Memo: PCBs Literature Review 2013-2015

Introduction

Polychlorinated biphenyls (PCBs) are industrial chemicals that were manufactured under the trade name Aroclor for use in transformers, electrical equipment, motor oils, plastics, paint, and numerous other applications. Although banned thirty-five years ago, these contaminants are still widely detected in humans and the environment.

PCB’s primarily accumulate in soils and sediment as a result of spills, leaking toxic landfills, or contamination from products containing the chemicals. While PCBs do pollute the air via volatization and dispersion, the contaminants are most problematic in soils and sediments where they adhere to organics and are very slow to degrade. The primary route of exposure for humans and wildlife is through the ingestion of contaminated dietary items. PCBs are highly lipophilic and dissolve in fatty tissues and bioaccumulate over an organism’s lifespan. This property is important to both human and ecological toxicology because bioaccumulation leads to biomagnification, the process by which persistent toxins increase in concentration upward through the food chain (Faroon et al., 2003). As a result, the highest concentrations of PCBs are often observed in top predators with long life-spans and high fat deposits such as dolphins, whales, and humans.

In the United States, PCBs are regulated by several different agencies and regulatory frameworks. The Environmental Protection Agency (EPA) requires drinking water to have a maximum contaminant level (MCL) of 0.5 parts per billion (EPA, 1996); fish consumption advisory numbers are also maintained in contaminated waters. States are increasingly being urged by EPA to develop PCB total maximum daily loads (TMDLs)-goals for reducing PCB concentrations in affected waterways. Disposal and remediation of PCBs is regulated under the Toxic Substances Control Act (TSCA) (EPA 2005). Finally, the Federal Drug and Food Administration (FDA) publishes tolerances for PCB concentrations and residues in foods such as milk, eggs, and poultry and enforces bans on the use of the compound in product packaging.

Brief Review of Human and Ecological Toxicology

PCBs are a broad category of compounds consisting of 209 individual congeners differentiated by the position and number of chlorine atoms that make up the molecule (Lauby-Secretan et al. 2013). Part of the complexity of studying PCB toxicity is recognizing that the chemical, physiological, and ecological effects of these distinct congeners can vary. PCBs are classified as endocrine disrupters because of their ability to mimic hormones and activate, deactivate, and even damage receptors that modulate and control cellular and body systems (Lauby-Secretan et al. 2013). The specific
receptors affected varies based on the congener or mixture of congeners involved and these multiple mechanisms of action result in a wide range of possible human and environmental effects. The following section provides an overview of toxicological effects of PCBs with the understanding that these general conclusions do not apply to all congeners.

**Carcinogenic Effects**

Increasingly the consensus points towards a strong link between cancer in humans and wildlife exposed to PCBs. In 2013 the International Agency for Research on Cancer (IARC) upgraded PCBs from “probable carcinogen to humans” to “carcinogenic to humans”. This decision was made based on 70 epidemiological studies which showed elevated risks of melanoma in both individuals with occupational exposure and the general public; increased risks of breast cancer and non-Hodgkin’s lymphoma were also noted (Lauby-Secretan et al. 2013). This report aligns and strengthens the position of EPA’s 1996 report which concluded that PCBs are likely carcinogenic with evidence of increased risk of thyroid, liver, and gastrointestinal cancer from PCB exposure (EPA, 1996).

**Non-Carcinogenic Effects**

PCBs have been shown to affect most of the major body systems including the respiratory, cardiovascular, gastrointestinal, renal, endocrine, and musculoskeletal (Faroon & Olson, 2000). PCBs can also affect the reproductive system; studies on rats have documented decreased litter sizes and body weight, as well as reduced sperm count and conception rates (Faroon et al. 2003). In both humans and rats, neurological and developmental deficits have been observed in children with high in-utero exposure (EPA, 1996). Children exposed to PCB’s at an early age have been reported to exhibit weaker reflexes, reduced memory, and a higher likelihood of attention deficit issues (Faroon et al, 2003). PCBs have also been linked to immunological effects that range from a weakening of the immune system to increases in inflammatory disorders such as tonsillitis and bronchitis (Faroon et al, 2003).

The toxicology of PCBs continues to be an area of extensive international research and each year brings numerous new studies on the contaminant.

