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Introduction to special issue: Neurotoxicity of brominated flame retardants and the quest for safer alternatives

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The term flame retardants (FRs) refers to a diverse class of chemicals that impede combustion by reducing the availability of fuel or oxygen, or by reducing the temperature of a growing fire, among other mechanisms. Although FRs have been used since antiquity, the recent decades have been very interesting for various stakeholders involved with the use, manufacturing, and safety of FRs. Relatively rapid changes have occurred in the use patterns of some FRs as concerns about toxicity (particularly neurotoxicity), environmental persistence, and bioaccumulation have reduced or restricted use. Consequently, alternative FRs are emerging, along with potential health and environmental risks that are often poorly characterized.

Because FRs include many different types of chemicals, it is difficult to classify them by chemical structure, mechanism of action, or physiologic effects. However, the need for classification exists and FRs are therefore often categorized by the toxicology community based on structure, resulting in groupings such as halogenated organic FRs (including brominated or chlorinated compounds), organophosphorus FRs (including halogenated or non-halogenated), nitrogen-based FRs, and inorganic FRs. Yet, because of the heterogeneous nature of FRs, these classifications do not imply that all chemicals within a class share the same toxicologic profile.

Much of the initial research on the toxic effects of FRs has focused on brominated compounds (BFRs), such as polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCDD). In recent years, research has begun to examine organophosphorus FRs, while research on other types of FRs remains limited. This special issue of Neurotoxicology and Teratology intends to advance the field in respect to the neurotoxicologic assessment of FRs, including both developmental and adult exposures. As such, we are pleased to present the work of several research groups employing a variety of methods, from *in vitro* assessments through *in vivo* models and epidemiologic investigations.

The first papers in this special issue address advanced research questions about select BFRs, including the role of PBDE metabolites in toxicity, mechanisms underlying the effects of different BFRs, and the neurobehavioral effects of developmental BFR exposure in animal models and human cohorts. This issue then presents studies that utilize alternative *in vitro* and *in vivo* assays to evaluate and compare select BFRs and organophosphorus FRs for developmental and neurotoxic effects. Finally, the issue concludes with a comprehensive review of this research that evaluates the neurotoxicity of select BFRs and what is known about the effects of alternative FRs, which are replacing certain BFRs in some applications.

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