.5、16.4 和 42.1 微克/升的十溴二苯乙烷中，以此研究了在发育阶段斑马鱼中诱导的活动过度，T24 时这些浓度分别下降至 1.0、2.3、6.2 和 10.2 微克/升。与对照组相比，接触 16.4 和 42.1 微克/升十溴二苯乙烷的斑马鱼幼体的畸形率、存活率和体长没有显著差异，但心率显著增加（$p<0.001$）。所有十溴二苯乙烷给药组的尾部弯曲发生频率在受精后 23 小时均与对照组接近，但 1.9 微克/升给药组的尾部弯曲发生频率在受精后 24–26 小时明显更高，7.5 微克/升给药组在受精后 24、25 和 28 小时明显更高，16.4 和 42.1 微克/升给药组在受精后 24–28 小时明显更高。在连续光照下接触 16.4 和 42.1 微克/升的十溴二苯乙烷后，斑马鱼幼体的平均自由游动速度显著增加。在暗明过渡期，接触 42.1 微克/升的十溴二苯乙烷后，所有三个暗期的平均游动速度均显着增加；接触 16.4 和 42.1 微克/升的十溴二苯乙烷后，第一个明期的平均游动速度也显著增加。在接触 1.9 微克/升十溴二苯乙烷的斑马鱼幼体中，多种神经递质的含量显著降低。在较高剂量（16.4 和 42.1 微克/升十溴二苯乙烷）下，只有乙酰胆碱水平显著增加，这与观察到的活动过度现象一致。在接触 42.1 微克/升十溴二苯乙烷的幼体中发现催化乙酰胆碱合成的胆碱乙酰转移酶（ChAT）活性增加（Agostini 等人，2018），这可能是导致乙酰胆碱含量增加的原因。分子对接研究表明十溴二苯乙烷对胆碱乙酰转移酶具有结合效力，这表明十溴二苯乙烷对斑马鱼可能具有兴奋活性。相比之下，乙酰胆碱酯酶（AChE，一种将乙酰胆碱催化为胆碱的限速酶）的活性在任何十溴二苯乙烷给药组中均没有出现明显变化。分子对接结果还显示十溴二苯乙烷与 α 1-微管蛋白和 SYN2a 之间有相互作用效力，结合能分别为-38.9064 和-18.6725 千卡/摩尔。综合来看，运动行为变化表明胚胎接触十溴二苯乙烷后会产生兴奋性毒性效应。

85. Zhang 等人（2026）表明，接触十溴二苯乙烷可能使发育阶段的斑马鱼出现神经行为异常，并导致心血管和发育毒性。心脏功能问题开始较早（Lima 等人，2026），心血管系统毒性的指征包括心包水肿、静脉窦-动脉球（SV-BA）距离增加，以及心脏射血分数、心跳节律和速度降低（Zhao 等人，2024）。还值得注意的是，成年斑马鱼能够完全心脏再生，而成年哺乳动物心脏的再生潜力有限（Zhao 等人，2024）。使受精的斑马鱼胚胎接触 0、5、50 和 500 微克/升十溴二苯乙烷，直至受精后 120 小时。接触十溴二苯乙烷没有显著影响幼体的存活率和孵化率。在受精后 120 小时，接触 50 和 500 微克/升十溴二苯乙烷的幼体表现出主要以脊柱弯曲和鳔未充气为特征的形态异常。在 500 微克/升组中，观察到躯干弯曲、眼球突出（眼部损伤）和心包水肿扩大。在评估神经行为影响时，运动轨迹热图显示，接触十溴二苯乙烷显著增强了幼体的运动活动。平均游动速度呈剂量依赖性增加，500 微克/升组在明期和暗期均表现出明显更快的速度。热图轨迹和速度增加表明十溴二苯乙烷引起了焦虑样行为。这

项研究还发现溶血磷脂胆碱的水平降低，这种水平降低可能会损害中枢神经系统并阻碍神经发育，这可能与观察到的行为异常有关。对于心脏毒性，形态学评估的量化显示，50 和 500 微克/升剂量下的心包面积均显著增加，500 微克/升剂量下的心率显著增加。此外，结果显示 50 和 500 微克/升给药组的静脉窦-动脉球距离均显著增加。KEGG 通路富集分析显示，铁死亡和自噬是显著富集的通路。十溴二苯乙烷诱导活性氧呈剂量依赖性上升。与此一致，在 500 微克/升剂量下发现了丙二醛的显著积累和谷胱甘肽的显著耗竭。同时伴随着磷脂酰乙醇胺水平的增加（这种增加与心脏毒性有关）以及铁死亡相关蛋白及其基因转录本水平的改变。然而，如果同时接触 500 微克/升十溴二苯乙烷和 2 微克/升铁死亡抑制剂（Fer-1），则可减轻十溴二苯乙烷引起的心脏毒性，改善全身氧化应激并逆转铁死亡相关基因的表达。这表明氧化应激和铁死亡可能对于观察到的心脏发育影响很重要。根据其蛋白质组学研究结果，作者认为接触十溴二苯乙烷通过协同下调视黄醇脱氢酶 12（RDH 12）和上调 UGT1B2 来扰乱视黄醇色素代谢和视觉循环，最终导致斑马鱼幼体出现眼球突出等发育异常。

86. Yang 等人（2023）使斑马鱼幼体（受精后 2 小时至 120 小时）接触十溴二苯乙烷（0、50、100、200 和 400 微克/升），发现其可诱导神经毒性，表现为斑马鱼幼体平均游动速度增加、神经递质含量受到干扰以及神经发育相关基因的转录发生改变。此外，接触 400 微克/升十溴二苯乙烷显著增加了斑马鱼幼体的畸形率（心包水肿、卵黄囊水肿、脊柱弯曲和尾部弯曲）和心率。在 200 和 400 微克/升十溴二苯乙烷给药组中，丙二醛和活性氧水平出现了明显升高，谷胱甘肽含量减少，超氧化物歧化酶活性降低。对线粒体活性进行评估发现，接触 400 微克/升十溴二苯乙烷的斑马鱼幼体的基础呼吸、三磷酸腺苷产生、最大呼吸、呼吸储备容量和质子泄漏均显著降低，表明接触后线粒体呼吸活性下降。以 400 微克/升剂量给药后，三磷酸腺苷含量和线粒体呼吸链复合体 I、II、III、IV 的活性显著降低。与此同时，接触 200 和 400 微克/升十溴二苯乙烷的斑马鱼幼体的线粒体膜电位（MMP）也显著降低（$p < 0.05$）。烟酰胺核糖（NR）是 NAD+的前体物质，被用于外源性补偿，以防止线粒体异常。同时接触 160 微克/升烟酰胺核糖和 400 微克/升十溴二苯乙烷（受精后 2 至 120 小时）可以阻止十溴二苯乙烷对线粒体功能的影响，减少氧化应激，并恢复十溴二苯乙烷对神经递质水平以及与神经发育和糖脂代谢相关的基因表达的影响。

87. 成年斑马鱼神经毒性：已证明十溴二苯乙烷对成年斑马鱼具有与神经毒性相关的影响，以及对斑马鱼幼体中具有上文所述影响。斑马鱼幼体大脑拥有与哺乳动物相似的神经调节回路，包括主要神经递质系统，例如谷氨酸、GABA、乙酰胆碱、多巴胺、5-羟色胺（5-HT）、去甲肾上腺素和组胺（Rosa 等人，2022）。上述神经递质与包括人类在内的哺乳动物中发现的神经递质非常相似（Lima 等人，2026）。

88. Sun 等人（2022）（见第 78 段）认为，活动减退（以 100 纳摩尔/升给药组平均游动速度和总游动距离下降（$p < 0.05$）来衡量）与 4 个月大雌性斑马鱼接触 1 纳摩尔/升和 100 纳摩尔/升十溴二苯乙烷 28 天时肌肉相关蛋白质和相关通路以及细胞内的钙稳态受到干扰有关。

89. Sun 等人（2023c）以与 Sun 等人（2023b）相同的方式使 F0 成年斑马鱼进行接触（见第 83 段），发现神经递质平衡被破坏。在成年斑马鱼（8 月龄）的大脑中，F0 代和未接触的 F2 代的神经递质含量变化最为显著，而 F1 代很少有显著变化。几乎所有测试的神经递质在 F1 和 F2 卵中均发生了变化，表明斑马鱼亲代向受精卵传递神经递质的过程受到干扰。十溴二苯乙烷导致雄性和雌

性成年斑马鱼的重量、体长和组织体指数（BST、GSI）发生显著变化。行为表现与神经递质的结果吻合，因为一般而言，在F1代中观察到的变化较少。在10纳摩尔/升浓度下，F0雄性在中间区域的停留时间显著增加，而F2雄性在近端区域和远段区域的停留时间显著增加。在10纳摩尔/升浓度下，F0雌性在近端区域的停留时间显著增加，但在F1或F2中没有观察到同样的情况。记录了根据两只斑马鱼确定的最近邻距离（NND）和个体间距离（IID）。在雌性成年鱼中，最近邻距离在F0代下降，在F1代上升，在F2代没有显著变化，而个体间距离在F0代和F2代中出现显著下降，但在F1代中没有显著下降。考虑到斑马鱼天然群居生活，社会互动（包括社会偏好和集群行为）的改变可能会使其更易受到捕食威胁。然而，观察到的社会偏好变化似乎并非不利，因为大多数变化增加了与同种较为接近的时间，但F2雄性除外。氧化性DNA损伤、总体DNA甲基化水平和转录谱证实了对成年后代大脑具有跨代影响以及雌性具有更强的敏感性。成年脑中成熟且已分化的神经元一般不再进行有丝分裂，而是长期停留在G0期。在三代成年斑马鱼脑中观察到细胞周期紊乱，F2雌性中细胞凋亡显著增加，表明十溴二苯乙烷可以对脑细胞凋亡产生跨代影响。

90. Wang等人（2026）使6月龄成年斑马鱼接触0、10和100纳摩尔/升浓度的十溴二苯乙烷，为期28天（n = 3，每次重复包含20条雄性加20条雌性），发现与中枢神经系统相关的基因转录水平和神经递质水平发生了变化。在雌性成年斑马鱼大脑中，100纳摩尔/升接触组中乙酰胆碱、DA、NE、5-HT和5-HIAA的水平在统计学上显著升高，而10纳摩尔/升接触组中只有5-HT和5-HIAA的水平显著升高。成年雄性斑马鱼大脑中的神经递质水平没有显著变化，这与Sun等人（2023c）的结果相反，其中斑马鱼接触该物质从受精后2小时开始，直至8个月。没有发现对雄性或雌性斑马鱼的社会偏好行为有明显的不利影响（Wang等人，2026）。在雌性斑马鱼中，几个对脑功能和修复有重要意义的基因出现上调，而在雄性中，只有两个基因出现显著上调。雌性和雄性某些基因的转录变化表明，两种性别都出现了与接触十溴二苯乙烷有关的神经毒性。相反，对神经递质水平的观察显示，某些转录水平呈现显著的性别依赖性变化，这表明雌性可能比雄性更易受到接触十溴二苯乙烷的影响。

91. 小鼠神经毒性：Sun等人（2026）发现，亚慢性接触十溴二苯乙烷会诱导小鼠的焦虑样行为，并损害其空间学习和记忆能力。使雄性C57BL/6J小鼠（45周龄）经口接触1%（体积分数）Tween-80中的十溴二苯乙烷，剂量为0、100、500和2 500微克/千克体重/天，持续12周（每组n= 10）。通过开放场和莫里斯水迷宫进行了行为测试。与对照动物相比，两个最高剂量组的动物表现出显著的行为改变，与焦虑样行为以及学习和记忆能力受损有关。海马体的免疫组织学检查显示，两个最高剂量组中的剂量依赖性神经元损伤最为严重。受影响的区域表现出核固缩增加以及神经元排列松动、肿胀和破裂。观察到海马氧化应激标志物（丙二醛和超氧化物歧化酶）显著增加，并且对神经元生存和记忆形成至关重要的关键神经营养蛋白和紧密连接蛋白出现下调。还发现十溴二苯乙烷会诱导小鼠海马内质网应激和线粒体功能障碍，出现Ca^{2+}超载和铁死亡。

2.4.2 对陆地生物、土壤生物和其他水生生物的不利影响

92. 对陆地和土壤生物的毒性：现有研究表明，即使在非常高的浓度下，土壤生物的死亡率也很低。然而，已在蚯蚓中观察到十溴二苯乙烷的氧化应激、脂质过氧化和 DNA 损伤，在接触环境相关浓度的蚕中观察到肠道受损。

93. Hardy 等人（2011）后来发表了几份调查对陆地生物毒性的行业报告。Hardy 等人（2011）评估了对土壤微生物、蚯蚓和植物的陆地毒性。未发现对土壤微生物的不利影响。使蚯蚓（E. fetida）接触 313、625、1 250、2 500 和 5 000 毫克/千克干土壤的十溴二苯乙烷，总共为期 56 天。平均测量浓度分别为 231、440、761、1 907 和 3 720 毫克/千克。在最高测试浓度下，第 56 天观察到繁殖能力显著减少（$p < 0.05$）。因此，56 天生殖最低观测效应浓度为 3 720 毫克/千克干土壤，无观测效应浓度为 1 910 毫克/千克干土壤。按照原始研究报告和欧洲化学品管理局（2008）的要求，将结果标准化至有机碳含量 3.4%时，得出无观测效应浓度为 649.4 毫克/千克土壤干重。E. fetida 没有其他终点在测试浓度下与对照组相比呈现差异。对于植物而言，在较高的测试浓度（3 0915 802 毫克/千克）下，对黄瓜、洋葱和西红柿的生长参数产生了一定影响。

94. Jiang 等人（2021）使 E. fetida 接触十溴二苯乙烷（5、10、20、50、100 毫克/千克），为期 28 天。蚯蚓体内十溴二苯乙烷浓度分别达到 1.31、1.69、1.72、2.32 和 2.60 微克/克。接触 100 毫克/千克的十溴二苯乙烷后，导致蚯蚓表皮的显微结构和超微结构损伤。在所有给药组中均观察到 CYP450 和 GST 活性的显著变化。蚯蚓的 CYP450 和 GST 随接触量的增加呈下降趋势，表明蚯蚓的解毒能力在 21–28 天的高剂量接触下被削弱和抑制。Zhao 等人（2020c）发现，通过人工土壤接触 2.5、5、10 和 20 毫克/千克十溴二苯乙烷，会导致 E. fetida 出现氧化应激、脂质过氧化和 DNA 损伤。即使在最低浓度下也能观察到影响。Wang 等人（2022c）发现，C. elegans 在接触十溴二苯乙烷（0、1、10、100、500 和 1 000 微克/升，0.01%（体积分数）二甲基亚砜）72 小时后，从 100 微克/升开始出现运动神经毒性。此外，100 微克/升组细胞膜损伤明显，增加了 24%（$p < 0.05$），并且与浓度的增加呈剂量依赖关系。

95. Luo 等人（2025）使蚕（Bombyx mori L.）通过用十溴二苯乙烷处理的桑叶接触 0、0.011、0.11、1.1 和 11 微克/克干重的十溴二苯乙烷，该浓度与之前在植物中检测到的水平相当，这些植物是红树林叶（A. marina）（1.072.4 微克/千克有机碳总量）和玉米叶（Z. mays L.）(4.16–31.9 微克/千克干重）（欧洲化学品管理局，2025）。幼虫处于第五龄期，用桑叶喂养了四天。该研究显示，在 0.011–11 微克/克干重范围内，蚕的肠道发生组织病理学变化，所有四种给药都改变了肠道微生物群的组成（$p < 0.05$）。化蛹率、茧层重或全茧重均未观察到显著变化。

96. 鸟类毒性：一份未发表的关于对鸟类长期毒性的研究报告（2013）发现，对于通过饮食接触十溴二苯乙烷的北美鹑（C. virginianus）而言，20 周无观测效应浓度为≥88.1 毫克活性成分/千克体重/天。然而，当用 0.1 毫摩尔/升十溴二苯乙烷处理鸡肝细胞时，观察到在与环境相关的浓度下对鸟类的甲状腺可能产生影响。在 0.1 和 0.2 微摩尔/升浓度下，DIO1 基因的信使 RNA 表达增加，CYPA4/5 的信使 RNA 表达显著上调（Eggloff 等人，2011）。

97. 对水生生物的毒性：在标准化工业研究报告中，十溴二苯乙烷表现出较低的急性毒性。这些标准化短期毒性测试后来已作为同行评审文章发表（Hardy 等人，2012）。Hardy 等人（2012）研究了十溴二苯乙烷对五个物种