**2013-2015 Literature Search**

The current literature search is an update of one conducted in August-September 2014 (Appendix B) that covered PCBs in the literature from 2013-2014 and one conducted in August-September 2013 (Appendix C) that covered PCBs in the literature from 2002 to 2013. The most recent review of the literature published in 2014 and 2015 on PCB toxicology returned over 100 relevant publications. These publications are listed in Appendix A for the reader’s convenience. While it is not within the scope of this memo to address them all, a few key studies are discussed in brief below.
Carcinogenic Effects
As stated above, IARC’s 2013 classification of PCBs as carcinogenic is significant and several recent studies support this classification. Dong et al. (2014) found some PCBs are both cytotoxic and genotoxic in liver cells and increased DNA and chromosome breaks were observed in cells exposed to this congener. Ruder, Hein, Hopf, & Waters (2014) examined a cohort of 24,865 workers exposed to PCBs at manufacturing plants in the U.S. and found elevated overall mortality and an increased risk of melanoma and stomach, prostate, and nervous system cancers. Similar studies conducted by Li et al., (2013) and Onozuka, Hirata, and Furue (2014) examined workplace exposure cohorts and found decreased net survival rates primarily caused by increased cancer rates. PCB exposure was also linked to chemoresistance of liver cancer, resulting in a poorer prognosis in patients with the disease (An et al., 2014).

Non-carcinogenic Effects
Several new studies have addressed the link between PCBs and neurological effects. Gaum et al. (2014) studied individuals with work-related exposure to PCBs and found a significant relationship between PCB burden and increased depression and psychosomatic symptoms. Wigestrand, Stenberg, Walaas, Fonnum, & Andersson (2013) found PCBs can inhibit uptake of dopamine in the same manner as cocaine; the researchers suggest this mechanism is a likely factor in PCB neurotoxicity and behavioral effects such as depression.

The effects of PCB’s on human development have been well-documented but several new studies provide an international scope to the literature. A 2014 study of toddlers in Japan found a relationship between prenatal exposure of PCB congeners in cord blood and decreased IQ (Tatsuta et al., 2014). This is significant because prenatal exposure continues to be a significant exposure pathway in the U.S.; Nanes et al. (2014) surveyed 43 human placentas from several U.S. locations and found PCBs in all specimens. Dallaire et al. (2014) studied a cohort of Inuit children and found a correlation between concentrations of PCB 153 in blood and lower weight, shorter height, and smaller head circumference across a range of ages and suggest PCBs are disrupting thyroid function. Decreased motor coordination was also positively correlated with PCB exposure; a study of 97 Dutch infant-mother pairs found high PCB 107 and 187 blood concentrations were associated with decreased motor coordination (Berghuis, Soechitram, Hitzert, Sauer, & Bos, 2013).

Finally, a 2014 paper corroborates previous epidemiological studies that suggested a link between exposure to PCBs and auditory impairment in children and adults; data surveyed from 1999-2004 indicated a positive relationship between serum PCB levels and hearing impairment in U.S. adults (Min, Kim, & Min, 2014).
Environmental and Ecological Effects
PCBs are potent contaminants in the environment as well; many of the same effects seen in humans have been documented in wildlife. However, international bans and cleanup efforts have resulted in a reduction of PCB levels in soils and sediments in some cases. Everaert et al. (2014) report two to threefold reduction in PCB concentrations between 1991 and 2010 in an open water ecosystem near Belgium; no significant decrease was observed in an industrial estuary receiving no remediation. As Bruckman et al. (2013) indicate in their survey of PCB soil depositions in Germany, PCB congeners have long half-lives and can be retained in sediment for decades unless the PCBs are cleaned up.

Remediation of PCB contamination has been shown to be effective in many cases. A 2013 study by Ficko, Luttmer, Zeeb & Reimer compared PCB concentrations in vegetation and field mice on an abandoned Air Force station before and after PCB remediation work was conducted; the study found vegetation concentrations were four times lower while concentrations in deer mice were three times lower.

Several new studies add to the well-established ecotoxicological profile of PCBs. A 2013 study of six arctic birds found that migration and opportunistic feeding increased PCB burden equivalent to one full increase in trophic level (Baert, Janssen, Borgà, & De Laender, 2013). Evidence of these effects on migratory birds reinforces the international scope of PCB contamination. Persson & Magnusson (2014) surveyed 101 wild mink and found that PCBs alter the size and shape of mink reproductive organs, likely leading to reproductive effects. Similarly, Carpenter et al. (2014) found high PCB concentrations in Illinois river otters and concluded the species is at risk of PCB toxicity.

Marine mammals such as whales and dolphins have been shown to retain high PCB concentrations decades after the PCB ban. Dorneles et al. (2013) found high accumulation of PCBs in false killer whales and rough-toothed dolphins off the coast of Brazil. Similarly, a survey of beluga whales found moderate levels of PCB exposure and confirmed the contaminant can disrupt vitamin profiles in the large mammals (Deforges et al., 2013). As Kubo et al. (2014) report in their study of Steller sea lions, marine mammals are also at risk of PCB exposure through maternal-to-fetal transfer.

