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Thyroid hormone-related mixture effects of some brominated fire retardants

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Several polybrominated diphenyl ethers (PBDEs), especially hydroxylated metabolites, have been shown to mimic thyroid hormone (TH). Most TH-active PBDEs mimic thyroxine (T4) and may bind to T4-transporting and -metabolizing hormones, and some can even mimic triiodothyronine (T3) thus activating the TH receptor (TR). In addition to these agonistic effects, recently antagonistic and potentiating TR-mediated mixture effects have been shown for some brominated flame retardants (BFRs). These effects have been studied *in vitro* in the T3-dependent T-screen and TRα/TRβ specific reporter gene assay, *ex-vivo* in isolated tadpole tail tissue, and in an *in vivo* proliferation assay with 1-week old tadpoles. The results will be presented for the following BFRs: 2,4,4'-tribromodphenylether (BDE28), the nona BDE#206, and hexabromocyclododecane (HBCD), as well as 4,4'-diiodobiphenyl (DIB) as a model compound. Interestingly, the potentiating mixture effects of BDE28 and DIB were TRα or TRβ-specific in the reporter gene assay, consistent with a molecular structure that resembles TH, while HBCD, a compound with a highly dissimilar molecular structure, did not induce any effect in this specific assay for TR activity. However, HBCD had potentiating effects in the T-screen and tail resorption assay, suggesting a cell-type specific effect of this compound that is not mediated directly via TR activation.