Pharmaceuticals and other Endocrine Disrupting Compounds in Natural Water Systems

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Executive Summary

Since the 1940's, there has been a vast number of new, human-made chemicals introduced into our world. Many of these chemicals have found their way into our drinking water and natural waterbodies, which has raised concern for the health of humans, wildlife, and aquatic species. It has been found that these chemicals have the ability to interfere with hormonal activity of the body thereby resulting in a variety of adverse effects, some of which may not become evident for decades or generations.

The endocrine glands of the body secrete hormones which serve as messengers, controlling and coordinating activities throughout the body. The widespread use of pesticides introduced many people to the effects of even *minute* doses of a chemical having endocrine disrupting effects. Subsequently, the research on the effects of endocrine disrupting compounds (EDCs) became largely centered on pesticides. As the science grew, it became apparent that there are many other EDCs introduced into our environment from pharmaceuticals (particularly estrogen products), personal care products, plastics, flame-retardants, heavy metals and many more. The adverse effects vary by species and also by the life stage at the time of exposure, with unborn and young children particularly vulnerable. The areas of most concern are the carcinogenic, reproductive, immunological, and neurological effects on the human body.

Endocrine disrupting compounds find their way into the watershed from household and personal care products washing down drains, from pharmaceutical dumping and excretion, from agricultural and feedlot discharges, and from industrial discharges. Wastewater from municipal treatment plants, septic systems, and discharges from sewers, industry, agriculture and feedlots all make their way into our natural waterways, which eventually become our drinking water. Upgrading wastewater treatment facilities can significantly reduce the load of EDCs into a watershed.

Awareness of the presence of EDCs and their effects on the health of people and wildlife is only the beginning. Research into various EDC effects on humans and different species of wildlife is monumental as the number of chemicals grows every day. Communication and education is vital for individuals, governments, and scientists to reduce exposure to EDCs, and to fill knowledge gaps.

1. Introduction

Water contaminated with pharmaceuticals, personal care products, and common household chemicals is an international concern, even at extremely low concentrations. Everything that passes through the body or is washed down the drain has the potential to end up in our environment, posing risk to human health and natural ecosystems. As demonstrated by Theo Colborn, Dianne Dumanoski, and John Peterson Myers (1996) in their book "Our Stolen Future", some synthetic chemicals can interfere with natural hormonal activities of the body's endocrine system, resulting in adverse effects such as reduced birth rates, feminization, behavioural changes, increased occurrences of cancers, and lowered immunity. Such chemicals are referred to as endocrine disrupting compounds (EDCs).

Pharmaceuticals are of primary concern, although other household chemicals, industrial chemicals, and personal care products (PCPs) can also act as endocrine disrupting compounds. Given their increased use and, in turn, their increased presence in our aquatic systems, these human-made chemicals are ingested unknowingly by humans and wildlife through drinking water and through absorption by microbiological organisms and creatures that live in a water-based environment (Colborn et al. 1996). These chemicals can adversely affect the propagation and growth of species living in the natural environment, threaten aquatic populations, and impact human health.

EDCs have been present in water and the environment as long as humans have been using them, with an explosion of uses and chemicals since WWII. Actions and activities by individuals using EDCs directly contribute to the combined level of chemicals found in the aquatic environment yet the importance of individuals adding chemicals to the environment has been largely overlooked. The discovery of pharmaceuticals and PCPs in water and soil shows that even simple activities like shaving, applying lotion, or taking medication ultimately affect the environment (Environmental Protection Agency 2015(a)).

Muskoka, as with all other communities, needs to be concerned with the use and disposal of pharmaceuticals and other human-made chemicals into the watershed, even in trace amounts. Given that Muskoka's water quality and natural environment, including fish and wildlife, are unique and need to be preserved, awareness of and attention to the use and disposal of chemicals is particularly applicable here. The tourism industry is a major contributor to the local economy, and much of the success of that industry is based upon the expectation of a clean and dynamic environment. Technology and expertise exists that could improve Muskoka's current water quality and assist in minimizing the impacts of EDCs.

2. Background

EDCs are bioactive and can affect living tissue. According to C.R. Propper (2005), the U.S. Environmental Protection Agency defines an endocrine disrupting compound as any substance that interferes with the *"synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development, and/or behaviour"*.

The endocrine system is a collection of glands in the body that secrete hormones into the circulatory system to be carried to target organs. Hormones are naturally produced by our bodies and have specific functions in the endocrine system including reproduction, responses to stress and injury, growth and sexual development, body energy levels, internal balance of body systems, bone density, and muscle strength (Endocrine Society 2016). EDCs are sometimes referred to as hormone mimickers because, once in the body, the body is unable to tell the difference between a real hormone and an EDC. The hormone mimicker binds to and stimulates receptor cells resulting in an unintended, or disrupted, cell function. EDCs do this by turning on, turning off, or modifying the signals that a normal hormone would carry (Diamanti-Kandarakis et al. 2009).