（虹鳟（O. mykiss）、淡水藻类（P. subcapitata）、水蚤（D. magna）、摇蚊（C. riparius）和寡毛类动物（L.variegates））的影响，但没有发现任何急性毒性作用。鱼类、藻类和水蚤急性接触 110 毫克十溴二苯乙烷/升的水适应组分（WAF）后未受影响。在最高测试剂量（5 000 毫克/千克干沉积物）下长期接触十溴二苯乙烷，没有影响摇蚊的平均发育时间、羽化率和发育速率，也未影响寡毛类动物的存活、繁殖和干重。然而，由于使用水适应组分方法来制备接触溶液，因此这项研究中的剂量存在不确定性，并且作者没有报告使用任何溶剂。

98. Nakari 和 Huhtala（2010）对 D. magna（ISO 6341，1996）和斑马鱼的卵和幼体（ISO 12890，1999）进行了急性毒性测试。十溴二苯乙烷对 D. magna 的 48 小时半数有效浓度值为 19 微克/升。卵和幼体测试显示，接触 25 微克/升浓度的卵的孵化率显著降低（$p < 0.05$）。两个测试组（12.5 和 25 微克/升）的卵和孵化幼体死亡率均显著较高（$p < 0.05$）。

99. Wang 等人（2023b）使贻贝（M. galloprovincialis）接触十溴二苯乙烷（1、10、50、200 和 500 微克/升，0.001%（体积分数）二甲基亚砜），为期 30 天。组织学观察、卵子和精子蛋白的性别特异性基因表达（VERL 和 VCL）以及组织学形态计量参数分析表明，十溴二苯乙烷促进了雄性和雌性的配子发生，这说明该物质可能会引起海洋贻贝的生殖内分泌干扰。Zheng 等人（2024）使章鱼（A. fangsiao）接触十溴二苯乙烷（0、1、50、100、300 微克/升，加入 0.2 %（体积分数）二甲基亚砜），为期 28 天。300 微克/升组在 28 天内表现出生长和食物摄入量显著下降。接触十溴二苯乙烷会损害肠道的完整性，促进细菌移位，并对消化腺造成组织学损害和炎症，这可能导致生长表现受到阻碍，食物摄入受到抑制。

100. 由于受体和信号通路存在若干保守特征，第 2.3.1 节包含了对斑马鱼的机制研究。

根据附件 D 标准得出的不利影响结论

101. 认为十溴二苯乙烷及其脱溴类似物被认为符合附件 D 第 1 (e) (i)和(ii)段中列出的不利影响标准。

102. 关于对人类健康和环境的不利影响，氧化应激在所有研究中都很普遍，并会对多种组织产生不利影响，线粒体功能障碍可能与观察到的大脑影响有关。还观察到了对下丘脑–垂体–甲状腺轴的影响，这可能导致肝脏代谢功能受损。

103. 关于对人类健康的不利影响，小鼠和大鼠的实验研究表明，十溴二苯乙烷有可能通过干扰睾酮的产生以及改变睾酮、促黄体生成素和促卵泡激素的血清水平，对生殖造成不利影响并降低精子质量。在接触 5 毫克十溴二苯乙烷/千克体重 7 周的小鼠中观察到精子数量减少和精子畸形增加以及睾丸中生殖细胞层减少和睾酮减少，血清中的促黄体生成素和促卵泡激素减少的最低观测效应浓度为 50 毫克/千克（Qi 等人，2025）。在另一项小鼠研究中，接触 0.5 毫克/千克体重的十溴二苯乙烷 12 周导致精子质量显著下降，睾丸精子生成受到影响（Shi 等人，2026）。

104. 使 ApoE 基因敲除小鼠接触 100 毫克/千克体重的十溴二苯乙烷 6 周后，观察到心血管影响，炎症、斑块和脂质积聚增加。脂质代谢以及促进巨噬细胞聚集的粘附分子水平也受到影响。使大鼠接触 50 和 500 毫克/千克体重的十溴二

苯乙烷 28 天的研究表明，十溴二苯乙烷可能损害线粒体功能并降低心脏组织中的三磷酸腺苷水平，诱导炎症反应，影响代谢（增加血糖和低密度脂蛋白）并诱导心脏组织的细胞凋亡。

105. 关于对环境的不利影响，对鱼类接触十溴二苯乙烷的实验研究表明，对生育能力、性腺发育、精子质量和精子生成、性激素水平、下丘脑-垂体-性腺轴基因表达和卵巢代谢组特征会产生影响（Yu 等人，2026，Yang 等人，2024，Zhou 等人，2026；Sun 等人，2022；Choi 等人，2021）。在几项鱼类研究中观察到与甲状腺激素相关的影响，接触环境相关浓度的十溴二苯乙烷会导致下丘脑–垂体–甲状腺轴和血浆甲状腺激素水平紊乱（Sun 等人，2024b，Wang 等人，2019c；2022a）。世代接触后，在发育中的幼体和成鱼中观察到神经递质含量和行为的改变。

106. 更加令人关切的是，发现在长须鲸和人类中，十溴二苯乙烷会通过胎盘从母体转移至胎儿，并且在全球范围内的人类母乳中都测量到了该物质。生物积累性物质在子宫内的母源转移对胚胎发育构成潜在风险，并且可能是后代出生后前几年阻燃剂输入的最大来源。

3. 关切的理由和采取全球行动的必要性说明

107. 根据现有数据，可以认为十溴二苯乙烷符合《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。

108. 过去十年，全球产量和使用量显著增长，预计未来仍将增加，主要是作为十溴二苯醚的替代品。十溴二苯乙烷用于许多应用，导致向环境排放。

109. 已在 1989 年至 2011 年意大利马焦雷湖的测年沉积物柱样（Poma 等人，2014）以及 2011 年至 2018 年渤海软体动物（Wang 等人，2021）中观察到增加趋势。环境中的十溴二苯乙烷水平超过或等于十溴二苯醚和其他已列入持久性有机污染物清单的溴化二苯醚。在城市化程度较高的地区，在环境和人体中观察到的浓度水平较高，说明该物质的释放没有得到控制。十溴二苯乙烷还可能导致在环境中形成具有持久性、生物积累性和固有毒性的转化产物，例如溴化程度较低的二苯乙烷类化合物。在偏远区域的空气、雪、土壤和生物群样本中广泛检测了该物质，证明发生了远距离大气迁移。

110. 对照研究中的接触情况表明，十溴二苯乙烷会诱导氧化应激、增加炎症、损害线粒体和代谢功能，从而导致观察到的心血管、生殖和大脑影响。有研究表明，十溴二苯乙烷可能影响哺乳动物、鸟类和水生物种的内分泌系统。

111. 十溴二苯乙烷会对啮齿动物和鱼类雄性的精子生成和下丘脑-垂体-性腺轴产生毒性，从而影响生殖。还有迹象表明，十溴二苯乙烷可能影响雌性生殖，在雌性鱼中观察到生育能力下降与性激素水平下降和卵母细胞发育改变有关。研究发现，接触十溴二苯乙烷会通过影响非哺乳动物和哺乳动物的下丘脑–垂体–甲状腺轴来干扰甲状腺系统。在鱼类和啮齿动物中都观察到了对神经系统的影响。已经证明十溴二苯乙烷会改变鱼类的神经递质平衡以及鱼类和啮齿动物的行为，并诱导小鼠大脑中与记忆相关区域的形态改变。

112. 在所有调查区域，十溴二苯乙烷仍在继续向环境中释放。十溴二苯乙烷可能导致在环境中形成具有持久性、生物积累性和固有毒性的转化产物，例如溴化程度较低的二苯乙烷类化合物。由于其持久性有机污染物特性以及与其广泛生产和使用相关的风险，有必要采取全球行动控制十溴二苯乙烷的进一步释放。

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Technical work: consideration of chemicals proposed for listing in Annexes A, B and/or C to the Convention: decabromodiphenylethane (DBDPE) and its related substance, 1,1'-ethane-1,2-diylbisbenzene, brominated

Proposal to list decabromodiphenylethane (DBDPE) and its related substance, 1,1'-ethane-1,2-diylbisbenzene, brominated, in Annexes A, B, and/or C to the Stockholm Convention on Persistent Organic Pollutants**

Note by the Secretariat

I. Introduction

1. The Government of Norway has submitted a proposal to list decabromodiphenylethane (DBDPE) and its related substance, 1,1'-ethane-1,2-diylbisbenzene, brominated, 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. 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 decabromodiphenylethane (DBDPE) and its related substance, 1,1'-ethane-1,2-diylbisbenzene, brominated, in Annexes A, B and/or C to the Stockholm Convention on Persistent Organic Pollutants

1. Introduction

1. Decabromodiphenylethane (DBDPE) is a brominated aromatic flame retardant consisting of two benzene rings fully substituted with five bromine atoms connected via a central ethane moiety. Brominated diphenyl ethyls including DBDPE and a related UVCB substance[1] (1,1'-ethane-1,2-diylbisbenzene, brominated) are widely used nonreactive brominated flame-retardant additives. Their extensive use spans electrical and electronic equipment, automotive components, building and construction materials, and textiles. Global production and use have grown significantly over the past decade, largely as replacements for decaBDE, which was listed in the Stockholm Convention in 2017 (ECHA, 2024a).

2. DBDPE is registered under REACH in the European Union, with imports between 10,000–100,000 tonnes annually. According to ECHA (2024a), brominated diphenyl ethyls account for 43% of the total estimated tonnage of aromatic brominated flame retardants placed on the EU market. Substantial quantities are also produced or imported in the United States (9000- 45 000 tonnes/y between 2016-2019, US EPA 2020). Import to Canada is estimated at 1,000–10,000 t/y (ECCC & HC, 2019), and 120 tonnes per year (AICIS, 2021) to Australia. China is the main producer of DBDPE with >50 % of the global production in 2012. Between 2006 and 2016, China produced approximately 230,000 tonnes of DBDPE, with about 20% (39,000 tonnes) exported in DBDPE containing products. Exports are projected to rise to 100,000 t/y primarily incorporated in exported electronic equipment (EEE) by 2026 (Liu et al., 2026). 1,1'-ethane-1,2-diylbisbenzene, brominated is registered under REACH with 1-10 t/y.

3. Regulatory scrutiny has increased internationally. In 2025, DBDPE was identified as a Substance of Very High Concern (SVHC) due to vPvB properties (ECHA, 2025) in the EU. Several jurisdictions, including Canada and Australia, have adopted or announced prohibitions with exemptions (ECCC & HC, 2025; AICIS, 2022). The U.S. continues to assess the substance under U.S. Toxic Substances Control Act, while most Asian countries have not yet introduced national regulations.

4. There are no known natural sources of DBDPE, which have been detected in all compartments of the environment including air, surface water, sediment, biota and humans and in remote Arctic and Antarctic regions (AMAP, 2016; ECHA, 2025). Widespread detection in remote air, snow, soil, and biota samples demonstrates long-range atmospheric transport. Increasing trends in dated sediments cores from Lake Maggiore in Italy from 1989 to 2011 (Poma et al., 2014) and in mollusks from Bohai Sea from 2011 to 2018 (Wang et al., 2021) have been observed. In environmental samples DBDPE is often detected in higher levels than other new BFRs (Wang et al., 2023a).

5. Releases during service life measured as indoor dust levels are reported in the range 307-540,000 ng/g, sewage sludge from <LOD to 220 ng/g dw and levels in biota (fish and mussels) reported from <LOD to 3300 pg/g lw (ECHA, 2024a, appendix G). Serum levels in human worker with occupational exposure was reported from 87-54,400 ng/g lw, indicating chronic exposure (Wang et al., 2019a).

6. Based on existing data DBDPE can be considered to meet the screening criteria in Annex D for persistence, bioaccumulation, long-range transport and adverse effects under the Stockholm Convention. DBDPE may also contribute to the formation of persistent, bioaccumulative, and inherently toxic transformation products (lower brominated BDPEs) in the environment.

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* 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] Substances of unknown or variable composition, complex reaction products or biological materials.

7. For the assessment of DBDPE, information from the support document for identification as a SVHC (ECHA, 2025) has been used as well as information from peer-reviewed scientific journals and grey literature. Unpublished studies are thoroughly described by ECHA (2025), where the authors had access to complete study reports during the SVHC process. The OECD TG 443 (Unpublished, 2026) was not part of the previous assessment and only a summary has been available.

Chemical identity

8. Brominated diphenyl ethyls consist of DBDPE registered as a mono- constituent in the public available registration dossier in ECHA CHEM database. The other member of the group is (1,1'-ethane-1,2-diylbisbenzene, brominated) registered as a UVCB substance containing DBDPE as a constituent above 0.1 % w/w as well as other structurally similar congeners (ECHA, 2024a).

Table 1. The chemical identity of decabromodiphenylethane (DBDPE)

CAS number:	84852-53-9
IUPAC name:	1,1'-(ethane-1,2-diyl)bis[pentabromobenzene]
EC number:	284-366-9
EC name:	1,1'-(ethane-1,2-diyl)bis[pentabromobenzene]
Molecular formula:	$C_{14}H_4Br_{10}$
Molecular weight:	971.226 g/mol
Synonyms:	1,1'-(ethane-1,2-diyl)bis[2,3,4,5,6-pentabromobenzene]; 1,2-bis(pentabromophenyl)ethane benzene; 1,1'-(1,2-ethanediyl)bis(2,3,4,5,6-pentabromo)-decabromodiphenylethane (DBDPE); 1,2,3,4,5-pentabromo-6-[2-(2,3,4,5,6-pentabromophenyl)ethyl]benzene
Trade names	DBDPE, DBDPE/RDT-3, Ecoflame B-971, Firemaster 2100R, SAYTEX 4010 Flame Retardant, SAYTEX 4010 ZD, SAYTEX 402 Flame Retardant (no longer marketed), SAYTEX 8010, SAYTEX 8010 Flame Retardant, SAYTEX 8010 ZD, SLFR-2, YCFR-03

Table 2. Overview of selected physicochemical properties

Property	Value [Unit]	Reference/source of information
Physical state at 20°C and 101.3 kPa	Solid colorless white powder	Visual inspection[2]
Melting/freezing point	350 °C	Differential Scanning Calorimetry[2]
Vapor pressure	**3.14×10^{-11} Pa at 20 °C** $<1 \times 10^{-4}$ Pa at 20°C 3.8×10^{-9} Pa 1.55×10^{-11} Pa at 20°C 9.33×10^{-9} Pa For comparison: 4.63×10^{-6} Pa at 21°C for decaBDE, melting point of 300-310°C	**Value selected:** OECD TG 104 Vapour Pressure – Effusion method: isothermal thermogravimetry, (AICIS, 2021) OECD TG 104, Vapour Pressure – Spinning rotor method[2] Prediction by Wania and Dugani, 2003 COSMOtherm prediction. (Glüge and Scheringer, 2023) Predicted from AEROWIN v1.00 (EC, 2002)
Water solubility	**<0.05 µg/L DBDPE/L at 20 °C** 0.72 µg/L at 25 °C <0.05 µg/L at 20°C	**Value selected:** OECD TG 105 Water Solubility Column Elution Method EPA OPPTS 830.7860 (Water Solubility Generator Column Method) [2] OECD TG 105 Water Solubility – Column Elution Method (AICIS, 2021)

[2] Search results for 84852-53-9 - ECHA CHEM.

