# HUMAN HEALTH IMPACTS OF EXPOSURE TO POPs: UNANSWERED QUESTIONS

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The Stockholm Convention[1] on persistent organic pollutants (POPs) was adopted in 2001 to protect human health and the environment from chemicals that are highly toxic, persistent, bioaccumulative, and undergo long range transport. These POPs include 9 pesticides, polychlorinated dibenzo-*p*-dioxins (PCDDs), dibenzofurans (PCDFs), and biphenyls (PCBs). They are grouped into three classes as to their risk management: most of the pesticides are slated for total elimination; because of a lack of effective alternatives, the production and use of DTT is to be restricted; and unintentional anthropogenic production of the dioxins, furans, PCBs, and hexachlorobenzene is to be reduced. However, these are not the only persistent contaminants of concern. The US EPA has also developed national action plans for other persistent and bioaccumulative toxicants (PBTs) such as alkyl-lead, benzo(a)pyrene, organic mercury compounds, and octachlorostyrene[2].

However, there are emerging chemicals which clearly meet the definitions used for POPs and PBTs. As for the original Stockholm POPs, these are all halogenated compounds. Several have already been nominated for inclusion under the Stockholm convention. The risk management evaluation has been approved for lindane, chlordecone, hexabromobiphenyl, pentabromodiphenyl ether (pentaBDE), and perfluorooctane sulfonate (PFOS), its salts and PFOS fluoride (PFOSF). This would lead to elimination or restriction of the production, use, export, and import of these chemicals. Four more chemicals are in the evaluation phase: commercial octabromodiphenyl ether, pentachlorobenzene, and alpha and beta hexchlorocyloohexane, and short chain chlorinated paraffins (SCCPs). Endosulfan has been newly proposed to the Stockholm convention.

The emerging POPs generally fall into two classes: perfluorinated surfactants[3] and brominated flame retardants[4]. The highly fluorinated compounds such as the perfluorinated alkly acids (PFAAs), including the carboxylates and the sulfonates, such as PFOA and PFOS, which have been extensively used as surfactants, but can also be unintentional degradation products of the precursor alcohols, amides and other derivatives. The perfluorinated chemicals (PFCs) are very different in their physical/chemical and biological properties from the classical POPs. PFCs have both a hydrophobic and a hydrophilic nature, so that they do not concentrate in lipid rich tissues, but instead appear at the interface between lipids and water. Thus, they are found in bodily fluids (highly bound to serum proteins), as well as in most body tissues (particularly the liver). Only low concentrations are found in adipose tissue or milk. They are very poorly metabolized. Thus, while they are persistent and can bioaccumulate to some degree, they do not biomagnify up the food chain to the same extent as the traditional POPs. Perfluorinated compounds have now been detected in environmental samples from around the world, including the Arctic, as well as in wildlife and people. Significantly, the resident time of PFC chemicals such as PFOS and PFOA are as long in humans as some of the traditional POPs, with half-life estimates of 4-6 years. While earlier work demonstrated rodent carcinogencity for some of the PFCs, recent studies have shown the potential for additional toxicities for these compounds at low exposure doses, including developmental and reproductive effects, neurotoxicity, and immunosuppression. An ongoing human study is suggestive of adverse effects in a population who have been exposed to highly contaminated drinking water. Much of the focus has been on the C6-C12 chain length compounds, but as industry has realized some of the potential concerns with the longer chain PFCs, studies have been initiated on the shorter chain compounds which have less ability to persist and bioaccumulate.

The other major class involves certain brominated flame retardants (BFRs). While there have been at least 75 BFRs, until recently the major products were tetrabromobisphenol A (TBBPA), hexabromocyclododecane (HBCD), and polybrominated diphenyl ethers (PBDEs). All have been detected in environmental samples and biota, and HBCD

and PBDEs have been found in the Arctic. This long range transport is likely a reflection of their additive use resulting in escape from the products in which they were used. This is in contrast to TBBPA which is primarily used in a reactive mode, thus chemically bonding to its matrix. The stereoisomeric composition of the commercial HBCD mixture is distinct from what is found in biota. Likewise, the congener composition of the commercial PBDE mixtures is very different from that found in various environmental matrices, wildlife, or people. To date, TBBPA and HBCD are essentially unregulated, although their release is captured under EPA's high volume chemical's program. In contrast, the commercial Penta and Octa PBDE mixtures have been formally banned in the EU and several US states. The sole manufacturer voluntarily ceased production nearly four years ago. Action on these two products was driven by the potential health concerns. Although studies demonstrating toxicity of the Deca PBDE product are more limited than for the lower brominated species, there is growing concern not only for its inherent toxicity, but for its ability to break down into the lower brominated congeners as well as be metabolized to reactive intermediates in biota. Health effects of PBDEs reported in invertebrates, fish, and mammals include hepatotoxicity, dermal effects, reproductive toxicity, immunotoxicity, endocrine disruption, developmental reproductive and neurotoxicity, and cancer. Several recent epidemiology studies have reported associations between PBDEs and developmental reproductive effects, as well as endocrine disruption. As concerns increase for these BFRs, industry is actively developing less persistent, bioaccumulative, and toxic alternatives in order to provide fire safety.

While the "classical" POPs and PBTs have been extensively studied for decades, there are still many uncertainties which surround their potential for health effects when exposures occur at the background level. Because of recent advances in biomonitoring, we have more information on the concentrations which are present in people from the general population. Certain countries have extensive biomonitoring programs, measuring a variety of contaminants in various biological fluids, but especially blood/serum/plasma, urine, and breast milk. Certain European countries have collected such samples for over 30 years. In the United States, the Centers for Disease Control now conducts a statistically based sampling of the population known as NHANES[5] which results in a biannual "report card" of over 100 contaminants in the general US population.

What are the remaining health concerns for all of the POPs and PBTs? It is clear that we need to be concerned with population effects, as well as effects on the individual. Subclinical effects, such as reduced potential or enhanced sensitivity, can have major population impacts. Exposure to POPs is on top of the presence of differential nutrition and pharmaceutical use, as well as personal care products, disinfection byproducts, as well as differential genetic susceptibilities. The same level of exposure can cause adverse effects in some, but not other, individuals. And the reality is that exposure is to a complex mixture of contaminants present in the environment, wildlife, and people. Development of relative potency approaches, as used in the dioxin toxic equivalency scheme, allows estimation of the total toxicity of one group of compounds. However, the brominated dioxins and furans, which are contaminants of the BFRs and produced upon their combustion, are not yet included in this approach. Use of the dioxin toxic equivalence says nothing about how the dioxins may interact with other classes of chemicals. For example, PCBs always have some dioxin-like congeners present. Do the dioxin and nondioxin-like PCBs interact? The PBDEs and the PCBs seem to cause a similar spectrum of effects. Can their toxicity be estimated by developing some quantitative additive approach? But the behavior of the higher brominated PBDEs is very different from the lower brominated ones. What about the PFCs? And do the PFCs and the PCBs/PBDEs/dioxins interact?

Knowing internal measures of exposures allows us to compare across populations and species. Population effects seen in wildlife can serve as sentinels for people. Focusing on body burdens in our laboratory studies enables us to relate administered doses to effects. Understanding that there are life stages with inherently greater vulnerability allows us to design experiments, both animal and human, in which we ask more subtle questions than in the past. Overall, nature is inherently conservative. Effects seen in several species of animals can indicate at least the potential for responses in the human population.

Disclaimer: The views expressed in this abstract are those of the author and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.

References

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