Studies have shown that pharmaceuticals and other EDCs are present throughout our aquatic environment: our lakes, rivers, streams, ground water, wetlands, coastal marine environments, and drinking water sources. They have been discarded or excreted into toilets, flushed into the wastewater system and then eventually find their way into natural waterways. For their targeted purpose, pharmaceuticals perform a desirable endocrine messaging function. However, it was never intended that the general population be exposed to them, even in small amounts. Due to the high rate of growth and development taking place, childbearing women and their fetuses, and young children are particularly at risk if exposed to complex pharmaceuticals on a continuing basis even at very low concentrations.

Where might you find EDCs?

- Natural and synthetic hormones (including birth control pills)
- Pharmaceuticals
- Personal care products (soaps, shampoos, perfumes, antimicrobials)
- Flame retardants
- Pesticides, herbicides, and other synthetic complex organics
- Nanoparticles
- And the list grows…

Soaps, perfumes, and other products contain many potential EDCs such as parabens, phthalates, and Triclosan. Such externally applied drugs and personal care products (PCPs) are washed down drains and into sewer lines and septic systems. Parabens are antimicrobial agents found in most cosmetics and food materials and they have demonstrated weak estrogenic activity in several assays (Daughton and Ternes 1999). Phthalates are a group of endocrine-disrupting compounds commonly used to render plastics soft and flexible (The Endocrine Disruption Exchange (TEDx) 2016). Triclosan is added to products to reduce or prevent bacterial contamination. Currently under review by the FDA, studies have shown that Triclosan alters hormone regulation in animal (US Food and Drug Administration 2016). In addition to PCPs, synthetic complex organics (such as pesticides, herbicides, nanoparticles, and detergents), phthalates (plastics), perchlorate (rocket fuel), fire retardants, and heavy metals (such as lead, arsenic and mercury) can all disrupt the endocrine system of humans and wildlife. These chemicals generally find their way into the watershed through household drains, discharges from manufacturing processes, and agriculture practices. They have been around for many decades with their use increasing every year. Some non-pharmaceutical EDCs such as polychlorinated biphenyls (PCBs) have been banned in some countries due to their known carcinogenic effect. This chemical was used as insulating material in electrical equipment and in a wide range of products such as plastics and flame-retardants (Eyles et al. 2011).

The number of chemicals that are used commercially is high, in the thousands, with hundreds of new chemicals developed every year. The vast majority of these chemicals have not been tested for endocrine disrupting effects. It is difficult to identify potential EDCs among these chemicals as there is an absence of endocrine disrupting testing data. Furthermore, EDCs can work in combination with their by-products or other EDCs. In 2012 the World Health Organization (WHO) reported that close to 800 chemicals are known or suspected to be capable of interfering with hormone receptors, hormone synthesis, or hormone conversion. Because of the need to analyse each chemical individually, only a few of all potential EDCs have been quantified in the environment, humans and/or wildlife. The lack of appropriate methods for measuring many EDCs is a major obstacle for assessing exposure to potential EDCs (Kidd et al. 2012). Scientific research continues to add knowledge on the identification, fate, and effects of many pharmaceuticals and chemicals.

Advances in analytical techniques have allowed for testing of some EDCs in the part-per-billion (ppb) or part-per-trillion (ppt) concentration levels. This is a very fine scale, but is essential since EDCs can have negative impacts on humans and natural species even at these extremely low levels. An experiment by Karen A. Kidd et al (2012) at the Experimental Lakes Area in Northwestern Ontario found that chronic exposure of fathead minnows to synthetic estrogen, ethinyl estradiol (EE2), led to feminization of the males, which led to a near collapse of the fish-breeding rate and ultimately the fish population. They were exposed to a mere 5-6 ppt for a period of seven years. It is not unusual to find 5-6 ppt of EE2 in municipal wastewater. The good news for this particular species is that the fish population was able to recover when moved into EE2 free water.

3. Terminology

As our understanding of EDCs has evolved, the collective group of compounds that cause endocrine disruption has been given many names in the literature and in public usage. Some examples include:

- EDCs and PPCPs
- Emerging Contaminants
- Trace Constituents / Trace Organics
- Contaminants of Emerging Concern
- Chemicals of Potential Concern

- Microconstituents
- Non-conventional Pollutants (used by the Ministry of Environment and Climate Change)
- Micropollutants

Originally, the term endocrine disrupting compounds, or EDCs, was commonly used because it referenced the undesirable effect of the target compounds. As stated above, dozens of alternate naming systems have since been used. The various names can be grouped into a handful of categories (as described below):