Property	Value [Unit]	Reference/source of information
	0.00000867 µg/L at 20°C For comparison:<0.1 µg/L at 25 °C decaBDE	COSMOtherm prediction (Glüge and Scheringer, 2023) (EC, 2002)
n-octanol/water partition coefficient (log K_{OW})	**9.23** 3.55 at 25°C >6.50 9.89 9.23 at 20°C For comparison: 6.27 – 9.19 decaBDE	**Value selected:** COSMOtherm prediction (Glüge and Scheringer, 2023) Generator Column Method[2] OECD TG 117 – HPLC Method (AICIS, 2021) Prediction by ECCC and HC, 2019 Prediction COSMOtherm (Glüge and Scheringer, 2023) (EC, 2002)
organic carbon/water partition coefficient (log K_{OC})	**6.86** 6.38 8.01 6.54 at 25°	Value selected: OECD TG 106 [2] PCKOC v1.66 v2.00 prediction KOCWIN v2.00 prediction and log Kow of 9.23 Prediction COSMOtherm (Glüge and Scheringer, 2023)
n-octanol/air partition coefficient (log K_{OA})	**13.81** 16.66 at 20°C	Value selected: KOAWIN v1.10 prediction; log Kow = 9.23 and HLC = 0.061 Pa m3/mol (= 0.00000060 atm-m3/mol) used, Prediction COSMOtherm (Glüge and Scheringer, 2023)

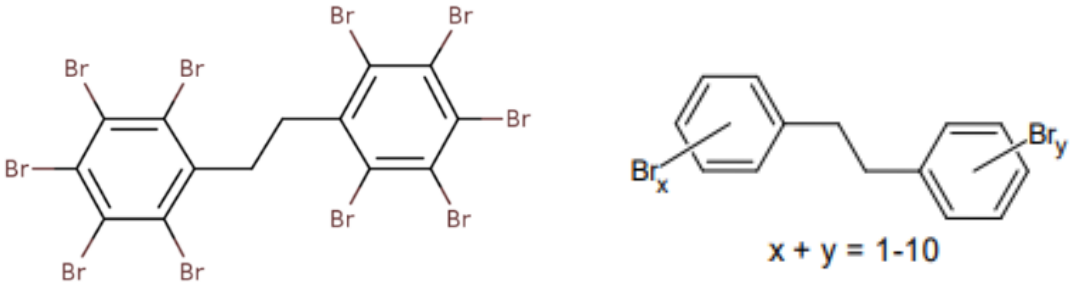

Figure 1. Structural formula of DBDPE (CAS No. 84852-53-9) and the UVCB substance 1,1'-ethane-1,2-diylbisbenzene, brominated (CAS No. 1092834-40-6)

2. Information on DBDPE and how it fulfils the Annex D screening criteria

2.1 Persistence

9. DBDPE is chemically very stable in environmental compartments and shows very limited degradation under both aerobic and anaerobic conditions. Available screening tests, simulation studies, and field observations consistently demonstrate that DBDPE is highly resistant to degradation and therefore environmentally persistent. Like for decabromodiphenylether, BDE-209, debromination has also been observed under various conditions, although BDE-209 seems to debrominate more easily than DBDPE.

10. DBDPE does not contain any readily hydrolysable functional groups, and hydrolysis is therefore not expected to be a relevant abiotic degradation process. This is further supported by its extremely low water solubility (≈ 0.05 µg/L at 20°C, ECHA, 2025) and its high log K_{OC} (6.86), leading to strong adsorption to suspended particulate matter and sediments, substantially limiting its availability for aqueous phase reactions (Unpublished, 2015a). Hydrolysis is therefore considered to be environmentally insignificant for DBDPE.

11. Phototransformation in air has been investigated by UV/visible absorption measurements, which indicate that DBDPE absorbs weakly at wavelengths above 290–295 nm, suggesting low sensitivity to direct photolysis under natural sunlight conditions (Dungey and Akintoye, 2007). Model estimates using AOPWIN predict an atmospheric half-life of approximately 4.5–6.7 days for reaction with hydroxyl radicals; however, due to DBDPE's very low vapor pressure (3.14×10^{-11} Pa at 20°C) and strong association with airborne particulates, gas phase phototransformation is considered of limited environmental relevance (ECHA, 2025). Due to the low water solubility of DBDPE, photolysis has not been studied in pure water and is expected to have limited importance for DBDPE.

12. Phototransformation of DBDPE in other media has been investigated in laboratory photolysis studies using artificial UV light and reactive matrices such as solvents and humic-acid/water systems. The studies show that DBDPE can undergo stepwise debromination under high-energy irradiation. For example, Wang et al. (2012) exposed DBDPE to UV light in solvents, humic-acid/water systems, and on silica gel (which simulates soil compartment) and observed rapid transformation with formation of nona- to heptabrominated diphenyl ethane congeners. Similar debromination patterns were reported by Kierkegaard (2004), Granelli (2011), Wei et al. (2012a), Li et al. (2019) and Klimm et al. (2019). Wang et al. (2010) used UV-light to generate DBDPE debromination products and study their uptake. Mainly debromination products such as nona- to heptabrominated diphenyl ethane were formed after UV-exposure, although some oxygen containing transformation products were observed by Klimm et al. (2019) and Li et al. (2019). Further, Zeng et al. (2025) demonstrated photolysis and debromination of DBDPE and used this to prepare reference standards for the debromination products. In contrast, when DBDPE was incorporated in a plastic matrix (High-impact polystyrene (HIPS)) and exposed to natural sunlight for up to 224 days, no measurable degradation of the parent compound was observed (Kajiwara et al., 2008), indicating that phototransformation is matrix dependent and may be of limited importance in most environmental settings as DBDPE will partition to particles and sediment. Overall, phototransformation of DBDPE is considered to be environmentally insignificant.

13. DBDPE is highly persistent in soils and sediments. In a water–sediment simulation study according to OECD TG308, no relevant degradation was observed under either aerobic or anaerobic conditions over a six-month period at room temperature, and the degradation half-life in sediment thus exceeded 180 days (Unpublished, 2015b). Similarly, two soil simulation studies conducted according to OECD TG 307 in multiple soil types showed no significant degradation under both aerobic and anaerobic conditions, with DT_{50} values exceeding 180 days in all cases (Unpublished, 2015c and 2015d), thereby fulfilling the Annex D criteria. Additionally, a soil study including growing plants also showed no enhanced transformation, indicating that plant–soil interactions do not substantially affect the environmental stability of DBDPE (Unpublished, 2019).

14. Ready and inherent biodegradation studies support the results from simulation studies, showing that DBDPE is neither readily nor inherently biodegradable. In a ready biodegradation test conducted according to OECD TG 301C (Unpublished, 1991), no biodegradation was observed based on oxygen consumption and only minimal primary degradation (~2%) was detected by chemical analysis. An inherent biodegradability test following the proposed OECD TG 302D (Unpublished, 2015e) showed only 2.2% mineralization after 90 days under aerobic conditions, with no evidence of formation of degradation products (as summarised in ECHA, 2025). In addition, a test for transformation and mineralization in anaerobic digester sludge according to OECD TG 314C (Unpublished, 2011, summarized in ECHA, 2025) showed no microorganism mediated mineralization over 63 days, indicating that DBDPE is not degraded under anaerobic wastewater treatment conditions.

15. Transformation of DBDPE to lower brominated congeners by organisms has been demonstrated. Wang et al. (2010) observed biotransformation in rats. While reductive debromination was observed, substitution with $MeSO_2^-$ was the primary metabolic pathway. Wang et al. (2019b) observed transformation of DBDPE in zebrafish larvae, although the identities were not determined. Wang et al. (2022a) also observed transformation in zebrafish larvae and identified nona-, octa and hepta-BDPE debromination products as well as other brominated compounds. Wang et al. (2020a) showed that debromination occurred in snails and here reductive debromination was the main pathway, forming nona- to heptabrominated and lower diphenyl ethane congeners. Wang et al. (2022b) showed a rapid debromination by the white rot fungi *Pleurotus ostreatus*, which was able to degrade 48% to 38% of DBDPE at concentrations ranging from 5 to 25 mg DBDPE/L. At higher concentrations the degradation slowed down, presumably due to toxicity. Both intercellular enzymes (P450) and extracellular enzymes (e.g. laccase and lignin peroxidase) were involved, with laccase playing an especially important part in the degradation. Degradation products formed from debromination and hydroxylation were the dominant types. Jiang et al. (2021) observed transformation products in both earthworms and earthworm casts corresponding to forming nona- to heptabrominated

and lower diphenyl ethane congeners. Other types of debromination products, such as OH-adducts, may have been formed as well but were not characterized.

Conclusion on persistence according to the criteria in Annex D

16. DBDPE meets the persistence criteria of Annex D with degradation half-lives in sediment and soil greater than six months (>180 days). The substance has also been detected across all environmental compartments, including remote regions such as the Arctic and Antarctica, which provides strong evidence of its persistence. DBDPE has previously been identified as a SVHC due to its vPvB properties according to REACH annex XIII (ECHA 2025).

2.2 Bioaccumulation

17. Under Annex D, substances with a bioconcentration factor (BCF) > 5 000 in aquatic organisms meet the bioaccumulative (B) criterion or may qualify based on high bioaccumulation in other species or monitoring data. DBDPE is extremely hydrophobic (log K_{OW} 9.23; water solubility ~0.05 µg/L), strongly partitions to organic matter, and exhibits very high adsorption to sediments and soils (log K_{OC} up to 6.86), limiting dissolved exposure but enabling dietary and particle-mediated uptake.

18. Multiple laboratory studies indicate that DBDPE fulfils the B criterion. Burkhard et al. (2023) performed an OECD TG 305 dietary study with rainbow trout and ECHA (2025) later modelled BCFs based on these results. ECHA (2025) found BCFs that exceeded 5 000 with slow depuration, indicating high bioaccumulation potential. Likewise, sediment-based testing with *Lumbriculus variegatus* yielded BCFs > 5 000 when normalized to pore water (Zhang et al., 2013).

19. Monitoring data show DBDPE in invertebrates, fish, amphibians, reptiles, birds, mammals, and humans, including Arctic wildlife, demonstrating environmental uptake despite low water solubility (KLIF, 2013; de Wit et al. 2020). Monitoring studies indicate that uptake of DBDPE in the environment via food exceeds what is observed in laboratory settings, likely due to the form of DBDPE exposure and exposure duration. Monitoring and field studies for DBDPE are thoroughly described in ECHA 2025, chapter "3.4.3 Monitoring data and field studies". Biomagnification factors (BMFs) greater than 1 have been reported for a range of predator–prey relationships across aquatic, terrestrial, and estuarine food webs, with BMFs reaching values up to 28.5 (Ding et al., 2022; Wu et al., 2024; Sun et al., 2024a), while other studies report BMFs below 1 (Wu et al. 2023; Sun et al 2023a). Trophic magnification has also been observed in marine food webs, with trophic magnification factors (TMFs) above 1 (up to 4.22–5.12; Hou et al., 2022[3]). However, other studies report trophic dilution (TMF < 1; e.g. Liu et al., 2020), illustrating that biomagnification may be species specific and dependent on food web structure and exposure conditions.

20. Burkhard et al. (2023) conducted a dietary OECD TG 305 study in rainbow trout exposed for 28 days to DBDPE along with several other halogenated compounds, including established POPs. Uptake was very low and variable for DBDPE. Superhydrophobic substances like DBDPE tend to have very slow uptake phases and need a very long time to reach equilibrium. DBDPE was added to the feed as a solid, and not dissolved, which likely reduced its uptake. The concerns for uptake duration and introduction through feed are supported by the available monitoring data demonstrating uptake in a wide array of biota but was very limited in this study. Elimination appeared to be more rapid than the uptake, and a k_2 of 0.084, resulting in lipid-normalized BMF values below 1. The k_2 value from this study was just below the suggested k_2 value (< 0.085) by Brooke and Crookes (2012) as corresponding to a BCF of 5000. Due to these concerns, as well as depuration data often being near detection limits and growth dilution was not accounted for (fish weight doubled during the test), the study was considered to be unsuitable for directly deriving definitive BMF values. The authors concluded that biomagnification was not expected under the laboratory conditions, although this contradicts several field studies reporting BMFs and TMFs > 1 for DBDPE.

21. ECHA (2025) reevaluated the Burkhard dataset using kinetic modelling aligned with OECD TG 305 and the OECD BCF estimation tool described in OECD GD 305, including lipid and growth correction. The modelling produced BCF estimates mostly >5000 and confirmed slow depuration ($k_{2g} \approx 0.045$ d^{-1}; biological half-life ≈ 15.5 days), consistent with a highly hydrophobic, poorly soluble substance. Despite uncertainties inherent to the mixed substance exposure design, the reassessment provides strong supporting evidence that DBDPE meets the B criterion of annex D.

[3] Hou et al. (2022) spans 2.14 trophic levels. According to Kidd et al (2018) et al 2.0 is sufficient for reliable TMFs.

22. Qiao et al., (2023) observed tissue specific BAFs ranging from approximately 6 500 to 12 900 in zebrafish and showed that DBDPE can be transferred to offspring, as it is found in roe. The study demonstrated clear concentration dependent accumulation of DBDPE across multiple tissues and was conducted under controlled laboratory conditions with analytical verification of exposure levels. Gradual debromination to nona-, octa-, hepta-, hexa- and pentaBDPE was also observed in the study. Although exposure levels exceeded environmental relevance, internal concentrations were analytically consistent and aligned with expectations for a highly hydrophobic substance. The study provides strong supporting evidence of bioaccumulation.

23. Zhang et al., (2013) calculated very high BCF values for uptake by *L. variegatus* from field collected sediment when normalized to estimated porewater concentrations. The study demonstrated pronounced uptake of DBDPE into tissue, despite low aqueous solubility and limited mobility from sediment, with logBCF values up to 9.87, far exceeding the BCF criteria of 5000. The exposure system did not strictly follow standard guideline procedures, and uncertainties remained regarding steady state attainment. Because porewater levels were not measured directly (via SPME fibres and back calculated) and the test system deviated from guideline conditions, some uncertainty remains about the resulting BCFs. The study was deemed unsuitable for deriving quantitative BCFs but found to be supportive of the qualitative conclusion of high bioaccumulation potential.

24. A laboratory food web study conducted by Zhou et al. (2023) examined DBDPE bioaccumulation in a constructed community including macrophytes, mollusks, and fish. Log BAFs ranged from 2.94 to 4.96, while the trophic magnification factor was TMF < 1, indicating biodilution rather than biomagnification within the constructed food web. The log BAF of 3.82 ± 0.329 for Chinese bitterlings (carp fish) exceeds the Annex D threshold for B. However, the simplified trophic structure and lack of increasing concentrations with trophic level indicate that steady state biomagnification was not achieved. Although the stated challenges reduce the reliability of the results, the study met basic analytical quality criteria and supports a qualitative conclusion of high bioaccumulation potential.

25. Wang et al. 2022a exposed zebrafish larvae for 144h to aqueous solutions of n-TiO_2 (100 µg/L) and DBDPE (0, 1, 10, or 100 µg/L). Accumulation of DBDPE was only detected above LOD in larvae exposed to 10 or 100 µg/L DBDPE with or without n-TiO2. However, in the group exposed to 100 µg/L DBDPE and n-TiO2, the DBDPE concentration was significantly higher than in the group exposed to only DBDPE. Co-exposure with particles is relevant as this could closer represent the natural environment where particles naturally occur in the water column. Due to their surface properties, particles can adsorb organic and inorganic pollutants, resulting in changes in bioavailability (Wang et al., 2022a). This is supported by observations made by Lu et al., (2026) who observed that DBDPE had a low presence in the diet of red footed boobies (fish and squid) but was found in elevated levels in the sampled birds and environmental samples of plastic. They concluded that accumulation in birds may have been increased by plastic ingestion, indicating an additional non-trophic exposure pathway. However, they note that the study only had samples from five birds that were found washed up on the beach post-mortem and are difficult to use for population-level inferences. The studies by Wang et al. (2022a) and Lu et al. (2026) are given a low weight in the overall evaluation.

26. Two studies by Fremlin et al. (2025a and 2025b) evaluate the bioaccumulation potential of DBDPE. The 2025a study used DBDPE as a model substance to investigate a new approach to how note ii[4] to Annex D criteria for bioaccumulation could be used for a difficult to test substance. The study applied a chemical-activity framework and concluded that DBDPE cannot bioaccumulate to levels of concern. It is noted that chemical activity is generally most relevant for acute baseline toxicity (also called non-polar narcosis) (Mackay et al., 2020), while a high level of uncertainty remains for chronic effects (ECETOC, 2016). According to the chemical activity approach, it is not possible for compounds with very high melting point to be toxic though non-polar narcosis, and DBDPE has a melting point of approximately 350 °C. The study also narrowed its toxicity assessment to 14 of 58 studies, excluding many that report biological responses but lacked classical dose–response endpoints. Typically, the studies that were excluded investigated "enzyme or hormone reactions, changes in biochemistry, histopathology of organs, behavioral responses, and changes in gene expression". These types of effects are important for DBDPE, as can be seen in the chapter on adverse effects, and also expected to be poorly described by non-polar narcosis. This filtering therefore reduces the sensitivity of the approach to subtle or chronic effects that might be more relevant for highly persistent, low-solubility chemicals. In addition, this proposed approach imports quantitative

[4] "Evidence that a chemical presents other reasons for concern, such as high bio-accumulation in other species, high toxicity or ecotoxicity; or".

risk assessment into the bioaccumulation assessment step. This is inconsistent with the general regulatory understanding of PBT/POP identification (ECHA, 2023), where bioaccumulation potential is evaluated independently of risk.

27. The Fremlin et al. 2025b study introduces a structured scoring system for evaluating the reliability of field TMF/BMF studies. While intended to standardize data quality, the approach removes more than half of the available studies and then averages biomagnification metrics across ecologically diverse food webs. The study concludes that DBDPE does not show magnification in the environment. Because accumulation varies substantially among ecosystems and species, averaging can mask genuine biomagnification observed in particular environments. Several included field studies do show accumulation in certain food webs, even if others do not.

