**EL1**

**Current understanding of perfluoroalkyl acid toxicology**

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The perfluoroalkyl acids (PFAAs) are a family of organic chemicals consisting of a perfluorinated carbon backbone (4-14 carbons in length) and an anionic head group (sulfonate, carboxylate or phosphonate). These compounds have excellent surface-tension reducing properties and have numerous industrial and consumer applications. However, they are chemically stable, persistent in the environment, ubiquitously distributed, and present in humans and wildlife. Two issues must be considered regarding PFAA toxicology: pharmacokinetics and potency of the chemicals. The rates of PFAA clearance and their body burden accumulation are dependent on carbon-chain length and animal species. In general, the serum half-life of PFAAs increases with chain length in both rodents and humans, but the estimates in humans are markedly higher than those in laboratory animals. Recent studies with laboratory animal models have indicated a number of toxic effects of PFAAs, including tumor induction, hepatotoxicity, developmental toxicity, immunotoxicity, neurotoxicity and endocrine disruption. The modes of PFAA actions are not well understood, but are thought to involve, in part, activation of nuclear receptor signals (such as peroxisome proliferator-activated receptor-α, PPARα). Based on PPARα activation, potency of PFAAs increases with carbon-chain length, carboxylates are stronger than sulfonates, and mouse receptor is more reactive than human receptor. Adverse effects of perfluorophosphonates in mice resemble those described for sulfonates and carboxylates, although potency of this congener appears to be weaker than the other two counterparts. *This abstract does not necessarily reflect US EPA policy.*

**EL2**

**A systemic review of the prothrombotic risk of xenobiotics: from cell to system**

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Thrombosis continues to represent a major cause of death in spite of the advanced medicine and pharmacotherapy of the modern era. Excessive thrombosis can cause life-threatening thrombotic events including deep vein thrombosis, stroke, myocardial infarction and pulmonary embolism. What is worse, it can lead to the exacerbation of the existing cardiovascular diseases through the degranulation of secondary vaso-active mediators and the stimulation of vascular remodeling.

Recently, we and several research groups have discovered that xenobiotics can manifest prothrombotic effects and efforts are being directed into the elucidation of the underlying mechanisms. Especially, prothrombotic effects of heavy metals and ROS-generating chemicals, nanomaterials and neurotoxicants are being extensively investigated in an effort to clarify the link between pro-thrombosis and their well-established cardiovascular toxicities. Platelets had been the main tissue of interest due to their major roles in thrombosis through forming platelet aggregates. However, the focus is being migrated into the involvement of erythrocytes and coagulation systems and their interaction with platelets and other cardiovascular tissues.

Exemplifying this, arsenicals which can induce platelet aggregation and thrombosis, also induces procoagulant activation in platelets, a series of events that culminate in phosphatidylserine exposure on outer membrane, the enhancement of thrombin generation and ultimately increased clot formation. It has been demonstrated that erythrocytes can also participate in the xenobiotic-induced thrombogenic activation through exhibiting phosphatidylserine exposure and resultant procoagulant activity. Interestingly, phosphatidylserine exposure is a key marker of apoptotic cells and it can increase cell-cell interaction and initiate phagocytosis by tissue macrophages, reflecting that the procoagulant activity induced by xenobiotic might be further related into other biological events like apoptosis and anemia.

These studies indicate the urgent need to expand our current understanding of prothrombotic risks of xenobiotics as a narrow scoped platelet aggregation into a general alteration of cardiovascular tissues as a system. In this context, a timely and comprehensive review on this subject will be informative and inspiring to the participants of the 6th Congress of Asian Society of Toxicology.