- Definition by specific effect: this category refers to the problem or effect to be eliminated, but does not lend itself to the public's understanding of the sources and pollutants being targeted. The term "endocrine disrupting compounds" remains a popular definition among the scientific research community and recently by the media.
- Definition by consumer products: this category refers to the broad types of products that make up the majority, but not all, of the chemicals being defined. Terms such as "pharmaceuticals", "pharmaceuticals and personal care products (PPCPs)", and "PPCPs and household products" are easy for the public to understand, however, they only refer to a portion of the chemicals of concern (for example, agricultural herbicides and pesticides, industrial detergents and plastics are EDCs but are not PPCPs). For reference, PPCPs include products such as sunblock, shampoo, and N,N Diethyl-3-methylbenzamide(DEET). Tables listing these types of products have been useful for the public's understanding.
- Definition by regulation: terms such as "trace organics", "microconstituents" and "non-conventional contaminants" have been used by regulators at the provincial and national levels for legislation (or in anticipation of legislation) related to drinking water treatment, wastewater treatment, and watershed management. The main purpose of the definition is to distinguish the compounds from other compounds already controlled in existing regulations, and therefore these terms are most useful when used in a regulatory context.
- Definition by the unknown magnitude of the problem: many terms have been developed to describe EDCs as an open-ended and ever-increasing collection of chemicals. Terms such as "emerging contaminants ", "compounds of emerging concern", or "chemicals of potential concern" recognize that the topic is evolving; however, the terms are also ambiguous and not restricted to EDCs.

The ultimate choice of the terminology likely depends on the target audience. Although the most scientifically accurate term is EDC, the target audience for this discussion is primarily the public and secondarily The District Municipality of Muskoka. In this case, it is suggested that the terms PPCPs and EDCs may be used interchangeably depending on the context, since both address our main focus, which is endocrine disrupting compounds.

4. Health Effects

With the widespread use of the EDC dichlorodiphenyltrichloroethane, better known as DDT, in the 1940s to early 1970s, a profound decline in bird populations was observed. It was determined that calcium metabolism was affected by DDT which resulted in thinning of eggs shells which could not survive through to hatching. Bird populations still suffer from bioaccumulation of DDT and other pesticides, affecting their sexuality, causing deformities and death of the young.

It took until the early 1970s before human health effects by EDCs were recognized. According to "Our Stolen Future" (Colborn et al. 1996), the *New England Journal of Medicine* reported that daughters of mothers who had taken diethylstilbestrol (DES, a synthetic estrogen) while pregnant were linked to a rare vaginal cancer. It was noted that these 15 to 22 year old daughters were very young for this type of cancer. An unusually high number of these daughters also had abnormally formed uteri. Making the connection to a drug taken by the mother a generation earlier was difficult to establish. The sons of DES mothers were not spared as they were born with anomalies of the reproductive system, reduced fertility, and they had a high rate of testicular cancer. Trans-generational verification of cause and effect is difficult if not impossible to prove. The impacts of EDCs on aquatic species and animals, both in the laboratory and in the wild, are repeatedly being recognized as happening to humans as well.

Knowing that EDCs are in water systems, the ensuing effects of EDCs on aquatic organisms are troublesome as these organisms have continual lifecycle multigenerational exposure which could go undetected until an irreversible change takes place (Daughton and Ternes 1999). Pharmaceuticals and pesticides are designed to be biochemically active leading one to question whether it would be restricted only to its intended use. In controlled laboratory conditions, EDCs have caused changes in growth, decreased levels of serotonin, and increased feminization of aquatic organisms (Connon, Geist and Werner 2012). A 2001 study by Jenkins et al. found that in samples closest to wastewater treatment plants' effluent, male mosquitofish showed impairment of endocrine and reproductive function, as evidenced by changes in sex steroid hormone levels, secondary sex characteristics, organosomatic indices (effects on the liver, heart, kidney and spleen), and sperm quality parameters. The study concluded that exposure to EDCs and consequent impairment showed the most significant effects at the wastewater treatment point sources, with gradually lesser effects further away from the point sources. Other studies found ethinyl estradiol (EE2), a synthetic estrogen, is readily taken up by algae which can then work up the food web (Maes 2011).

Scientists were slow to accept that EDCs were a different breed of danger to humans and animals. EDCs do not have a dose-response curve typical of previously recognized toxic chemicals. A minimal dose of an EDC can cause an undesirable hormonal effect, such as the rate of reproduction or immunity to disease of the affected organism. At a higher dose, the EDC mechanism could result in a different endocrine effect. In the case of DES, which was previously mentioned, Frederick vom Saal (Colborn et al. 1996, pp 169) found that the response increases with dose for a time and then, at still higher doses, begins to diminish, a response contrary to traditional expectations. Birth defects may have been considered in the past, however invisible damage at birth such as delayed endocrine, immune and nervous systems effects was not considered. In an affected watershed, we won't necessarily see dead fish or frogs on the

Traditional Toxicology

Early in the 1500s, Paracelsus is credited for coining the phrase "the dose makes the poison" i.e. things that are not poisonous in small quantities can be lethal in large doses. This formed the basis for the study of toxicology encompassing dosage, acute or chronic exposure, routes of exposure, species, age, sex, and environment. Simplified, the process required exposure of different concentrations (dosages) of a chemical to lab animals noting the highest dosage before the first adverse effect was observed (NOEL, no observed (adverse) effects level), and when lethal dose of 50% of the population was observed (LD50), among other points. Many dose-response curves are then used to determine acceptable levels of exposure and/or need for special handling protocols.

beaches, but rather we will simply see that the population of a particular species is disappearing. The danger of a chemical can no longer be observed as a rash, illness, or even cancer. Rather, the effects of EDC exposure today may not be fully observed or understood for generations.