28. Experimental animal studies indicate that DBDPE is poorly absorbed after both single and repeated oral exposure (Unpublished, 2004; 2012; 2025 as referred in ECHA 2025; Wang et al., 2010; Knudsen et al., 2017). The unpublished study from 2025 found no uptake after 14 days of exposure, while Wang et al. (2010) found uptake after 90 days. Both these studies used corn oil to dissolve DBDPE. Knudsen et al. (2017) used a lower dose of 100 nmol/kg (~0.01 mg/kg[5], n=4) than the Unpublished (2025) study at 100-1000 mg/kg. Knudsen et al. (2017) also administrated orally by gavage but observed uptake after one and 10 days. These studies suggest that repeated exposure over longer periods leads to higher uptakes, but that exposure route and dose formulation are also important. DBDPE was predominantly eliminated via feces in the Knudsen et al. (2017) study, with more than 90% of the administered dose recovered unchanged within 72 hours and only minimal urinary excretion. Intravenous dosing in rats showed slow excretion and extensive retention in tissues, with 70% being retained in tissues after 72 hours. This indicates a whole-body half-life of 5 - 5.8 days. According to ECHA's PBT-guidance R.11 (ECHA, 2023), a whole-body terminal elimination half-life longer than 4 days in rats is supporting evidence for vB-properties in a WoE-assessment for bioaccumulation. By comparison in the same study, 30% of BDE-209 was retained after intravenous dosing in tissues after 72 hours, indicating a whole-body half-life of 2.1 – 2.5 days. It is noted that the slow clearance of DBDPE may be attributed to saturation of metabolic and elimination pathways at high internal concentrations, mimicking intrinsically slow clearance. Uptake after dermal exposure was also demonstrated after exposure to 5µl of DBDPE dissolved in toluene to 2.7 nmol/cm². 17±10% of the administered dose was adsorbed to the skin and 5±2% penetrated the skin and was found in internal tissues, demonstrating that dermal uptake can contribute to the total uptake. The limited metabolism and reliance on fecal elimination may contribute to the persistence of DBDPE once internalized in humans.

29. Maternal transfer has been documented in wildlife including birds, amphibians and marine mammals (Zheng et al., 2018; Sun et al 2023a; Sala et al., 2022). DBDPE has also been shown to accumulate in humans and to undergo maternal transfer, raising concern for exposure during sensitive life stages which are of special concern as the fetus and newborns are highly vulnerable to exposure by xenobiotic substances. The substance has been detected in human serum, umbilical cord blood, breast milk, hair, and nails (e.g. Zhou et al., 2014, Leung et al., 2020, Hammel et al., 2024; Wang et al., 2020b; Wemken et al., 2020; Mannetje, et al., 2013; Rawn et al., 2024; Tao et al., 2017; Schreder et al., 2023; Zhao et al., 2020b, Salah et al., 2026), with particularly high concentrations reported in occupationally exposed workers (Chen et al., 2019; Wang et al., 2019a).

30. Biotic and abiotic debromination to more bioaccumulative congeners have been demonstrated. Both biotic and abiotic debromination for DBDPE to nona-, octa-, hepta- and even hexa-BDPEs has been demonstrated, e.g. Qiao et al., (2023), Jiang et al., (2021), Wang et al. (2012), Wang et al., (2020a), Wang et al. (2022a) and Zeng et al. (2025). Wang et al. (2019c) observed that in zebrafish larvae, 88.2% of the brominated compounds in the DBDPE treated group was composed of transformation products after 14 days exposure. These debromination products are assumed to be more accumulative than DBDPE but there is limited information on the properties of debromination products from DBDPE. However, it is reasonable to expect a similar increase in bioaccumulation potential for the debromination products of DBDPE as seen with the debromination products of BDE-209. BDE-209 is a close structural analogue and is a recognized POP based on bioaccumulation of the parent substance and that it was transformed to lower brominated diphenyl ethers that are more bioaccumulative and are listed in the Stockholm Convention.

31. Numerous laboratory and field studies indicate that DBDPE has a high potential for bioaccumulation, but not all available investigations show this consistently. Several studies report low bioconcentration or even apparent trophic dilution under certain experimental conditions. However, these findings typically arise from study designs that limit environmental relevance—such as

[5] Knudsen et al. (2018) report the value as 0.02 mg/kg, but this seems to be a misprint.

aqueous-only exposure routes, short exposure durations, or test concentrations exceeding water solubility. Such conditions are not appropriate for evaluating a highly hydrophobic substance like DBDPE. The available TMF and BMF values greater than 1 provide robust support for biomagnification when interpreted within a weight of evidence framework. There are multiple lines of evidence demonstrating DBDPE's high bioaccumulation potential—including long elimination half-lives, widespread detection in biota (including humans), and clear biomagnification in several food webs. In fact, several studies indicate that DBDPE biomagnifies to a degree comparable to known POPs such as BDE-209 (POPRC, 2014), MCCP (ECHA, 2021; de Wit et al., 2020), SCCP (ECHA, 2008; de Wit et al., 2020) and PCB-153 (Stockholm convention, 2001; Ding et al., 2022). Because these substances have also been sampled in the same field studies as DBDPE, this benchmarking provides strong support for identifying DBDPE as bioaccumulative. Moreover, molar concentration comparisons from field data show that DBDPE occurs at concentrations similar to recognized vB substances, as described by ECHA (2025). Taken together, these results—spanning environmentally relevant laboratory studies, field observations, and toxicokinetic evidence—form a consistent weight of evidence demonstrating that DBDPE meets the annex D criteria for bioaccumulation.

Conclusion on bioaccumulation according to the criteria in Annex D

32. The combination of BCFs >5000, BMFs and TMFs>1, long elimination half-lives, widespread detection in biota (including top predators and humans), and documented maternal transfer show that DBDPE fulfils the bioaccumulation criteria of Annex D. This is further supported by its identification as a SVHC due to its vPvB properties according to REACH annex XIII (ECHA 2025).

2.3 Potential for long-range environmental transport

33. Monitoring data: DBDPE has been detected in remote areas in air, snow ice and biota. Several publications report findings of DBDPE in air in remote locations despite its low vapor pressure. DBDPE has been detected on Svalbard in the Arctic by Salamova et al. (2014) at concentrations up to 2.2 pg DBDPE/m^3 (2012-2013, n=34, detection frequence (DF) 88%; particle concentration), by Hao et al. (2020) at concentrations up to 3.5 pg DBDPE/m^3 (2014-2015, n=5, detection rate 100%; passive air-samplers), and by Halvorsen et al., (2020) at concentrations up to 7.27 pg DBDPE/m^3 (2022, n=26, detection rate 17%; gas + particle). DBDPE has been detected by Vorkamp et al. (2019) on Northern Greenland at mean concentrations of 3.1 pg DBDPE/m^3 (monthly 2014, n=13, detection rate 100%, gas + particle) and 9.7 pg DBDPE/m^3 (spring 2016, n=13, detection rate 100%, gas + particle). DBDPE has been detected annually on Antarctica from 2011-2018 at maximum concentrations of 0.44 – 2.1 pg DBDPE/m^3 (Zhao et al., 2020a; n=24/year, detection rate 94%; particle + gas phase).

34. DBDPE was detected in ice cores from the remote glacier in Arctic at Holtedahlfonna, Svalbard Norway and showed nearly continuous input growth in the recent core segments since 1988 of ~3.5 pg/cm^2/y indicating long range transport of particle bound DBDPE to the site during the Arctic haze period (March and April) (Hermanson et al., 2010). The sampling location of the ice-core was about 40 km northeast of Ny-Ålesund on the west coast of Spitsbergen. Ice core subsampling for analysis included combining contiguous sections of the core from the upper 34 m into 6 distinct samples with liquid volumes of 11-15 L each. This depth was estimated to cover the period of 1953 to 2005. The analysis of DBDPE (and 18 other BFRs) yielded net ng/L units. They were converted to a flux (pg cm^{-2} yr^{-1}) by dividing the amount of BFR by the surface area of the core (86.6 cm^2) and the years represented in the core segments analysed. To account for possible background contamination from transport, storage, and other handling, including in the laboratory, two deeper ice core segments representing the pre-BFR period from about 1900 to 1914 at depths of 52.3 to 59.2 meter (m) were analyzed. The largest BFR concentration in these deep samples represented the procedural detection limit, or background, which was subtracted from amounts in the upper 34 m of the core. The input flux of DBDPE was below background level or not detected until the sub core 1988-1995 where it was about 3.6 pg cm^{-2} yr^{-1} and a similar level (3.4 pg cm^{-2} yr^{-1}) was measured in the surface layer of the ice core, representing years 1995-2005.

35. DBDPE has been detected in snow core samples from the Arctic Devon Island, Canada, in concentrations up to 0.024 ng DBDPE/L (Meyer et al., 2011; 2005-2006; concentrations given as water equivalents). DBDPE was detected in one snow core in 2005 (0.002 ng DBDPE/L, 1.1-1.75 m depth) and in two in 2006 (0.024 ng DBDPE/L, 0-0.75 m depth and 0.00092 ng DBDPE/L, 3.2-4.2 m depth).

36. DBDPE has been detected in soil on Svalbard in the Arctic by Hao et al. (2020) at concentrations up to 0.147 µg /kg dw (n=10, DF 100%). Xiong et al., (2021) detected DBDPE in soils from Fildes Peninsula, Antarctica, in concentrations up to 0.19 µg DBDPE/kg dw and a detection frequency of 100% (n=7). Levels in lichen (n=8, DF= 100%) and moss (n=9, DF = 100%) range from

about 0.1 – 0.3 µg DBDPE/kg dw (Xiong et al., 2021). DBDPE was also the predominant BFR in soil and moss in Himalayan valley in samples taken 500 m to 1 km away from main roads (Chen et al., 2024).

37. DBDPE has been measured in Atlantic cod (*G. morhua*) liver (n=10, DF = 90%) up to 15 µg DBDPE/kg lw, and in Polar cod (*B. saida*) whole body (n=1, DF=100%) from Svalbard (Arctic) at 25 µg DBDPE/kg lw (KLIF, 2013). It has also been found in eggs from Common eider (*S. mollissima*) (n=12, DF = 100%) up to 12 µg DBDPE/kg lw, and Kittiwake (*Rissa tridactyla*) (n=12, DF = 100%) up to 72 µg DBDPE/kg lw and in plasma from Glaucous gull (*L. hyperboreus*) (n=12, DF=100%) up to 76 µg DBDPE/kg lw in samples from Svalbard (KLIF, 2013).

38. KLIF (2013) detected DBDPE in concentrations up to 1293 µg /kg lw in plasma of Ringed seals (*P. hispida*) (n=10, DF=100%) and up to 4300 µg DBDPE/kg lw in plasma of Polar bears (*U. maritimus*) (n=20, DF=95%) from Svalbard. Vorkamp et al. (2015) measured DBDPE in Ringed seal blubber in East Greenland (Arctic) (n=5, DF=20%) up to 0.17 µg DBDPE/kg lw and in West Greenland (Arctic) (n=4, DF=25%) up to 0.33 µg DBDPE/kg lw.

39. Vorkamp et al. (2019) reported concentrations of DBDPE up to 5.9 µg /kg lw in muscle from landlocked Arctic char *(S. alpinus)* (n=6, DF=100%) from a small lake in Greenland (Arctic). They also measured DBDPE in liver of glaucous gull up to 0.56-1.0 µg DBDPE/kg lw (n=6-8, DF=25-33%, Northwest and East Greenland). DBDPE was also detected in blubber up to 0.68 µg DBDPE/kg lw in ringed seal (n=6, DF = 50%), up to 1.6 µg DBDPE/kg lw in harp seal*(P. groenlandicus)* (n=4, DF=100%), up to 0.52 µg DBDPE/kg lw in Bearded seal (*E. barbatus*) (n=5, DF=80%), and up to 0.41 µg DBDPE/kg lw in killer whale *(O. orca* (n=11, DF=9.1%).

40. Sala et al. (2022) provided LRTP data via migratory species when measuring transplacental transfer of DBDPE in fin whales *(B. physalus)* from the North Atlantic Ocean, with concentrations in maternal blubber (n=8, DF=62.5%) up to 1.61 µg DBDPE/kg lw and in fetal skin (n=8, DF=87.5%) up to 97.1 µg DBDPE/kg lw. DBDPE was present in four killer whale samples (range <1.60-12.9 ng/g lw, n=24, DF=16%) and one humpback whale *(M. novaeangliae)* sample (3.39 ng/g lw, n=5, DF =20%) from the Svalbard Archipelago and northern Norway (Lippold et al., 2022).

41. Modelling: Dungey and Akintoye (2007) estimated the atmospheric half-life of DBDPE using AOPWIN v1.91(US EPA, 2012) to be 53.6 hours (4.5 days with a 12-hr day with 1.5×10^6 OH/cm^3) in the gas phase. Using a lower concentration of OH radicals, 5×10^5 OH/cm^3 as recommended in ECHA guidance chapter R.16 (ECHA, 2016b), results in a slightly higher half-life of 6.7 days. Modelling predicts that 100% will be sorbed to airborne particulates (AEROWIN v1.00; US EPA, 2012), and that the sorbed fraction may be resistant to atmospheric oxidation. The AOPWIN half-life value based on reaction with hydroxyl radicals in the gas-phase is therefore most probably an underestimation of the half-life of DBDPE in air as the fraction of DBDPE sorbed to particulates may increase its residence time and potential for atmospheric long-range transport. This is confirmed by monitoring data in remote areas far away from point sources. The atmospheric half-life of 4.5 – 6.7 days for DBDPE exceeds the criterion in the Stockholm Convention of >2 days and is indicative of a potential for long-range atmospheric transport.

42. Environment and Climate Change Canada, Health Canada (ECCC & HC, 2019) estimated the characteristic travel distance (CTD) to be 2860 km using the OECD Pov and LRTP Screening Tool (Wengman et al., 2009), which is below the boundary (5097 km, CTD of PCB 28) in their evaluation of DBDPE. They also calculated the overall persistence (Pov) to 277 days and the transfer efficiency (TE) to 12.7%, which is above the boundary of 2.248% (PCB-28). The high TE means that DBDPE may deposit to Earth´s surface in remote regions. The conclusion on long-range transport was that while DBDPE may not be predicted to have a long CTD, the high predictive transfer efficiency and its presence in remote areas indicate that the role of particle bound transport allows for long-range transport. Furthermore, the results from the modelling are associated with uncertainty due to the uncertainty of the input parameter such as the half-life in water is unknown. Furthermore, the OECD Tool does not contain a sediment compartment while DBDPE is persistent in sediment.

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

43. DBDPE has been detected in air in locations remote from known point sources, such as the Arctic and Antarctica. It has also been detected in other media such as snow, biota and endangered species in the Arctic, and soil and biota in Antarctica.

44. Models predict an environmental half-life for DBDPE of 4.5 – 6.7 days with a (12-hr day) in the gas-phase. However, >99.9% of DBDPE is predicted to be sorbed to airborne particulates, which likely increase the residence time in air and its potential for atmospheric long-range transport. The

atmospheric half-life for DBDPE exceeds the criterion in the Stockholm Convention of >2 days demonstrating its potential for long-range atmospheric transport.

45. In summary, findings from the Arctic and Antarctica and migratory species provide evidence that DBDPE can be transported far from its point source of initial emission, demonstrating its long-range transport potential.

2.4 Adverse effects

46. Available acute toxicity studies in experimental animals indicate low concern for acute toxicity via oral, inhalation, and dermal exposure (ECHA, 2024b; ECCC & HC, 2019). However, for bioaccumulative and persistent substances, chronic exposure is more relevant for assessing potential hazards to the environment and human health. Superhydrophobic substances such as DBDPE exhibit very slow uptake and may require extended periods to reach equilibrium (paragraph 28). U-shaped dose–response relationships have been reported for substances capable of forming colloidal particles (Owen et al., 2014), and DBDPE is a large, poorly soluble molecule. Consequently, the relevance of effects observed at the highest test doses may be questioned, particularly considering the uptake characteristics described in paragraph 28 and the potential for crystallization at high concentrations. Chronic exposure to lower doses is therefore considered more appropriate for characterizing potential hazards. No chronic exposure studies in rodents are available for DBDPE. Existing rodent studies have generally used corn oil as a vehicle, while aquatic studies discussed here have used DMSO to prepare stock solutions. Although some aquatic studies include concentrations exceeding the water solubility of DBDPE, the use of solvents is considered reasonable. The results suggest that aquatic effects may occur in environments where solubilizer-like substances co-occur with DBDPE (e.g. co-solvation in waste effluents, interactions with dissolved organic carbon or surfactants), or where long-term exposure allows steady-state conditions (ECCC & HC, 2019).

