Dose-Response Relationships for DNA-Adducts formed by Mono-, Di- and Tri-Chlorobiphenyls: Do Common Indoor and Outdoor PCB Vapor Exposures Pose a Significant Cancer Risk?

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Scott, PK, A Bernal, T Cheng, E DeGandiaga and BD Kerger

Abstract:
Mono-, di- and trichlorobiphenyls are reported to create DNA adducts from reactive oxygen species generated during liver metabolism, resulting in concerns that exposures to vaporized PCBs from environmental sources may pose an appreciable cancer risk in humans. We analyzed the available published reports on airborne PCB measurements, identified the range of upper bound daily intake of lower-chlorinated species during appropriate human exposure scenarios, and determined associated liver concentrations using a one-compartment pharmacokinetic model. We also compiled dosimetry data from in vitro and in vivo studies that identified significantly increased adduct formation from lower-chlorinated congeners, and assessed the minimum conditions of dose necessary to generate such adduct formation. We found that DNA adducts were only significantly increased from lower-chlorinated PCBs when rats were pretreated with agents that increased oxidative liver metabolism or when administered PCBs at doses orders of magnitude higher than upper-bound doses of the same congeners reported during environmental exposures to humans. We determined that internal doses of lower-chlorinated congeners from estimated upper bound environmental exposures are at least 2-3 orders of magnitude lower than the effective doses necessary for adduct formation. The compiled dosimetry data also indicated that PCB mixtures elicit an attenuated dose-response for enzyme induction and adduct formation when compared to single congeners administered at high tissue doses. Similarly, vaporized PCBs constitute a mixture of congeners that vary in their ease of oxidative metabolism depending on the pattern of chlorination, and competitive inhibition may limit potential for generating reactive oxygen species and significant adducts. Considering these dose-response elements, we conclude that ambient environmental sources of PCBs are not likely to pose a significant risk of liver enzyme induction, DNA adduct formation, or cancer risk in humans.