EDCs are considered pollutants of concern in many municipalities around the world. Based on results using research animals, the possible effects on humans could include reductions in male fertility, declines in the number of males born, abnormalities in male reproductive organs, and increases in female reproductive diseases including fertility problems, early puberty, and early reproductive senescence, as well as increases in memory loss, ovarian, breast and prostate cancers. EDCs can transfer from a pregnant woman to the fetus or child through the placenta or breast milk (WHO 2016). This could disrupt critical development at the time of exposure. Endocrine systems are very similar across vertebrate species and endocrine effects manifest themselves independently of species (WHO 2012). EDC research is ongoing because there is still much about how these chemicals interact in humans, the natural environment, and each other that is not understood. The cumulative, synergistic, and antagonistic effects are generally not known.

Many known and suspected EDCs are compiled in Appendix B. The chemicals were chosen based on their presence in the Ontario Drinking Water Systems Regulation O. Reg. 170/03, the Rotterdam Convention 1998 (Annex III chemicals) and the Stockholm Convention 2004 (12 initial persistent organic pollutants).

5. Sources and Pathways

People excrete both metabolized and un-metabolized pharmaceuticals via urine and feces, but EDCs also get into septic and wastewater systems from people flushing expired prescriptions, other medicines, and other chemicals down the toilet or drain. Excretion of pharmaceuticals varies depending on the individual drug. Pharmaceuticals of most concern are hormones, anti-inflammatories, antibiotics, and lipid regulators.

Health Canada's (2016) Drug Product Database currently contains over 47,000 products that include human pharmaceutical and biological drugs, veterinary drugs, radiopharmaceutical drugs, and disinfectant products. Depending on their function, these products can enter the

So, what happens when you take a pharmaceutical pill?

There are many routes that a drug can take. A very general and simple route for an ingested pill is to be absorbed into the bloodstream. The blood quickly carries it through the liver or kidney where the parent drug may go through a chemical change called metabolism creating a 'metabolite'. Depending on the drug, this could happen quickly or slowly and there could be one metabolite or many or possibly none. At this point, the drug and/or metabolite(s) can proceed to their targeted function. The time for half the drug to be metabolised or eliminated from the body is called the half-life. Most drugs have a half-life of hours or days. The most common route of elimination of the drug and/or its metabolites is through urine and/or feces. The opinion of some medical and research personnel is that 20 to 50% of a dose is excreted. Also, as a person ages, metabolism and elimination processes slow down making it hard to predict how much of a drug or metabolite is actually finding its way into our water. Some pharmaceuticals are absorbed well by the body, and may be stored in the fatty tissue of the body to be excreted much later, if ever.

body by being ingested, injected, inhaled, or absorbed. Each person's reaction to a given chemical (drug) and its metabolites is difficult to ascertain as indicated by a wide range of possible side effects of the drugs we use. Age, gender, lifestyle, and effects due to other drugs used at the same time are just some of the factors that make it so difficult to know what proportion of a drug is actually utilized and what proportion passes through the body without being utilized. Estrogen (EE2), the widely used birth control pill, is largely passed as by-products or metabolites which are considered hormonally active but on different functions of the body.

Typically, EDCs enter our natural environment through one or more of the following pathways:

Source	Pathway to the Natural Environment
Household PPCPs	o Wastewater Treatment Plant (WWTP) Discharges o Septic System and Tile Field Leachate to Groundwater and Surface Water o Combined Sewer Overflows o Biosolids/Land Application (Surface Runoff/Groundwater Infiltration)
Livestock Pharmaceuticals (Growth Hormones)	o Livestock Manure (Surface Runoff/Groundwater Infiltration)
Household Pesticides and Herbicides	o Storm Sewer Discharges o Combined Sewer Overflows o Wastewater Treatment Plant (WWTP) Discharges o Septic System and Tile Field Leachate

Source	Pathway to the Natural Environment
Agricultural Pesticides and Herbicides	o Surface Runoff/Groundwater Infiltration
Industrial Products	o Wastewater Treatment Plant (WWTP) Discharges o Septic System and Tile Field Leachate o Industrial WWTP Discharges

EDCs in Drinking Water Sources	o Water Treatment Plant Residuals/Landfill
	o Or, if residuals are sent to the sewer:
	    o WWTP Discharges
	    o Combined Sewer Overflows
	    o Biosolids/Land Application

Other EDCs	o Wastewater Treatment Plant (WWTP) Discharges o Septic System and Tile Field Leachate o Combined Sewer Overflows o Biosolids/Land Application (Surface Runoff/Groundwater Infiltration)

Muskoka: Pathways for EDCs

Muskoka is fortunate as it does not have major industrial facilities nor agricultural and livestock facilities within the watershed. As well, The District Municipality of Muskoka has done well eliminating sewer system overflows. As a result, Muskoka's primary pathways would be wastewater treatment plant discharges and septic system releases. Wastewater treatment plant discharges are of major concern because of their concentrated discharge to a single location at the discharge point of the plant. In Muskoka, septic system releases may be of even greater concern, both because of their widespread release throughout the watershed and also because a larger segment of the population is serviced by septic systems than by sewers connected to a wastewater treatment plant. Current treatment technologies have a widely varying capability to eliminate EDCs during the wastewater treatment process, nominally between 20% and 80%. Traditional septic tank and tile field systems would eliminate EDC's at the low end of that range.