2.4.1 Adverse effects on human health and the environment

47. Due to the presence of several conserved features of receptors and signaling pathways, mechanistic studies in zebrafish are included in this section. Oxidative stress has been observed in most organisms tested and may be an underlying mechanism for several effects observed on thyroid and other endocrine systems, cardiovascular, neurological and liver systems, as well as on reproduction, development and behavior.

48. Mutagenicity and genotoxicity: DBDPE has been tested for mutagenicity in two well conducted *in vitro* studies as summarized in ECHA (2024b) and ECCC & HC, (2019). In an Ames test, no effects were observed with DBDPE with and without metabolic activation. Similarly, no clastogenic activity was evident in a chromosome aberration assay in Chinese hamster lung cells. There is no data on the carcinogenic potential of DBDPE in humans or animals. However, the absence of indications for carcinogenicity from repeated exposure studies (for example, proliferative changes) and the lack of genotoxic activity in the available *in vitro* mutagenicity data would suggest that DBDPE is unlikely to be carcinogenic. Based on the available information regarding genotoxicity, DBDPE is not considered genotoxic (ECHA 2024b; ECCC & HC, 2019).

49. Liver effects: In a guideline study, Sprague-Dawley (SD) rats exposed to 0, 100, 320, 1,000 mg/kg body weight (bw) DBDPE by gavage for 90 days, mean absolute liver weight, liver weight relative to bw, and liver weight relative to brain weight in the high-dose female group were statistically greater than that of the controls ($p < 0.05$). After 28 days recovery, the increased liver weight was similar to control (Hardy et al. 2002). The liver changes were characterized by minimal to slight hepatocellular vacuolation (high-dose males) and minimal to slight centrilobular hepatocytocellular hypertrophy (high- and possibly mid-dose males). No treatment-related changes were found in the livers of female rats at any time point (Hardy et al., 2002). In another guideline study (OECD TG443, Unpublished 2026), dose-related minimal or slight macrovesicular/microvesicular fatty change was observed in the liver of males given 100, 300 or 1000 mg DBDPE/kg bw/day in the F0 and F1 group. For F0, this was considered to correlate with the higher than control mean absolute and body weight relative liver weights observed in males at 1000 mg/kg/day.

50. Several per-reviewed studies indicate potential for DBDPE to impair liver function by inducing oxidative stress altering glucose and lipid metabolism, and enzyme expression and activity in rodents and fish. Wang et al. (2010) exposed SD rats orally to 0 or 100 mg DBDPE/kg bw/d by gavage. DBDPE levels in tissues were elevated 13 to 1444 folds over the control levels, with DBDPE concentrations of 11.2 in kidney, 177 in liver, and 549 ng/g lw in adipose tissue. A significant alteration of some serum parameters in the DBDPE group, indicating possible oxidative stress due to the accumulation of DBDPE or its metabolites, included a decrease in chrom, aspartate

aminotransferase (AST), alkaline phosphatase (ALP) and an elevation in total bile acid (TBA) ($p < 0.05$) and glucose was not altered. Liver cytochrome P450 (CYP)3A2 mRNA were increased in DBDPE exposed group.

51. In Balb/C mice orally exposed to 0, 5, 20, 100 and 200 mg DBDPE/kg bw/day (n=16 pr group) for 30 days, liver weight was increased at the highest dose, and histological changes were characterized by hepatocellular hypertrophy and cytoplasmic vacuolization (Sun et al., 2018). Levels of blood glucose were significantly increased in the treatment groups of 200 mg/(kg/day) starting from the 15th day, and 100 mg/(kg/day) from the 20th day, and 20 mg from the 30th day compared to control, but insulin levels were not affected. Increased blood glucose without alterations in insulin level has also been observed in several studies in rat (Sun et al., 2014; 2020; Gao et al., 2022; Li et al., 2021). Liver activity of alanine aminotransferase (ALT) and AST was significantly increased from the groups exposed to 20 mg and 5 mg/kg, respectively. Liver microsome activity of major xenobiotic metabolizing enzymes (Glucuronosyltransferase, (UDPGT), 7-pentoxyresorufin O-dependentylase (PROD), and ethoxyresorufin-O-dealkylase (EROD) were increased significantly in the higher dose groups, suggesting that DBDPE cause some impairment to liver function and thyroid hormone levels (see paragraph,60) (Sun et al., 2018). Increased EROD activity were also observed in an *in vitro* experiment with brown and rainbow trout male hepatocytes exposed for 96h to DBDPE (0, 6.3, 12.5, 25 and 50 μg/L) (Nakari and Huhtala, 2010).

52. In SD rats exposed to 0, 5, 50, 500 mg/kg DBDPE by gavage once a day for 28 days (Sun et al., 2020). Liver morphological changes, oxidative stress, increase of γ-glutamyl transferase and glucose levels in serum, and down-regulation of pregnane x receptor (PXR), constitutive androstane receptor (CAR) CYP3A1 and CYP3A gene expression were observed in the DBDPE exposed groups. In the 50 mg DBDPE group, the liver showed feathery necrosis, and 500 mg/kg bw/d caused obvious pathological changes in the form of irregular arrangement of hepatic cords, feathery necrosis, and inflammatory cell infiltration. However, no changes were observed in liver weight. Liver malondialdehyde (MDA) and glutathione (GSH) levels were significantly increased in the 50 and 500 mg DBDPE group, and superoxide dismutase (SOD) activity was significantly increased at 500 mg. Liver mRNA expression of CYP3A1 were reduced by all doses, while CAR and PXR were reduced at 50 and 500, and CYP3A2 significantly only at 500 mg DBDPE /kg bw/ d group. Serum g-glutamyl transferase was significantly increased in the 50 and 500 mg/kg bw group indicating liver damage, and serum glucose level increased in the 500 mg kg DBDPE group.

53. In male Wistar rats, orally gavaged for 8 weeks to 0, 5, 50 or 500 mg DBDPE /kg bw/d, liver-to-bw ratio increased significantly from 5 mg/kg in a dose dependent manner (Cui et al., 2025). Lipid accumulation in liver (oil-red O staining) increased in dose dependent manner from 5 mg/kg. In medium-dose exposure, a substantial accumulation of lipid vacuoles was detected in the liver, indicative of steatosis. High-dose exposure resulted in prominent lipid vacuole formation within hepatocytes, also consistent with steatosis, accompanied by marked alterations in cellular morphology. In addition, inflammatory infiltration and ballooning degeneration were observed in some areas of the liver. Dose dependent increase occurred in liver for levels of total cholesterol (TC), triglyceride (TG), and low-density lipoprotein (LDL), significant different from control in the 50 and 500 mg DBDPE group, and from 5 mg for LDL. High density lipoprotein (HDL) was only significantly reduced in the 5 mg/kg group. Expression of key-genes for lipid metabolism were altered fatty acid synthase (FASN), peroxisome proliferator-activated receptors (PPAR)γ, and acyl-CoA oxidase 1 (ACOX1) were significantly increased, and LDLR, (the rate-limiting enzyme for cholesterol synthesis) were reduced (Cui et al., 2025).

54. Zhou et al. (2026) utilized wildtype (wt) and transgenic zebrafish (zf) models to further explore liver effect in zf larvae exposed from 2 hour post fertilization (hpf) to 72 hpf to 0, 0.25, 0.5, 1, 5, 10 mg/L DBDPE or BDE-209. Neither BDE-209 nor DBDPE causes observable morphological abnormalities, but BDE-209 significantly reduced the survival rate and hatching rate in a dose-dependent manner. To evaluate the hepatotoxic effects of DBDPE on zf larvae, the authors utilized transgenic zf, a model for studying chemical-induced liver injury. Treatment led to a marked reduction in both liver area and fluorescence intensity, indicating impaired liver development. Lipid homeostasis was evaluated by oil-red O staining and showed that DBDPE exposure led to marked yolk sac expansion and ectopic lipid accumulation, particularly within the yolk sac region. Impaired liver function disrupts the metabolism and absorption of yolk lipids, leading to their abnormal retention (Lima et al., 2026), as shown here. In addition, DBDPE treatment elevated both ALT and AST activities in a dose-dependent manner from 1 mg/L, indicating hepatocellular injury. Liver function-related genes showed a strong upregulation following DBDPE exposure, along with genes related to detoxification and redox homeostasis. This gene-expression profile suggests a disruption of hepatic detoxification and redox homeostasis. The study demonstrated that BDE-209 and DBDPE

exhibit distinct toxicity profiles, where BDE-209 posed a greater risk to development and DBDPE exhibited more pronounced hepatotoxicity.

55. Li et al. (2023) exposed adult female zf to 1 or 10 nM DBDPE for 28 days, resulting in mean livers loads of 307 and 398 ng DBDPE/g dw, respectively. Effects on liver regeneration were studied by performing partial hepatectomy (PHx) after one day fasting, and animals were unexposed during the 28 days recovery. Compared with the control group, the hepatic somatic index (HSI) of the 1 and 10 nM DBDPE exposure group decreased by 16.9 % and 17.4 % 28 days after PHx, indicating that DBDPE significantly suppressed the liver's regenerative capacity in adult zebrafish. Meanwhile, transcriptomic bioinformatics analysis showed that the pathways significantly enriched by differentially expressed genes (DEGs) included glycerolipid metabolism-related pathways, ABC transporter, cell apoptosis, DNA replication and ferroptosis pathways related to cell proliferation. The above findings demonstrated that exposure to 1 and 10 nM DBDPE disrupted lipid metabolism and cell proliferation-related processes in zf, consequently inhibiting hepatic regeneration. Impaired capacity of repair and regeneration in aquatic organisms would make them more vulnerable to harsh environmental damage, thus increasing their survival risks.

56. Taken together, available results indicate that DBDPE may impair liver function in both rodents and fish, alter glucose and lipid metabolism and promote steatosis. The increase in enzyme activity for detoxification may also contribute to removal of thyroid hormones (TH), and down regulation of PXR/CAR, may further contribute with the potential for producing hypothyroidism by hepatic metabolism of thyroxine (T4).

57. Effects on hypothalamic-pituitary-thyroid (HPT)-axis: Effects related to the thyroid hormone system have been observed after exposure to DBDPE in several studies both in rat and mice studies, mechanistic *in vitro* studies, epidemiology studies as well as fish studies.

58. Mechanistic *in vitro* studies indicate a potential of DBDPE to interfere with TH receptors (THR) and enzymes important for TH effects at the cellular level. In a luciferase reporter assay system using HEK293 cells expressing the human THRα and THRβ, antagonistic effect of DBDPE were observed with IC_{50} 0.83 mM and 0.40 mM for THRα and THRβ, respectively (Coi et al., 2026). In human liver microsomes deiodination (DIO) activity were measured and inhibition of both outer and inner ring deiodination (O and IRD) of T3 and 3,3′-T2 formation from T4 were observed, respectively, with an estimated IC_{50} of 160 nM DBDPE (Smythe et al., 2017).

59. In an OECD TG 443 (Unpublished 2026) SD rats were exposed orally by gavage to 0, 100, 300 and 1000 mg DBDPE/kg bw/d. A marginal but significant increase in serum T4 level (115% of control) were observed in F0 males at the highest dose, and thyroid stimulating hormone (TSH) levels were reduced in F0 females receiving 100 mg/kg bw/d. In F1 males T4 were slightly increased in the animals receiving 300 or 1000 mg/kg bw/d (119% and 108%, respectively). No morphological alteration was observed in thyroids. However, other non-guideline mice and rat studies observed more pronounced effects to the thyroid system (Wang et al., 2010; 2019b; Sun et al., 2018).

60. Sun et al. (2018) exposed Balb/C mice orally to 0, 5, 20, 100 and 200 mg DBDPE/kg bw/d for 30 days (n= 16 pr group, 8 each sex) and observed reduced serum levels of free triiodothyronine (fT3) at 100 and 200 mg, increased TSH at 200 mg and T4 (both total and free) were dose-dependent reduced, although not significantly. No histopathology changes were observed in thyroid glands. Similar effects on serum THs were observed by Wang et al., (2019b) in male SD rats orally exposed DBDPE or BDE-209 at 0, 5, 50 and 500 mg /kg bw for 28 days (n= 12 pr group). Observations included reduced serum levels of fT3 ($p<0.01$) at 50 and 500 mg, and an increase in TSH ($p<0.01$) and thyrotrophin-releasing hormone (TRH) ($p<0.05$) at 500 mg for both DBDPE and BDE-209. This was accompanied by significant dose-dependent alteration in mRNA level for genes related to TH homeostasis in the thyroid and pituitary gland. Histopathological alterations in the thyroid gland with disordered structures of thyroid gland were observed in the 5 mg/kg bw/d group and swollen vacuolized epithelium with exfoliation and increased levels of mast cells were observed at 500 mg/kg. The average colloid area was significantly decreased. In ultrastructure, compared to the control group, exposure to BDE-209 or DBDPE in 5, 50 mg/kg bw/d resulted in dilatation of the rough endoplasmic reticulum, swelling of mitochondria and disappearance of mitochondrial crests. 500 mg/kg bw/d BDE-209 or DBDPE-treated rats showed atrophy of the rough endoplasmic reticulum and vacuolation of the mitochondria. For oxidative stress markers in the thyroid, a significant dose-dependent increase in MDA levels (a marker for lipid oxidative degradation) and reduction in SOD activity appeared (Wang et al., 2019b). In contrast to the reduced serum levels of T3 observed in the above studies with 28 and 30 days of exposure, Wang et al. (2010) observed of significant increase in serum T3 levels ($p < 0.05$), and an non-significant increase was also observed in T4 compared to control after 90 days exposure of male SD rats to 0 or 100 mg DBDPE /kg bw/day in orally administrated. The HPT-axis is

regulated by feedback mechanisms, and both dose and duration of exposure will affect observed response.

61. In a two-generation zf study (Sun et al. 2024b), life-time exposure to DBDPE at environmentally relevant concentrations disturbed thyroid homeostasis in all generations, and induced anxiety-like behavior further described in paragraph 82 in unexposed F1 and F2 offspring. In F0, a significant increase in plasma T4 was observed at 0.1 and 10 nM in females and at 1 and 10 nM for males, while T3 was not altered. In the F1 eggs a significant elevation in T3 and T4 was noticed at 10 nM, while no significant changes of TH were found in F1 larvae. Plasma T3 and T4 was notably elevated at 10 nM in adult F1 females, while T3 was significantly decreased in adult F1 males at 0.1 nM. In F2 eggs, TH-levels showed no significant changes, while the T4 levels were significantly increased in F2 larvae. Gene transcription related to the HPT-axis in brain and liver of adult zf and 5-dpf larvae showed dose- and generation-dependent changes consistent with the observed hormone levels. The findings indicate that thyroid disruption in F1 larvae were mainly driven by excessive maternal TH transfer, whereas effects in F2 larvae were primarily linked to transgenerational epigenetic inheritance via hypomethylation and hypermethylation of related genes.

62. Wang et al. (2019c) also found altered TH levels in zf embryos, exposed to 0, 3, 10, 30, 100 and 300 nM DBDPE in 0.1% DMSO from 2hpf to 6 and 14 dpf (n = 4). For the whole-body TH contents, DBDPE statistically increased T3 and T4 levels after both 6 and 14 days for the 30, 100, and 300 nM treatment groups. Transthyretin (TTR) protein was increased significantly and dose-dependent compared to control from 10 nM. DBDPE also statistically significantly affected the gene expression pattern related to the HPT-axis. Similar effects on TH levels and gene-expressions were observed by Wang et al. (2022a) who studied whether 100 µg/L n-TiO2 affected the potential toxicity of DBDPE (0, 1, 10 or 100 µg/L) in zf larvae, exposed from 2 hpf to 144hpf (n = 3; 300 larvae per n). Single exposure to DBDPE significantly elevated tT4 (total T4, bound and unbound) and tT3, and response was further attenuated in co- exposure with n-TiO2. The transcript levels of genes related to the HPT-axis were significantly increased upon single exposure to 100 µg/L DBDPE compared to the control group, coinciding with Wang et al. 2019 and Sun et al. 2024. Transcript levels of genes related to neurodevelopment (*syn2a and a1-tubulin*) were significantly elevated in co- exposure of 100 nM DBDPE and n-TiO2. Molecular docking results indicated that DBDPE can bind to the corticotropin-releasing hormone receptor 1 (CRHR1) and the THRβ, and its mode of interaction may be similar to that of T4. Both single exposure to DBDPE and combined exposure with n-TiO_2 induced hyperactivity in zf larvae, and increased content of neurotransmitters. These results coincide with the pattern demonstrated in Sun et al. (2024b) and Wang et al. (2019c).