Summary
As investigations into all aspects of PCBs continue around the globe, new information continues to reveal several trends:
- PCBs are toxic at lower levels than previously believed
- PCBs cause a wider range of toxic effects on wildlife and humans, including cancer
- Remediating PCB contamination is effective in reducing the PCB burdens

PCB contamination is a local, regional and global problem- the PCBs in one locality will contaminate the living and non-living environment, contribute to the regional PCB burden, and add to the global PCB burden for generations to come.
Appendix A
Literature Search and References –2014-2015 Publications on Toxicology of Polychlorinated Biphenyls

The following is a reference list of materials resulting from a literature search conducted in January 2015 on the toxicology of Polychlorinated Biphenyls (PCBs), individual PCB congeners, and frequently associated compounds. This reference list is an update and addition to prior literature searches conducted on the toxicology of PCBs, which are listed below in Appendices B and C. Included in the search are references pertaining to the effects of PCBs on both human health and the environment, including persistence, fate and transport, and specific effects on ecological systems and organisms.

A number of studies focused specifically on early exposure to PCBs and effects on development in both humans and animals. In human health, Casas et al. (2015) studied prenatal exposure to PCB-153 and p,p'-DDE in order to evaluate the relationships between organochlorine compounds and birth outcomes. These authors observed an inverse linear exposure-response relationship between prenatal exposure to PCB-153 and birthweight, even at low levels of exposure. The association was modified by maternal smoking and ethnicity; the most susceptible subgroup was girls with mothers who smoked while pregnant. Elnar et al. (2015) conducted a study on juvenile male mice and found that lactational exposure to low levels of the six indicator non-dioxin-like (NDL) PCBs led to over expression of genes involved in the repair and response to DNA damage as well as repression of neuronal activity. The level used in the study was lower than the guidance level for human consumption of contaminated fish. Lastly, Poon et al. (2015) investigated the effects of a PCB mixture composed of Aroclors 1242, 1248, 1254, and 1260 on developmentally-exposed rats and observed that they were more susceptible to audiogenic seizures when exposed to loud noise as adults; female rats were also more susceptible than males.

The literature search was conducted through the Virginia Commonwealth University Library System using the VCU multi-database search tool as well as the specific database Science Direct. All of the following materials are peer-reviewed journal articles.

ESC, LLC makes no claims about the research in these citations in terms of validity and does not necessarily agree with the conclusions within. We note that readers need to confirm that authors of scientific papers are free of conflicts of interest, financial or otherwise. We advise readers to determine if the authors receive funding from the industries or companies that may be affected by the results of their research.

References are cited in Chicago format and numbered for convenience.


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Dichlorodiphenyldichloroethylene (DDE) Concentrations in Maternal and Umbilical Cord Serum in a Human Cohort from South Portugal.


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**Appendix B**

**Literature Search and References –2013-2014 Publications on Toxicology of Polychlorinated Biphenyls**

The following is a reference list of materials resulting from a literature search conducted in late August 2014 on the toxicology of Polychlorinated Biphenyls (PCBs), its
congeners, and frequently associated compounds. The reference list includes primarily publications from 2013-2014 but a few key reports from agencies such as EPA and WHO have been included for background information. Toxicology is loosely defined as those materials documenting the effects of PCBs on both ecological systems as well as human health. While toxicological reports were the primary focus of this search, some related materials describing environmental prevalence, fate, and transport are also included.

This literature search was conducted via the Virginia Commonwealth University Library system using the VCU multi-database search tool, as well as specific databases such as BIOSIS and Science Direct. The majority of these materials are peer reviewed journal articles; however, government/NPO reports and white papers are included where appropriate and relevant.

ESC, LLC makes no claims about the research in these citations in terms of validity and does not necessarily agree with the conclusions within. We note that readers need to confirm that authors of scientific papers are free of conflicts of interest, financial or otherwise. We advise readers to determine if the authors receive funding from the industries or companies that may be affected by the results of their research.

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Appendix C
Literature Review on Toxicology of Polychlorinated Biphenyls (PCBs), 2002-2013
The following is a bibliographic listing of articles resulting from an extensive literature search, conducted during the period August-September 2013, on recent research regarding Polychlorinated Biphenyls (PCBs) during the period 2002 to present (2013). Research was narrowly defined as professional (peer-reviewed) journal articles relating to the toxicological effects on living organisms, which included human health effects, other aquatic and land animals, plants, microorganisms, etc. This literature search was conducted via the Virginia Commonwealth University Library system, specifically utilizing the BIOSIS reference database which includes abstracts of literature in biological and biomedical areas of specialty. The literature search also includes documents available in Environmental Stewardship Concepts, LLC’s in-house resource files.

ESC, LLC makes no claims about the research in these citations and does not make any blanket claims as to their veracity, nor necessarily agree with the conclusions. We note that readers need to confirm that authors of scientific papers are free of conflicts of interest, financial or otherwise. We advise readers to determine if the authors receive funding from the industries or companies that may be affected by the results of their research.


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