6. Wastewater Treatment and EDCs

All municipal wastewater treatment plants in Ontario must comply with Ontario regulations, which include specific requirements for the quality of the treated water being discharged to the respective lake or river. New quality requirements are generally only implemented at the time of major upgrades or expansions of any particular plant, and therefore it is typical that older plants may not produce as high a quality of treated water as do newer plants. The following regulations on wastewater treatment exist in Ontario:

- All plants in Ontario meet similar criteria in terms of solid materials and carbon (carbon is measured as biochemical oxygen demand or BOD).
- All plants in Ontario must remove phosphorus to achieve a maximum concentration of 1 mg/L or part per million. In sensitive areas such as Muskoka, much lower phosphorus concentrations (0.3 mg/L) are usually required. To achieve these lower concentrations, filtration by sand or synthetic membranes is often required. Such filtration has a positive effect on the removal of PPCPs.

When any wastewater treatment plant (WWTP) is designed, the treatment or removal of nitrogen is permitted at one of three general classifications:

1. Unrestricted, which means that ammonia passes through the plant unchanged. It has been found that wastewater treatment plants with no ammonia restrictions are relatively ineffective at reducing PPCPs.
2. Restriction on ammonia but without restriction on other nitrogen compounds such as nitrates. The ammonia is substantially converted to nitrate within the plant and then discharged.
3. Restriction on total nitrogen content, which means that ammonia is essentially converted to nitrate, which is then converted to nitrogen gas and released to the atmosphere. Such plants achieve greater PPCP reductions. It has been found that plants in pH-sensitive areas such as Muskoka will benefit by going directly to this standard even if the Ministry requires them to meet only a restricted ammonia level of treatment. This level of WWTP has some reduced operating costs compared to the second classification, and slightly easier operation; however the plants are larger and have higher construction costs.

Using the above information as a guide, one can predict the effectiveness of PPCP removal by various District wastewater treatment plants, and also by extrapolation, typical residential septic systems. All nine wastewater treatment plants in Muskoka have tertiary treatment

- The **Bracebridge** and **Port Carling** WWTPs remove nitrogen and also filter the water before discharge. These two plants have membrane filtration equipment and therefore enhanced ability for the removal of PPCPs.
- While Huntsville's **Mountview** and **Golden Pheasant** WWTPs are classified as unrestricted, they, along with the remaining five WWTPs in Muskoka, have some ability to convert ammonia to nitrate, but are likely not as effective in the removal of PPCPs as newer

plants. The District Municipality of Muskoka is planning an upgrade and expansion of the Golden Pheasant WWTP and decommissioning of the Mountview WWTP. It is anticipated that the Ontario MOECC will impose an ammonia restriction for the upgraded plant, and that the District could consider going to a total nitrogen removal design for maximum removal of EDCs.

Traditional septic tank/tile field systems are largely ineffective for the removal of EDCs. Alternative systems exist which filter the wastewater and reduce ammonia and nitrogen. One system includes an aerobic stage within what otherwise appears to be a traditional septic tank system. Another option is an ozone wastewater treatment system which is known to significantly reduce many chemicals of emerging concern (G.C. Balch and B.C. Wootton 2013). Such systems would greatly improve the removal of PPCPs by single unit residential septic systems.

7. Regulations and Management

As discussed in previous sections, the science indicates that EDCs pose a threat to health and the sustainability of the natural environment, wildlife, and humans. Despite this, few measures or solutions can be found in the form of regulation or policy in any jurisdiction to mitigate this problem.

There are no formal USA Federal regulations that limit the concentrations of EDCs, though 1996 Amendments to the Safe Drinking Water Act explicitly dictated that the USA Environmental Protection Agency (EPA) must:

> *"… develop a screening program, using appropriate validated test systems and other scientifically relevant information to determine whether certain substances may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effect as the Administrator may designate."*

The USA EPA has tried to establish an official EDC screening method for over 80,000 compounds in wastewater and surface water. However, there are many EDCs with diverse characteristics, which make the detection and analysis procedures difficult and challenging.

While American Federal regulations specifically designed for pharmaceuticals and potential EDCs in drinking water are essentially non-existent, the Contaminant Candidate List (CCL) process provides an evaluation of unregulated contaminants, some of which are EDCs. The CCL is a list of drinking water contaminants that are known or anticipated to occur in public water systems and are not currently subject to EPA drinking water regulations (EPA 2015(b)). Other jurisdictions, such as the European Union (EU), have developed a list of priority substances that are regulated under the Water Framework Directive (European Commission 2015).

The Canadian Environmental Protection Act (CEPA) (1999, article 3 subsection 44[3]) requires research on "hormone disrupting substances" to be a Ministerial duty of both Environment Canada and Health Canada. While gaps and research needs have been prioritized, information on the persistence of EDCs in the environment and their long-term effects on humans and other organisms are not yet sufficiently available.