63. Thyroid effects epidemiology: Measurements in humans have found that increasing DBDPE serum concentrations mainly, but not exclusively, results in increased levels of T3, T4 and thyroid antibodies (TG-Ab, TPO-Ab), (Chen 2019; Zhao et al., 2020b). Serum concentrations of DBDPE ranged from 3.148 to 54,360 ng/g lw, with a geometric mean (GM) of 332.6 ng/g lw in Chen et al., (2019). DBDPE was detected in 100% of the serum and hair samples, GM was 3.69 ug/g lw and 672 ug/g dw, respectively in Zhao et al., (2020b). The epidemiology results from workers with heavily and continuous exposure to DBDPE give some indications for possible effects on the HPT-axis.

64. Furthermore, in a case−control study, 481 serum samples were collected from patients with thyroid cancer (n=242) and healthy controls (n=239) in Shandong Province, eastern China. DBDPE exhibited median concentrations of 47 and 45 ng/g lw in the case and control groups, respectively, which were higher than those of other NBFRs by at least an order of magnitude. In sex-stratified logistic regression, in contrary to other alternative FRs, DBDPE exhibited significantly increased odds-ratios (ORs) in the third and fourth quartiles in both male and female participants for thyroid cancer (Liu et al., 2022).

65. Cardiovascular effects: Available studies indicate that DBDPE increases oxidative stress, inflammation and gives lesions in aorta and the heart tissue of male SD rats (Jing et al., 2019; Gao et al., 2022; Zheng et al., 2021). In these studies, SD rats were exposed to 0, 5, 50 or 500 mg/kg bw DBDPE in corn oil for 28 days (n=12 pr group). Heart histology showed that 50 and 500 mg DBDPE /kg bw/d exposure resulted in endothelial cell nucleus swelling, subendothelial space expansion, endothelial cell shedding, and internal elastic lamina thinning. Ultrastructure revealed mitochondrial swelling and crista disorder in the 50 and 500 mg/kg bw group (Jing et al., 2019; Gao et al., 2022). Jing et al., (2019) observed a significant increase in serum Low Density Lipoprotein (LDH) levels in animals exposed to 500 mg/kg DBDPE as well as increases in MDA and SOD, GHS-OX activity. The key inflammators Interleukin (IL)1-b, IL-6 and Tumor Necrose Factor (TNF)-a were significantly upregulated, suggesting oxidative stress and activated inflammatory response. Gao et al. (2022) observed that the level of uncoupling proteins (UCPs), which are essential transport proteins involved in energy metabolism on the inner mitochondrial membrane, decreased in the 5, 50 and 500 mg/kg/d

DBDPE group in a dose-dependent manner ($p < 0.05$) and the ATP level in heart tissue of rats was significantly reduced in the 500 mg/kg/d DBDPE exposure group compared to the control group ($p < 0.05$). There was also a dose-dependent increase in apoptosis (TUNEL positive cells), significant from the 50 and 500 mg/kg bw DBDPE group, as well as alterations in protein expression of MYH6 and SERCA2, indicating that myocardial systolic and diastolic function were affected. Serum glucose was significantly increased in the 500 mg DBDPE group, and HDL-C were significantly reduced in the 50 and 500 mg group, TC and triglyceride were unchanged. Gene expressions related to glucose metabolism (IRS-1, PI3K, p-AKT were significantly reduced, GLUT2 and RXR-a significantly increased compared to control (Gao et al., 2022).

66. Zheng et al. (2021) observed damage to the abdominal aorta morphology and ultrastructure in the groups exposed to 50 and 500 mg/kg bw DBDPE accompanied by increasing protein levels of IL1-beta and interleukin 18 (IL-18). Further *in vitro* studies of human vascular endothelial cells (HAECs) treated with DBDPE (0, 6.25, 12.5, 25, 50, and 100 mM) for 24 h indicate that DBDPE not only induced cytotoxicity and reactive oxygen species (ROS) but also caused HAECs pyroptosis, which was evidenced by the elevated expression of Nod-like receptor protein -3 (NLRP3), and canonical inflammasome components (ASC, and caspase-1) in DBDPE-treated group (Zheng et al., 2021).

67. DBDPE has also been shown to promote development of atherosclerosis (Li et al., 2025). ApoE−/− mice (8-week-old males) were orally single exposed to 0 or 100 mg/kg bw DBDPE, BDE-47 or BDE-209 in corn oil for 6 weeks. Single exposure of all tested BFRs significantly increased the plaque area and lipid content in the aortic root of mice compared to control. BFRs significantly increased the ROS level in plaques and promoted the expression level of adhesion molecule ICAM-1, which enhanced the recruitment of macrophages. DBDPE transcriptome analysis showed that differentially expressed genes (DEGs) were significantly enriched in signaling pathways related to oxidative stress and lipid metabolism. Results indicate that BFRs exposure can promote the development of atherosclerosis by increasing macrophage recruitment and foam cell formation BFRs exposure causes damage to vascular endothelial cells, induces ROS production and ICAM-1 expression, and thus promotes macrophage recruitment. On the other hand, BFRs exposure leads to lipid metabolism disorder, increases the content of Ox-LDL in macrophages, and thus promotes the formation of foam cells (Li et al., 2025).

68. Toxicity to reproduction (effects on fertility and developmental toxicity): No effects on organ weight or histological by light microscopy of reproductive organs were observed in a 90-day rat study at doses up to 1,000 mg/kg/d (Hardy et al., 2002).No treatment effects were observed at doses up to 1,000 mg/kg/d for estrous cycle, sperm measures or reproductive performance in F0 or F1 generation in a rat, OECD TG 443 study according to study author (Unpublished, 2026). However, there are other studies indicating effects of DBDPE on both sperm and oocytes development in rats, mice and fish. The studies indicate that exposure to DBDPE can affect male reproduction by inducing oxidative stress and activate apoptotic signal pathways and alter gonadotropic hormone signals (GHS). Damage to testicular structure and reduction in sperm quality has been observed in both rat and mice studies (Li et al., 2021; Xue et al., 2022; Qi et al., 2025; Shi et al., 2026) as well as fish studies.

69. Testicle toxicity in rodents: Li et al. (2021) exposed male SD rats orally to DBDPE at 0, 5, 50 and 500 mg/kg bw for 28 days by gavage (n= 12/ group). No effects were observed on testis weight by treatments, however, at 50 and 500 mg/kg bw DBDPE exposed rats showed significant deletion of the seminiferous epithelium compared to control animals. Significant decreased sperm number and decreased sperm mobility were also observed at the same doses as well as reduced telomerase activity and shortened telomers indicative of germ cell senescence. Increased DNA stand brakes (TUNEL positive cells) and apoptosis were also observed. Xue et al. (2022) used the same doses and exposure scheme as Li et al., (2021) and observed that sperm concentration was significantly reduced in the 50 and 500 mg/kg bw/day group. In addition, sperm motility was reduced by all doses, and sperm malformation was increased in 50 and 500 mg/kg/bw/day groups. In the histological examination of the testes, alterations of seminiferous epithelial were observed in 50 and 500 mg/kg bw groups, ultrastructural changes were observed, consisting of expanded and vacuolized mitochondria. Furthermore, mitochondrial damage and dysfunction and a significant increase in serum glucose and LDL-C level. In addition, DBDPE caused meiotic failure through testicular DNA damage, reduced the expressions of meiotic regulatory factors (Sohlh1, MILI, CDK2, and CyclinA), and synaptonemal complex proteins (SYCP1 and SYCP3). DBDPE induced glycolipid metabolism disorder and promoted apoptosis of spermatogenic cells through the mitochondrial-mediated apoptosis pathway, leading to reproductive toxicity by decreasing sperm quantity and quality (Xue et al., 2022).

70. Qi et al. (2025) exposed C57BL/6 J male mice for 0, 5 or 50 mg/kg bw DBDPE in corn oil by oral gavage for 7 weeks, dosed 5 days per week (n = 6 in each group). Sperm counts were reduced by

34% and 73% compared to control at 5 and 50 mg/kg bw (p=0.01) as well as a dose dependent increase in sperm malformation (p=0.01). Serum and intra-testicular testosterone (T) levels exhibited a strong negative correlation with increased DBDPE dosage ($p < 0.05$ and $p < 0.01$, respectively). The 50 mg/kg DBDPE group showed a 50 % reduction in serum luteinizing hormone (LH) and 29% reduction in follicle stimulating hormone (FSH) levels compared to controls ($p < 0.01$). Steroidogenic acute regulatory protein (StAR) which is a key enzyme in Leydig cells steroid hormone production was significantly decreased in DBDPE treatment groups compared to control ($p < 0.01$). This may prevent the Leydig cells from responding appropriately to gonadotropin signals. Lowest Observed Effect Concentration (LOEC) for reduced sperm count and increased sperm malformation as well as reduced germ cell layer and reduction in T in testis is 5 mg/kg bw, LOEC for serum reduction of LH and FSH is 50 mg/kg (Qi et al., 2025).

71. Shi et al. (2026) observed significant reduction in sperm quality and testicular structure in C57BL/6J mice exposed orally to 0 and 0.5 mg DBDPE /kg bw /day for 12 weeks. Testicular germ cells were disorganized or absent, with a substantial reduction in spermatocytes and spermatids. A significant reduction in key proteins involved in gap-junction and cellular oxygen homeostasis were affected in the DBDPE exposed group.

72. Toxicity to female reproductive organs: Effects of DBDPE on oocyte and fetus development have also been studied. Shi et al. (2021) exposed female Kumming mice during puberty (3-7 weeks old), for DBDPE (0, 0.05, 0.5, 5, 50 μg/kg bw/day in corn oil) for 30 days and super ovulated with hormone treatment. The ovaries were separated at specific timepoints after injection of human chorionic gonadotropin to harvest oocytes at onset and in anaphase I, and polar body extrusion (PBE) oocytes. DBDPE exposure injured the development of blastocysts, leading to blastocyst apoptosis. Asymmetric division of oocytes was markedly impaired in 5 and 50 μg/kg bw/day DBDPE exposed group, which resulted in oocytes with larger polar bodies (PBs). Thus, the large PB produced by abnormal asymmetric meiosis will take away a large amount of maternal material, leading to abnormal embryonic development, infertility, or abortion.

73. In another study Shi et al. (2022) exposed female Kumming mice during puberty (3-7 weeks old), for DBDPE (0, or 50 μg/kg bw/day in corn oil) for 30 days and divided animals into two groups. Group one was super ovulated and the females were mated. The next morning, females with vaginal plugs were collected (E 0.5day) with hormone treatment, and 1, 2 and 8 stage embryos were sampled and after 96h blastocytes were collected. DBDPE exposure did not affect spindle rotation after fertilization but led to decreased pronuclei (PN) size in zygotes. DBDPE interfered with the self-assembly of F-actin in PN, resulting in PN reduction, DNA damage, and reduced expression of zygotic genome activating genes, and finally led to abnormal embryonic development. DNA damage, measured as an increase in γ-H2AX, was observed in both female and male zygotes and were negative correlated with F-actin levels. In group 2 females were directly paired with males and mated after the 30 day exposure, and fetus were delivered by caesarean section at E11.5, E14.5 and E18.5. Litter size was significantly lower in DBDPE-exposed mice than in control mice, and embryo lengths were significantly shorter at E14.5 and E 18.5 compared to control. F1 pups born from control and DBDPE-exposed dams were raised to 6 weeks of age and then subjected to behavioral testing. DBDPE exposure leads to increased motor activity and social deficiency in female F1 mice but has no effect in motor activity and social behavior of male F1 mice.

74. Development/teratology in mammals: Two GLP- and OECD-compliant studies according to OECD TG 414 (as adopted in 1981) have evaluated the teratogenic effects of DBDPE in the rat and the rabbit were summarized in (Hardy et al., 2010). No treatment-related effects on fetal weight, sex ratio and early, litter size or late resorption in these studies. In the rat study, no external or visceral abnormalities were observed. Regarding skeletal abnormalities, a statistically significant increase in the number of litters with unossified hyoid and reduced ossification of the skull was noted at 400 mg/kg/d. This observation was considered to be incidental, as a similar increase was not seen at the top dose. In the rabbit study, no treatment-related mortality or clinical signs of toxicity were seen in the dams. Abortion occurred in one animal each of the 125 and 400 mg/kg/d groups and in two animals of the 1,250 mg/kg/d group. However, in view of the low incidence of this observation and given that rabbits are known to have a high spontaneous abortion rate, this finding is considered incidental. The only statistically significant difference was an increased number of litters with the 27th presacral vertebra at 1,250 mg/kg/d (9 litters compared to 4 in controls). Given that this increase (by 56.3%) was within the laboratory historical control range (12.5-93.8%), it was not considered adverse by the study director. A low incidence of vascular abnormalities was observed in the mid- and high-dose groups. Enlarged aortic valve, bulbous aortic arch and poorly developed right ventricle were observed in one fetus from the 400 mg/kg/d group. Malformation of the aortic arch and undeveloped right ventricle were seen in two fetuses from a single litter of the 1,250 mg/kg/d group. Based on these

low incidences, the reported malformations were considered not to be indicative of a treatment-related effect (Hardy et al., 2010).

75. In the available summary of a rat OECD TG 443 (Unpublished 2026) study, SD rats were exposed orally by gavage for 0, 100, 300 and 1000 mg/kg/bw DBDPE. In F1 no adverse treatment related effects were observed. Some treatment-related haematology findings were observed in males with non-dose responses Treatment related biochemical and urine analysis were also indicated. A marginal increase in anogenital distance was observed in both males and females in the 1000 mg/kg group, as well as nipple retention evaluated at perinatal day 13, with the highest incidence in the 100 mg/kg group. Histopathology of liver showed minimal or slight macrovascular /microvascular fatty changes in males, with no clear dose response. In F1 males only, from the 300 and 1000 mg DBDPE/kg bw group, a slightly higher serum T4 level (119% and 108%, respectively compared to control) were measured. For developmental immunotoxicity, a significant increase in absolute relative frequence of granulocytes was observed for all DBDPE groups compared to control, as well as an increase in the relative frequence of monocytes in males in the 300 and 100 mg DBDPE group. Other endpoints, differences in brain morphology parameters were considered incidental as they were inconsistent between sexes, inconsistent between cohorts, the magnitude was considered small, had no histopathological correlates, and/or had no significant mean brain weight differences. Study author concluded that the No-Observed-Adverse-Effect-Level (NOAEL) for both systemic toxicity and reproductive/developmental toxicity in this study is 1000 mg/kg/day.

76. Toxicity to fish reproduction: Throughout its life cycle, the zf produces key reproductive hormones homologous to those in humans, including gonadotropin-releasing hormone (GnRH), FSH, LH and the sex steroids testosterone (T), estrogen, and progesterone (Hara et al., 2016, Lima et al. 2026). DBDPE has been reported by multiple studies to induce reproductive toxicity. Altered estradiol (E2) and T levels in serum have been found in studies using adult zf (Sun et al. 2022; Yu et al. 2026; Choi et al., 2021). Disrupted steroidogenesis, leading to lower plasma levels of E2 and T in females, has been linked to changed hypothalamic–pituitary–gonad (HPG) axis gene expression (Sun et al. 2022; Yu et al. 2026). Fecundity and gonado-somatic index (GSI) have also been negatively affected by DBDPE exposure (Yu et al. 2026), and zf exposed to DBDPE suffered impaired sperm quality and spermatogenesis (Yang et al. 2024; Choi et al., 2021).

77. Yu et al. (2026) investigated the reproductive toxicity of DBDPE by assessing fecundity, gonadal development, sex hormone levels, HPG axis gene expression, and ovarian metabolomic profiles. Adult zf (4 months) were exposed to 0, 1, 10, and 100 μg/L DBDPE for 21 days (n = 3; 15 males + 15 females per n). The gonads showed a concentration-dependent accumulation of DBDPE. Fecundity, measured as cumulative egg production, and serum E2 levels and GSI were dose-dependent decreased from 1 μg /L and significantly reduced at 100 μg/L in female fish. In addition, this exposure group showed an increase in proportion of perinuclear oocytes (POs) and a significant decrease in late vitellogenic oocytes (LVOs). GSI and plasma sex hormones were not altered in males. These results indicate that DBDPE exhibits reproductive toxicity in female zf. The follicular cell dysplasia observed in DBDPE exposed fish may be attributed to significantly reduced E2 levels. 100 μg/L DBDPE significantly impaired the reproductive capabilities of female zf by disruption of estrogen synthesis and secretion via interference with the HPG-axis. Expression of several genes related to HPG-axis were significantly reduced in brain, gonads and liver. Furthermore, genes involved in the steroid hormone regulation were significantly altered in the gonads of females. Metabolomic and lipidomic analysis of female gonads indicated altered lipid metabolism and taurine and hypotaurine metabolism, as well as GSH metabolism within the ovary. Collectively, these factors lead to a reduced proportion of mature oocytes in the ovary, ultimately resulting in a significant decrease in cumulative egg production.