A recent study by the Ontario Ministry of the Environment and Climate Change (MOECC) determined that there were no known countries in the world that regulated the treatment or discharge of EDCs (MOECC 2014). As expected, then, there are no policies or regulations specific to the treatment of EDCs or PPCPs in Ontario, and the MOECC maintains Provincial Water Quality Objectives through Environmental Compliance Approvals (ECA) which restrict sewage treatment plant effluent. An ECA is a permit issued by a Ministry under a specific provision in an Act or regulation that allows the permit holder to legally discharge a limited volume of polluting substances or carry out an activity that may adversely impact the environment.

The MOECC's recently released report may serve to strengthen the regulation of wastewater treatment facilities in Ontario and, if implemented, may affect development and infrastructure in Muskoka (MOECC 2014). One result of the report might be a requirement for all wastewater treatment plants in Ontario to remove ammonia, which the report suggests is a valid indicator compound, or surrogate, for the substantial removal of pharmaceuticals and other EDCs. Some District of Muskoka plants, including the Mountview and Golden Pheasant plants serving Huntsville, would be affected. Further, an ammonia limit would likely be imposed upon any new industrial developments, and may be required for any new shoreline residential developments, requiring a higher level of treatment than is achieved by conventional septic tank and tile field systems.

Watershed monitoring

Long-term monitoring of the health of watersheds and sub-watersheds relative to EDCs is essential in order to be able to rank and prioritize watersheds for management and control. Chemical analysis, even for a subset of the thousands of pharmaceuticals and chemicals in the marketplace, is clearly impractical. Around 2005, the ELISA test (Enzyme-linked immunosorbent assay) was adapted to detect hormonal and immune responses to watershed samples containing pharmaceuticals. ELISA is a biochemical technique used mainly in immunology to detect the presence of an antibody or an antigen in a sample. Attempts were made to use the method as a measurement technique for the presence of pharmaceuticals and EDCs in watersheds. More recently, researchers such as Mark Servos at the University of Waterloo have been developing watershed monitoring techniques that are based upon one of the most common symptoms of EDC contamination, which is the feminization (or "intersex") of fish when exposed to EDCs. The method includes the capture of wild fish (often rainbow darters) in key watershed locations and the quantification of gonad size, severity of intersex, and relative androgen production (Fuzzen et al. 2015).

8. Defining the Issue

Communities are exposed to ever-changing patterns of creation and use of EDCs. The issue is multi-faceted and confusing to many people, but it is important when engaging the public that the message be clear and that all communication be truthful and transparent. Through public education and discussion it should be possible to define what actions, if any, will be required to address the impacts of EDCs in Muskoka. There are four paths that could be taken:

1) Minimize impact on human health
2) Minimize impact on wildlife and the natural environment
3) Minimize impact on human health, wildlife and the natural environment
4) No action

1. *Minimize impact on human health* – this scenario would see the focus on our drinking water. O. Reg. 170/03 dictates maximum limits on close to 70 inorganic and organic parameters. Many of these tested parameters are pesticides known to be EDCs. Levels of EDCs from pharmaceuticals and personal care products are unknown for our drinking water. It is unlikely that Muskoka's drinking water treatment plants would require upgrading in the foreseeable future to best available technology in order to maximize EDC removal for protection of the public. The high costs associated with this capital investment as well as ongoing PPCP testing would have long term effects on residential and industrial water rates. Consideration would need to be given to the rural population that does not have treated municipal drinking water and must rely on well water. The cost of reducing EDC and PPCP impacts for this segment of the population would be borne by the homeowner.

2. *Minimize impacts on wildlife and the natural environment* – this scenario leads to considerations of sources, pathways, and control measures for EDC exposure. At the minimum, this should address wastewater treatment (both centralized treatment plants and septic systems) to remove as many EDCs as current technology allows before discharge into the environment. Because there is so little information about EDCs in Muskoka's watershed, monitoring and testing would be prudent to determine which EDCs are present, their concentrations, where they are, possible undesired effects, and likely sources.

3. *Minimize impact on human health, wildlife and the natural environment* – a merging of the above two options allowing for maximum protection of human health and the environment from EDCs. It needs to be recognized that there are many cases where human and environmental health are intertwined; e.g. if it's found that the fish in our lakes contain high levels of EDCs, they would pose a health risk to any humans that may consume them.

4. *No action* – the public regards EDCs as no risk or insufficient priority to warrant action.

9. Recommendations

Muskoka has the opportunity to build on programs that other communities have been using to decrease the release of unwanted chemicals into their water. Muskoka Watershed Council views the issue of EDCs in the environment as important and encourages actions that would minimize impacts on both human health, wildlife and the natural environment. The following recommendations provide for a set of actions to be undertaken by individuals, by community groups and by various levels of government.

Communication and Education- potential initiatives for Muskoka Watershed Council and other local organizations

- Promote the "I Don't Flush" Campaign - The public is asked to return unwanted and unused prescription drugs to their pharmacy rather than flushing them down the toilet or throwing them into the garbage. This campaign has been successful in many communities across Canada.
- The creation of an educational video such as https://www.youtube.com/watch?v=CKnxEjrhhmc from the British Columbia Pharmacy Association is an effective way of communication.
- In Ontario, the Health Products Stewardship Association provides information at www.healthsteward.ca and a pamphlet which could be made more available on where and how to discard medications.
- Materials, such as posters, pamphlets, newspaper articles, as well as online discussions on Facebook, Twitter and on municipal websites can all help to educate the public on how to minimize their contribution of EDCs into the environment.
- Communicate with the public through radio commercials, talk shows or community and school presentations.
- Encourage the development of regulations and policies for industries to decrease the quantity and variety of EDCs used in personal care products.

Knowledge Gaps

There is limited information on EDCs in Muskoka. The following recommended actions may assist in developing comprehensive knowledge on EDCs. Actions include:

- The Ministry of Environment and Climate Change (MOECC) require testing for EDCs, specifically PPCPs, in our drinking water.
- Provincial Ministries (MOECC and MNRF) undertake EDC testing on a watershed basis. Tests could include assays such as the ELISA (enzyme linked immunosorbent assay) test, which measures general hormonal levels, or intersex testing of wild fish. Provincial data could be shared with the community.

- Interested parties, including Muskoka Watershed Council and individuals, monitor current research and available literature on EDCs, and, as possible, share findings and knowledge with the Muskoka community and beyond.
- Interested individuals and community organizations (local anglers, hunters, and birders, among others) develop local data of EDC impacts on water and land species. Information could include notes on anatomical deformities including feminization, population changes, unusual behaviour, etc. The Ontario Federation of Anglers and Hunters could be approached to undertake this work.
- Muskoka Watershed Council promote science and research to develop assays that assess multiple chemicals at hormone targets.

Local Governance

Under official plans, local municipalities could:

- Encourage developers to provide treated wastewater quality that is better than that provided by traditional septic tank systems for all new developments.
- Restrict or prevent the development of agricultural feedlot operations.

Personal

Concerned individuals can:

- Review, learn, and adopt best practices to effectively minimize the impacts of EDCs on individual health.
- Return unused prescriptions and other pharmaceuticals to local pharmacies for disposal.
- Reassess and reduce the need for personal care products and choose natural products.
- Maintain private septic systems and, when possible, upgrade systems to reduce EDC leaching into the environment.
- Eliminate the use of herbicides, insecticides, and fertilizers or, when used, dispose products properly at a hazardous waste collection site.
- Reduce the consumption of food products that include herbicides, pesticides, and veterinary drugs such as hormone and antibiotics.

References

Balch, G.C., Wootton, B.C. (2013). A literature review of ozone deactivation of waterborne pathogens and the oxidative removal of trace organic contaminants within raw drinking water supplies. (pp. 14-17). Retrieved from https://static1.squarespace.com/static/5575fb8ce4b0e287457dfcac/t/561e7fc5e4b007e546e70367/1444839365355/Ozone+Lit+Review.pdf.

Cai, Xiyun, Weiping Liu, Meiqing Jin, and Kunde Lin (2007). Relation of diclofop-methyl toxicity and degradation in algae cultures. *Environmental Toxicology and Chemistry* 26(5):970-5 · June 2007

Colborn, T., Dumanoski, D. and Myers, J.P. (1996). Our Stolen Future. Dutton, ISBN 978-0-525-93982-5.

Conley, J., et al. (2015). Endocrine Activity of Bisphenol S (BPS) Using In Vitro Estrogenic/Anti-Androgenic Transcriptional Activation Assays and the In Vivo Uterotrophic Assay. Society of Toxicology Annual Meeting, San Diego, CA, March 22 - 26, 2015.

Connon, R.E., Geist, J. and Werner, I. (2012). Effect-based tools for monitoring and predicting ecotoxicologic effects on chemicals in the aquatic environment. *Sensors 12* (12741-12771). Doi: 10.3390/s120912741.

Daughton, C.G. and Ternes, T.A. (1999). Pharmaceuticals and personal care products in the environment: agents of subtle change? *Environmental Health Perspectives*, 107(6): 907- 938.

Diamanti-Kandarakis, E., Bourguignon, J.P., Giudice, L.C., Hauser, R., Prins, G.S. Soto, A.M., Zoeller, R.T., Gore, A.C. (2009). Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement. *Endocrine Reviews,* 30(4): 293-342. Doi: http://dx.doi.org/10.1210/er.2009-0002#sthash.vOHymw31.dpuf.

Endocrine Society (2016). *Hormones and Health.* Retrieved from http://www.hormone.org/hormones-and-health.

Environment and Climate Change Canada (2008). Threats to Sources of Drinking Water and Aquatic Ecosystem Health in Canada: 5. *Endocrine Disrupting Substances*. Retrieved from http://www.ec.gc.ca/inre-nwri/default.asp?lang=En&n=235D11EB-1&offset=1&toc=show.

EPA (Environmental Protection Agency) (a) (2015). *What is endocrine disruption?* Retrieved from http://www.epa.gov/endocrine-disruption/what-endocrine-disruption#chemicals.

EPA (Environmental Protection Agency) (b) (2015). *Drinking water contaminant list (CCL) and regulatory determination*. Retrieved from http://www.epa.gov/ccl.