78. Sun et al. (2022) exposed female zf to nominal concentration of 1 and 100 nM DBDPE (0.01% v/v DMSO) for 28 days. The detected concentrations of DBDPE in the brain of female zf (2411± 190 and 4127 ± 547 ng/g dry weight) were comparable to brain levels measured in carp and tilapia from an e-waste recycling site (Tao et al., 2019). The concentrations of plasma E2 and T were significantly decreased in both 1 and 100 nM DBDPE treatments. Expression of genes related to HPG-liver axis were altered. The authors hypothesized that DBDPE exposure suppressed the process of steroidogenesis by inhibiting the transcription of related genes in the brain. However, the altered gene expression and lowered levels of E2 and T did not lead to statistically significant follicular dysplasia, although a weak downward trend on POs and a weak upward trend in vitellogenic oocytes (VOs) was seen, coinciding with Yu et al., (2026). Atretic oocytes were prevalent in DBDPE exposed group (both 1 and 10 nM) indicating that DBDPE may cause follicular dysplasia in female zf.

79. Choi et al. (2021) exposed male zf (n = 4, four male fish per n) to 0, 0.031, 0.31, and 3.1 µM DBDPE (0.1 % v/v DMSO) for 14 days (OECD 204 with minor modifications). In addition, two human tissue cell lines, i.e., H295R (human adrenocortical carcinoma) and MVLN (human breast carcinoma) cells, were used to evaluate the effects on sex hormones synthesis and the related mechanisms. The concentration of plasma E2 was significantly increased in male zf exposed to 0.31 and 3.1 µM of DBDPE, with a clear increasing trend across all treatments (though not significant for the 0.031 group). There were no significant changes in concentration of 11-KT (the principal T in fish) or E2/11-KTratio. Levels of related gene transcriptions (vtg, erα, and erβ) in liver showed no significant difference from control. In H295R cells exposed to DBDPE, the E2/T ratio showed an increasing trend ($p < 0.05$), whereas the genes related to steroidogenesis were not statistically significantly changed. In MVLN cell line assay, binding affinity to ER was observed at below 0%, indicating that DBDPE does not have direct ER agonistic effects. Results showed that exposures to DBDPE increased E2 levels in the male zebrafish and the E2/T ratio in H295R cells. However, the analysis of genes related to steroidogenesis and the ER binding affinity did not show any significant results. According to the authors, the results indicate that levels of sex hormones might be mediated by mechanisms other than the alteration of the steroidogenesis pathway. However, induction of vitellogenin were observed in an *in vitro* experiment with brown and rainbow trout male hepatocytes exposed for 96h to DBDPE (0, 6.3, 12.5, 25 and 50 µg/L) with a significant induction of vitellogenin at 6.3 µg/L (Nakari and Huhtala, 2010).

80. Yang et al. (2024) exposed adult male zf with nominal concentrations of 0, 0.1, 1, 10 and 100 nM DBDPE for 2 months. After the 2-month exposure, DBDPE content in testes were 871, 1284, 1411 and 3252 ng/g lw in the DBDPE exposed groups, respectively. Significantly lower total motility and progressive motility of zf spermatozoa were observed at all the tested concentrations as well as an increase in head width of sperms. However, when DBDPE-exposed males were paired with unexposed females, reproductive behavior was unaffected, while the F1 offspring larvae showed a significantly lower hatching rate in the 100 nM group (from 99.81 to 83.78 %). Other parameters, such as fertilization, malformation, and survival rates, did not differ from control. Effects on the germ cells were observed in histology of testes with certain differences in germ cell types. The proportion of spermatogonia was significantly greater in the 1 and 100 nM DBDPE-exposed fish, and that of spermatozoa was significantly lower in the 100 nM DBDPE-exposed fish, with a lower trend in the fish exposed to 0.1–10 nM DBDPE, which might suggest inhibition of spermatogenesis following DBDPE exposure. Increase in DNA strand breaks were observed using g-H2AX from 1 nM, and TUNEL staining at 100 nM. Proteins related to apoptosis showed a significant dose-dependent increase from 1 nM. Exposed zf testes showed DNA damage responses and energy metabolic disorders, with differentially expressed proteins enriched in necroptosis and phosphatidylinositol-signaling pathways, and significant down-regulation of proteins involved in F-actin assembly that may underlie the observed DNA damage. It remains unclear whether these effects stem directly from DBDPE or from associated cell death. *Ex-vivo* exposed zf spermatozoa to 0.01, 0.1, 1 and 10 µM DBDPE for 3 h was followed by artificial fertilization with eggs from unexposed females. Total motility (0.1 and 1 µM) and progressive motility (0.1 µM) of zf spermatozoa were significantly lower than those of the control, but spermatozoa sperm linearity was not significantly different. Although no significant differences were observed in spermatozoa velocity parameters, a significant dose-dependent reduction in fertilization rates were observed from 0.1 µM DBDPE-exposure groups. Survival rates, malformation rates and hatching rates were not different from control (from 24-120 hpf). Taken together, the results suggest that zf exposed to DBDPE could suffer impaired sperm quality and spermatogenesis, and the underlying mechanism could be related to DNA damage and energy metabolic reprogramming in testicular germ cells.

81. Developmental, neuro- and behavioral toxicity in fish: As described above, TH related effects have been observed in several fish studies, where exposure at environmentally relevant concentrations of DBDPE have been observed to cause disruption of the HPT-axis and plasma TH levels (Sun et al., 2024b, Wang et al 2019c; 2022b). Developmental effects have been demonstrated and include changes to the thyroid system, neurotransmitters, mitochondrial function, morphological deformities and behavioral changes such as hyperactivity. Hyperactivity could be an adverse effect through increased energy expenditure, exhaustion, and increased predation risk through erratic movements and altered social behavior.

82. In a two-generation zf study (Sun et al. 2024b), life-time exposure to DBDPE at environmentally relevant concentrations induced anxiety-like behavior and thyroid disruptions in unexposed F1 and F2 offspring (see paragraph 61). Zf embryos were exposed to environmentally relevant concentrations of DBDPE (0.1, 1, 10 nM) up to 8 months of age (400 embryos in each group, n=3). The measured contents of DBDPE in water samples were 0.15, 0.68 and 7.60 nM (146, 660 and 7381 ng/ L). Higher-order behaviors such as anxiety-like responses can be quantified in older larvae

(e.g., 5 dpf) by measuring thigmotaxis, which is the propensity to remain near the edges of an arena, a conserved vertebrate behavior analogous to rodent open-field test behavior (Han et al., 2021, Lima et al. 2026). When testing thigmotaxis, Sun et al. (2024b) found that ancestral exposure to 10 nM DBDPE significantly increased the proportion of time spent in the outer zone for F1 larvae (5 dpf) under both light and dark conditions and for the F2 larvae under both light and dark conditions. Thigmotaxis (also called "wall-hugging" or "wall-following" behavior) is part of defensive/anti-predatory behaviors and indicates anxiety or stress related behavior (Champagne et al. 2010). The findings indicate that thyroid disruption and anxiety-like behavior in F1 larvae were mainly driven by excessive maternal thyroid hormone transfer, whereas effects in F2 larvae were primarily linked to transgenerational epigenetic inheritance via hypomethylation and hypermethylation of TH-related genes. presented study shows a potential relationship between thyroid disruption and the multi- and transgenerational anxiety-like behavior.

83. Sun et al. (2023b) exposed zf F0 generation to 0.1, 1 and 10 nM DBDPE (100 larvae per replicate, n = 3) from 2 hpf to 8 months of age and reared the F1 and F2 generation without further exposure. Total body burden of F0 larvae was 160, 237 and 876 ng/ g dw, respectively, and in F1 and F2 larvae total body burden of DBDPE was below LOD. Acute exposure of F0 to DBDPE did not cause significant changes in development parameters, except for increased heart rate at highest dose. However, increased malformation was observed in F2 larvae, where pericardial and yolk sac edema ($p < 0.01$), spine and tail bending ($p < 0.01$), and anophthalmia ($p < 0.05$) were the major malformations after ancestral DBDPE exposure (1 and 10 nM). Heart rate increased in the F0 and F1 larvae, while it decreased in the F2 larvae. This was in accordance with the results of changing profiles of neurotransmitter levels and locomotor activity. In the 0.1 and 10 nM treatments, the F1 generation showed significant increases in GABA, Choline, ACh, NE, 5-HT, Epi and 5-HIAA, while the F2 generation showed significant decreases of the same transmitters and also Glu. Considering the role of neurotransmitters in regulating cardiovascular function, the homeostasis of neurotransmitters may have contributed to the inappropriate heart rates in zebrafish larvae. When looking at dark-to-light behavioral essays, the normal locomotor pattern of zf larvae is characterized by a distinct phenotype: immediate and robust hyperactivity during dark periods followed by significantly lower activity during light periods. Deviations from this pattern are indicative of neurotoxic or psychoactive effects (Lima et al. 2026). In F1 larvae (5 dpf), who experienced direct exposure through multigenerational exposure in F0, hyperactivity was observed during both light and dark cycles in the 10 nM treatment. However, in F2 larvae (5 dpf), without direct exposure to DBDPE, the light− dark stimulated locomotor activity were significantly decreased. Analysis for both transcriptome and DNA methylome demonstrated a gradually increased number of significantly affected pathways from F0 to F1 and F2 larvae. In general, more extensive responses were observed in F2 larvae compared with F0 larvae at both transcription and DNA methylation levels. Taken together, the results demonstrated multigenerational imbalance in neurotransmitters resulting in excitatory effects in F0 and F1 larvae but a transgenerational inhibitory effect in F2 larvae upon ancestral DBDPE exposure. In addition, multi- and transgenerational imbalance in glycolipid and energy metabolic disruption was observed by alterations in levels of TG, glucose, hepatic lipase, succinate dehydrogenase, cytochrome c oxidase and ATP. Oxidative stress has been found to result from DBDPE exposure and might be one of the mechanisms underlying the toxic effects of DBDPE. ROS was increased in F0 larva, glutathione peroxidase (GSH-px) and GHS was markedly increased in F1 larvae, but only GSH-px was affected in F2 by a significant decrease. The alteration in TH and TH-axis described in Sun et al., (2024) may contribute to the observations in Sun et al., (2023b). TH's are crucial for early neural development, neurotransmission and particularly anxiety-like behavior control (Leach and Gould, 2015).

84. Hua et al. (2022) investigated induced hyperactivity in developing zf by exposing embryos from 2 hpf to 120 hpf to measured concentrations of DBDPE at 1.9, 7.5, 16.4 and 42.1 µg/L at T0, which decreased to 1.0, 2.3, 6.2 and 10.2 µg/L at T24, respectively. No significant differences were observed in the malformation rates, survival rates and body length, but the heart rates were significantly increased in zebrafish larvae exposed to 16.4 and 42.1 µg/L of DBDPE compared to control ($p<0.001$). The tail bending frequency in all DBDPE treated groups was close to the control at 23 hpf, but significantly higher at 24–26 hpf in 1.9 µg/L treatment, at 24, 25 and 28 hpf in 7.5 µg/L treatment, at 24–28 hpf in 16.4 and 42.1 µg/L treatment groups. Under continuous light, the average free-swimming speed of zebrafish larvae was significantly increased following exposure to 16.4 and 42.1 µg/L DBDPE. During the dark-light transition period, the average swimming speeds were significantly increased in all three dark phases upon 42.1 µg/L DBDPE exposure, and also in the first light phase upon 16.4 and 42.1 µg/L DBDPE exposure. Contents of multiple neurotransmitters were significantly decreased in zf larvae exposed to 1.9 µg/L DBDPE. At higher doses (16.4 and 42.1 µg/L DBDPE) only the ACh levels were significantly increased, which coincides with the observed hyperactivity. Increased activity of the enzyme ChAT, catalyzing ACh synthesis (Agostini et al., 2018), was found in larvae exposed to 42.1 µg/L DBDPE, and may be responsible for the increased

ACh contents. Molecular docking study suggested binding potency of DBDPE against ChAT, implying possible excitatory activity of DBDPE in zebrafish. In contrast, the activity of AChE, a rate-limiting enzyme catalyzing acetylcholine into choline, showed no obvious changes in any of the DBDPE treatment groups. Molecular docking results also revealed interacting potency of DBDPE against α 1-TUBULIN and SYN2a with binding energies of -38.9064 and -18.6725 kcal/mol, respectively. Taken together, the motor behavioral changes pointed to an excitatory toxic effect upon embryonic exposure to DBDPE.

85. Zhang et al. (2026) showed that DBDPE exposure could cause neurobehavioral abnormalities, cardiovascular and developmental toxicity in developing zf. Cardiac functions begin early (Lima et al. 2026) and indications of toxicity to the cardiovascular system include pericardial edema, increased sinus venosus-bulbus arteriosus (SV-BA) distance, decreased cardiac ejection fraction, heartbeat rhythm and velocity (Zhao et al. 2024). It is also worth noting that adult zf are capable of complete heart regeneration, whereas adult mammalian hearts have only limited regenerative potential (Zhao et al. 2024). Fertilized zf embryos were exposed to 0, 5, 50, and 500 μg/L DBDPE for 120 hpf. DBDPE exposure did not significantly affect the larval survival or hatching rates. At 120 hpf, larvae exposed to 50 and 500 μg/L DBDPE exhibited morphological abnormalities characterized primarily by spinal curvature and swim bladder non-inflation. In the 500 ug/L group bent trunk, exopthalmia (eye damage) and enlarged pericardial edema were observed. When assessing neurobehavioral effects, movement trajectory heatmaps showed that DBDPE exposure significantly enhanced larval locomotor activity. Average swimming speed increased dose-dependently, with the 500 μg/ L group showing significantly higher speeds during both light and dark phases. The heatmap trajectory and increased speeds indicate DBDPE-induced anxiety-like behavior. The study also found reduced level of lysophosphatidylcholine, where reduced levels could impair the central nervous system and hinder neurodevelopment, which could be tied to the observed behavioral abnormalities. For cardiotoxicity, quantification of morphological evaluations, showed significantly increased pericardial area at both 50 and 500 μg/L, as well as significantly higher heart rate at 500 μg/L. Furthermore, the results showed significantly increased SV-BA distance in both 50 and 500 μg/L treatment groups. KEGG pathway enrichment identified ferroptosis (cell death) and autophagy (cellular recycling) as significantly enriched pathways. DBDPE induced dose-dependent rise in ROS. In line with this, significant accumulation of MDA, and significant depletion of GSH was found at 500 ug/L. This was accompanied by increased level of phosphatidylethanolamine (where increased levels have been tied to cardiotoxicity) and altered levels of ferroptosis-related proteins and their gene transcripts. However, co-exposure with 500 ug/L DBDPE and 2 ug/L ferroptosis inhibitor (Fer-1) alleviated DBDPE-induced cardiotoxicity, improved systemic oxidative stress and reversed the expression of ferroptosis related genes. This indicates that oxidative stress and ferroptosis may be important for the effects observed for cardiac development. Based on their proteomic findings, the authors suggested that DBDPE exposure disrupted retinol metabolism and the visual cycle through synergistic downregulation of retinol hydrogenase 12 (RDH12) and upregulation of UGT1B2, ultimately causing developmental abnormalities such as exophthalmos in zebrafish larvae.

86. Yang et al. (2023) exposed zf larvae (2 hpf – 120 hpf) to DBDPE (0, 50, 100, 200, and 400 μg/L) and found that neurotoxicity was induced by increased average swimming speed, interfered neurotransmitter contents, and transcription of neurodevelopment-related genes in zf larvae. In addition, exposure to 400 μg/L DBDPE significantly increased the malformation rates (pericardial edema, yolk sac edema, spine bending and tail bending) and increased heartbeat rates in zf larvae. They showed significantly increased MDA and ROS levels and decreased GSH content and SOD activity in 200 and 400 μg/L DBDPE-treated groups. Mitochondrial activity was evaluated, and the basal respiration, ATP production, maximum respiration, spare capacity, and proton leak were all significantly reduced in zf larvae exposed to 400 μg/L DBDPE, indicating a decrease of mitochondrial respiratory activity upon exposure. ATP-contents, and activity of mitochondrial chain complex I, II, III, IV were significantly reduced by 400 μg/L treatment. Meanwhile, the mitochondrial membrane potential (MMP) was also significantly decreased in zf larvae exposed to 200 and 400 μg/L DBDPE ($p < 0.05$). Nicotineamide riboside (NR), a substrate for NAD+, was used for exogenous compensation to prevent mitochondrial abnormalities. Co- exposure to 160 ug/L NR and 400 ug/L DBDPE from 2 to 120 hpf prevented DBDPE effects on mitochondrial function, reduced oxidative stress and restored effects from DBDPE on neurotransmitter levels and expression of genes related to neurodevelopment and glycolipid metabolism.

87. Neurotoxicity in adult zebrafish: DBDPE has been shown to have effects related to neurotoxicity in adult zf, as well as the abovementioned effects seen in zf larvae. The larval zf brain possesses neuromodulatory circuits homologous to those in mammals, including major neurotransmitter systems such as glutamate, GABA, ACh, dopamine, serotonin (5-HT), noradrenaline,

and histamine (Rosa et al., 2022). The above-mentioned neurotransmitters are very similar to those found in mammals, including humans (Lima et al. 2026).

88. In Sun et al. (2022) (*see paragraph 78*) hypoactivity, measured as decreased average swimming speed and total distance in the 100 nM treatment group ($p < 0.05$), has been linked to disruption of muscular-related proteins and related pathways and intracellular calcium homeostasis when 4-month-old female zf was exposed to 1 nM and 100 nM DBDPE for 28 days.

89. Sun et al. (2023c) exposed F0 adult zf in the same manner as in Sun et al. 2023b (*see paragraph 83*) and found that neurotransmitter balance were disrupted. The F0 and the unexposed F2 generations showed the most significant changes in neurotransmitters content in the brain from adult zf (8 months), while the F1 generations seldom had significant changes. Almost all tested neurotransmitters were altered in the F1 and F2 eggs, indicating that the parental transfer of neurotransmitters to zygotes were disturbed in zf. DBDPE induced significant changes in weight, length and tissue SI (BSI, GSI) of adult zf in both male and female across generations. Behavior performance coincides with the neurotransmitter results, as fewer changes were observed in the F1 generation in general. F0 males spent significantly more time in the middle section at 10 nM, and F2 males in both the near and far section. F0 females spent significantly more time in the near section at 10 nM, but the same was not seen in F1 or F2. The nearest-neighbor distance (NND) and the interindividual distance (IID) determined from two zf were recorded. In the female adults, the NND showed decreases in the F0 generation, increases in the F1 generation, and no significant changes in the F2 generation, whereas the IID showed significant decreases in the F0 and F2 generations but not in the F1 generation. Considering that zf naturally live in groups, altered social interactions, including social preference and shoaling behavior, could make the fish more vulnerable to predation threats. However, the observed changes in social preference behavior does not appear adverse as most changes increased the time spent closer to conspecifics, except for the male F2. Oxidative DNA damage, global DNA methylation and transcription profile confirmed transgenerational effects in the brain of adult offspring and higher sensitivity of the females. Mature and differentiated neurons of adult brain are usually postmitotic and held in G0 phase. Cell cycle disturbances were observed in adult zf brain of the three generations, and apoptosis was significantly increased in F2 females indicating DBDPE can induce transgenerational effects on the cell apoptosis in brain.

90. Wang et al. (2026) exposed six-month old adult zf to DBDPE concentrations of 0, 10, and 100 nM 28 days (n = 3, 20 male + 20 female per n) and found alterations in the transcriptional levels of genes associated with the central nervous system and levels of neurotransmitters. In female adult zf brains the levels of ACh, DA, NE, 5-HT, and 5-HIAA were statistically significantly upregulated in the 100 nM exposure group, while only the levels of 5-HT and 5-HIAA were significantly upregulated in the 10 nM exposure group. Neurotransmitters levels were not significantly altered in the brains of male adult zf, in contrast to results in Sun et al. 2023c where zf had been exposed from 2hpf until 8 months. No obvious adverse effects were found on the social preference behavior in the male or female zf (Wang et al., 2026). In female zf, several genes important for brain function and repair were upregulated, while only two genes exhibited significant upregulation in males. The transcription changes of certain genes in both females and males suggest neurotoxicity associated with DBDPE exposure in both genders. Conversely, some transcription levels exhibited significant sex-dependent variations, as observed for the level of neurotransmitters, indicating that females may be more susceptible to DBDPE exposure than males.

91. Neurotoxicity in mice: Sun et al. (2026) found that subchronic exposure to DBDPE induces anxiety-like behaviors and impairs spatial learning and memory capabilities in mice. Male C57BL/6J mice (4 - 5 weeks of age) were orally exposed to 0, 100, 500, and 2, 500 µg / kg bw / day DBDPE in 1% (v / v) Tween-80 for 12 weeks (n= 10 pr group). Behavior was tested in Open field test and Morris water maze test. Animals in the two highest doses showed significantly altered behavior compared to control animals associated with anxiety-like behavior alongside impairment in learning and memory ability. Immunohistology examination of hippocampus showed dose-dependent neuronal damage most severe at the two highest doses. Affected regions exhibited increased nuclear pyknosis, loosened arrangement, swelling and rupture of neurons. Significant increase in hippocampal oxidative markers (MDA and SOD) was observed as well as downregulated key neurotrophic and tight junction proteins vital for neuronal survival and memory formation. DBDPE were also shown to induce ER stress, mitochondria dysfunction, with Ca^{2+} overload and ferroptosis in mice hippocampus.

2.4.2 Adverse effects to terrestrial, soil and other aquatic organisms

92. Toxicity to terrestrial and soil organisms: Available studies indicate low mortality to soil organisms even at very high concentrations. However, DBDPE oxidative stress, lipid peroxidation and DNA damage has been observed in earthworms, and damaged intestines in silkworm exposed to environmental relevant concentrations.

93. Several of the industry reports investigating the toxicity to terrestrial organisms have later been published in Hardy et al. 2011. Hardy et al. (2011) evaluate terrestrial toxicity of soil microorganisms, earthworms and plants. No adverse effect was found for soil microorganisms. Earthworms (*E. fetida*) were exposed to DBDPE at 313, 625, 1250, 2500 and 5000 mg/kg dry soil for a total of 56 days. The mean measured concentrations were 231, 440, 761, 1907 and 3720 mg/kg, respectively. At the highest test concentrations, a significant reduction in reproduction at day 56 was observed ($p < 0.05$). This resulted in a 56-day reproduction LOEC of 3720 mg/kg dry soil and a NOEC of 1910 mg/kg dry soil. Normalized to an organic carbon content of 3.4%, as done in the original study report and according to ECHA (2008), the NOEC comes to 649.4 mg/kg soil dw. No other endpoints for *E. fetida* showed differences compared to control at the tested concentrations. For plants, certain effects on growth parameters of cucumber, onions and tomatoes at the higher tested concentrations (3091 – 5802 mg/kg) was shown.

94. Jiang et al. (2021) exposed *E. fetida* to DBDPE (5, 10, 20, 50, 100 mg/kg) for 28 days. The DBDPE concentrations in the earthworms reached 1.31, 1.69, 1.72, 2.32, and 2.60 μg/g, respectively. 100 mg/kg DBDPE exposure led to microscopic and ultrastructural damage of earthworm epidermis. Significant changes to the CYP450 and GST activities were observed in all treatments. A descending trend of CYP450 and GST with increased exposure indicates that the detoxification capacity of earthworms was weakened and inhibited by high exposure of DBDPE during 21–28 d. Zhao et al. (2020c) found that DBDPE exposure led to oxidative stress, lipid peroxidation and DNA damage in *E. fetida* when exposed through artificial soil to 2.5, 5, 10, and 20 mg/kg DBDPE for 28 days. Effects were seen at even the lowest concentrations. Wang et al. (2022c) found that *C. elegans* exposed to DBDPE (0, 1, 10, 100, 500, and 1000 μg/L, 0.01 % (v/v) DMSO) for 72 hours showed locomotion neurotoxicity from 100 μg/L. Furthermore, significant cell membrane damage with a 24 % increase in the 100 μg/L group ($p < 0.05$) and a dose-dependent relationship with increasing concentrations was found.

95. Luo et al. (2025) exposed silkworm (*Bombyx mori L.)* through DBDPE-treated mulberry leaves to 0, 0.011, 0.11, 1.1, and 11 μg/g dw DBDPE, comparable to levels that has been detected in plants previously, i.e. mangrove leaf (*A. marina*) (1.07-2.4 μg/kg TOC) and corn leaf (*Z. mays L.)* (4.16 – 31.9 μg/kg dw.) (ECHA, 2025). The larva was in their fifth instar stage and fed mulberry leaves for four days. The study showed histopathological changes to the silkworm intestine from 0.011 - 11 μg/g dw, and all four treatments altered intestinal microbiota composition ($p < 0.05$). No significant changes were observed in pupation rate, cocoon layer weight or whole cocoon weight.

96. Toxicity in birds: An unpublished study report (2013) on long-term toxicity to birds determined a 20-week NOEC of ≥88.1 mg active ingredient/kg bw/day for northern bobwhite (*C. virginianus*) exposed to DBDPE in the diet. However, potential for thyroid effects in birds at concentrations that are environmentally relevant were observed when chicken hepatocytes were treated with 0.1 mM DBDPE. DIO1 mRNA was increased and CYPA4/5 mRNA was significantly upregulated at 0.1 and 0.2 uM (Eggloff et al., 2011).

97. Toxicity to aquatic organisms: DBDPE exhibit low acute toxicity in standardized industrial study reports. These standardized short-term toxicity tests have later been published as a peer-reviewed article (Hardy et al. 2012). Hardy et al. (2012) investigated the effects of DBDPE on five species (rainbow trout (*O. mykiss),* freshwater algae *(P. subcapitata),* water flea *(D. magna),* chiromids *(C. riparius)*, and oligochaetes (*L. variegates*)) but did not find any acute toxic effects. Fish, algae or water fleas were unaffected by acute exposures to water accommodated fractions (WAF) of 110 mg DBDPE/L. Chronic exposure to DBDPE at the highest dose tested, 5000 mg/kg dry sediment, did not affect midge mean development times, emergence or development rates or oligochaete survival, reproduction or dry weight. However, there is uncertainty of dosing in this study as a WAF method was used to prepare exposure solution, and they do not report the use of any solvent.

98. Nakari and Huhtala (2010) performed an acute toxicity test of *D. magna* (ISO 6341, 1996) and a zf egg-larvae-test (ISO 12890, 1999). The DBDPE 48-h EC_{50} value to *D. magna* was 19 ug/L. The egg-larvae test showed that hatching was significantly reduced ($p <0.05$) in eggs exposed to 25 μg/L. The mortality of eggs and hatched larvae was significantly higher ($p < 0.05$) in both test groups (12.5 and 25 μg/L).

99. Wang et al. (2023b) exposed mussels (*M. galloprovincialis*) to DBDPE (1, 10, 50, 200 and 500 µg/L, 0.001% (v/v) DMSO) for 30 days. DBDPE promoted gametogenesis in both sexes shown by histological observation, gender-specific gene expression of egg and sperm protein (VERL and VCL) and histological morphometric parameter analysis, indicating that DBDPE may evoke reproductive endocrine-disruptions in marine mussels. Zheng et al. (2024) exposed octopus (*A. fangsiao*) to DBDPE (0, 1, 50, 100, 300 µg/L, with 0.2 % (v/v) DMSO) for 28 days. The 300 µg/L group showed significantly reduced growth and food intake over 28 days. DBDPE exposure impaired intestinal integrity, promoted bacterial translocation and caused histological damage and inflammation to the digestive gland, which may have led to inhibited growth performance and suppressed food intake.

100. Due to the presence of several conserved features of receptors and signaling pathways, mechanistic studies in zebrafish are included in section 2.3.1.

Conclusion on adverse effects according to the criteria in Annex D

101. The criteria for adverse effects listed in paragraph 1 (e), (i) and (ii) of Annex D are considered to be met for DBDPE and its debrominated analogs.

102. For adverse effects to both human health and environment, oxidative stress is prevalent in all studies and initiates adverse effects in several tissues, and dysfunction of mitochondria may be linked to brain effects observed. Effects on HPT-axis have also been observed and may contribute to liver impairments seen on metabolic function.

103. For the adverse effects to human health, experimental studies in mice and rats suggest that DBDPE has the potential to cause adverse effects to reproduction and reduce sperm quality by interfering with testosterone production in testis and altered serum levels of T, LH and FSH. Reduced sperm count and increased sperm malformation as well as reduced germ cell layer and reduction in T in testis were observed in mice exposed 7 weeks for 5 mg DBDPE /kg bw, LOEC for serum reduction of LH and FSH is 50 mg/kg (Qi et al., 2025). In another mouse study, 12 weeks exposure to 0.5 mg/kg bw DBDPE resulted in significant reduction in sperm quality and testicular spermatogenesis were affected (Shi et al., 2026).

104. Cardiovascular effects, with increased inflammation, plaque- and lipid accumulation have been observed after 6 weeks exposure to 100 mg/kg bw DBDPE in ApoE-/- mice. Lipid metabolism was also affected as well as levels of adhesion molecules which enhance the recruitment of macrophages. Studies in rats exposed for 28 days to 50 and 500 mg/kg bw DBDPE suggest that DBDPE can impair mitochondria function and reduce ATP level in the heart tissue, induce inflammation responses, affect metabolism (increase serum glucose and LDH) and induce apoptosis in heart tissues.

105. For the adverse effects to the environment, experimental studies in fish to DBDPE indicate effects on fecundity, gonadal development, sperm quality and spermatogenesis, sex hormone levels, HPG-axis gene expression, and ovarian metabolomic profiles (Yu et al. 2026, Yang et al. 2024, Zhou et al. 2026; Sun et al., 2022; Choi et al., 2021). Thyroid hormone related effects have been observed in several fish studies, where exposure at environmentally relevant concentrations of DBDPE leads to disruption of the HPT-axis and plasma TH levels (Sun et al., 2024b, Wang et al 2019c; 2022a). Alteration of neurotransmitter content and behavior has been observed both in developing larvae and in adult fish after generational exposure.

106. Adding to the concern, DBDPE was found to be transferred from mother to fetus via transplacental transfer in fin whales and humans and it was measured in human breast milk globally. Maternal transfer of bioaccumulative substances *in utero* represents a potential risk to embryonic development and may represent the largest source of FR input to offspring during the first few years of life.

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

107. Based on existing data DBDPE can be considered to meet the screening criteria in Annex D for persistence, bioaccumulation, long-range transport and adverse effects under the Stockholm Convention.

108. Global production and use have grown significantly over the past decade and are projected to still increase in the future, mainly as replacement for decaBDE. DBDPE is used in many applications resulting in emission to the environment.

109. Increasing trends has been observed in dated sediments cores from Lake Maggiore in Italy from 1989 to 2011 (Poma et al., 2014) and in molluscs from Bohai Sea from 2011 to 2018 (Wang et

al., 2021). Levels of DBDPE in the environment exceed or are equal to decaBDE and other listed POP-BDEs. High levels are observed in the environment and in humans in more urbanized locations indicating that releases are not controlled. DBDPE may also contribute to the formation of persistent, bioaccumulative, and inherently toxic transformation products, such as lower brominated BDPEs, in the environment. Widespread detection in air, snow, soil, and biota samples from remote regions demonstrates long-range atmospheric transport.

110. Exposure in controlled studies show that DBDPE induces oxidative stress, increase inflammation, impair mitochondria and metabolic function which can lead to cardiovascular-, reproductive- and brain effects observed. There are studies indicating that DBDPE may affect endocrine systems both in mammals, birds and aquatic species.

111. DBDPE affects reproduction through toxicity to spermatogenesis and HPG-axis in males of both rodents and fish. There are also indications that DBDPE may affect female reproduction, where reduced fecundity has been observed in female fish linked to reduced sex-hormone levels and alteration of oocyte development. DBDPE exposure has been found to interfere with thyroid system by affecting HPT-axis in both non-mammalians and mammalians. Effects on the neural system have been observed in both fish and rodents. DBDPE has been shown to alter neurotransmitter balance in fish, behavior in fish and rodents and induce morphological alterations in mice brain in areas linked to memory.

112. Releases of DBDPE to the environment are continuing in all regions investigated. DBDPE may contribute to the formation of persistent, bioaccumulative, and inherently toxic transformation products, such as lower brominated BDPEs, in the environment. Due to the POP properties and risks related to its widespread production and use, global action is warranted to control further release of DBDPE.

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