EPA (Environmental Protection Agency) (c). Dioxin. Retrieved from https://www.epa.gov/dioxin.

European Commission (2015). *The EU water framework directive- integrated river basin management for Europe.* Retrieved from http://ec.europa.eu/environment/water/water-framework/index_en.html.

Eyles, J., Newbold, K.B., Toth, A. and Shah, T. (2011). *Chemicals of Concern in Ontario and the Great Lakes Basin - Emerging Issues.* Retrieved from http://hamiltonharbour.ca/resources/documents/admin_1/Chemicals_of_Concern_Update_2011.pdf.

Fuzzen, Meghan L.M., Charles J. Bennett, Gerald R. Tetreault, Mark E. McMaster, Mark R. Servos (2015). Severe intersex is predictive of poor fertilization success in populations of rainbow darter (*Etheostoma caeruleum*). *Aquatic Toxicology*, Volume 160, March 2015, Pages 106-116.

Fuzzen Meghan L.M., Leslie M. Bragg, Gerald R. Tetreault, Paulina A. Bahamonde, Rajiv N. Tanna, Charles J. Bennett, Mark E. McMaster, Mark R. Servos (2016). An Assessment of the Spatial and Temporal Variability of Biological Responses to Municipal Wastewater Effluent in Rainbow Darter (*Etheostoma caeruleum*) Collected along an Urban Gradient. *PLoS ONE* 11(10): e0164879.

Health Canada (2016). *Drugs and Health Products, Drug Product Database.* Retrieved from http://hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php.

Jenkins, R., Angus, R.A., McNatt, H., Howell, W.M., Kemppainen, J.A., Kirk, M. and Wilson, E.M. (2001). Identification of androstenedione in a river containing paper mill effluent. *Environmental Toxicology and Chemistry*, 20(6): 1325-1331.

Keegan A. Hicks, Meghan L. M. Fuzzen, Emily K. McCann, Maricor J. Arlos, Leslie M. Bragg, Sonya Kleywegt, Gerald R. Tetreault, Mark E. McMaster, and Mark R. Servos (2017). Reduction of Intersex in a Wild Fish Population in Response to Major Municipal Wastewater Treatment Plant Upgrades. *Environmental Science & Technology* 2017, 51 (3), 1811-1819.

Kidd, K.A., Becher, G., Bergman, A, Muir, D.C.G., Woodruff, T.J. (2012). Human and wildlife exposures to EDCs. In Bergman, A., Heidel, J.J., Jobling, S., Kidd, K.A. and Zoeller, R.T (eds.). State of the Science of Endocrine Disrupting Chemicals (189-250). United Nations Environment Program.

Kidd, Karen A, Blanchfield, Paul J., Mills, Kenneth H., Palace, Vince P., Evans, Robert E., Lazorchak, James M., and Flick, Robert W. (2007). Collapse of a fish population after exposure to a synthetic estrogen. PNAS, May 22, 2007, vol. 104, no. 21, 8897–8901.

Lyons, G. (1999). Endocrine disrupting pesticides. Retrieved from http://www.pan-uk.org/pestnews/Actives/endocrin.htm.

Maes, H. (2011). Fate of ethinylestradiol in the aquatic environment and the associated effects on organisms of different trophic levels. Unpublished doctoral thesis. Aachen University.

MOECC (Ministry of Environment and Climate Change) (2011). Literature review and jurisdictional practices of technologies to reduce non-conventional contaminants at Municipal sewage treatment plants. Prepared by CH2MHILL.

Precision Nutrition Inc. (2016). All about endocrine disruptors. Retrieved from http://www.precisionnutrition.com/all-about-endocrine-disruptors.

Propper, C.R. (2005). The study of endocrine-disrupting compounds: Past approaches and new directions. *Integrative and Comparative Biology*. 45 (1): 194-200.

PubChem (2016). PubChem Compound. Retrieved from https://www.ncbi.nlm.nih.gov/pccompound.

Rotterdam Convention (2013.) Annex III Chemicals. Retrieved from http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals/tabid/1132/language/en-US/Default.aspx.

Stockholm Convention (2008). The 12 Initial POPs under the Stockholm Convention. Retrieved from http://chm.pops.int/TheConvention/ThePOPs/The12InitialPOPs/tabid/296/Default.aspx.

The Endocrine Disruption Exchange (TEDx) (2016). TEDx List of potential endocrine disruptors. Retrieved from http://endocrinedisruption.org/endocrine-disruption/tedx-list-of-potential-endocrine-disruptors/overview.

US Food and Drug Administration (2016). *Triclosan: what consumers should know.* Retrieved http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm205999.htm.

Waterloo Biofilter Systems Inc. (2016). *Waterloo Biofilter Systems Inc. On-site wastewater treatment.* Retrieved from http://waterloo-biofilter.com/.

WHO (World Health Organization) (2016). *Children's environmental health – Endocrine disrupting chemicals.* Retrieved from http://www.who.int/ceh/risks/cehemerging2/en/.

WHO (World Health Organization) (2012). *State of the Science of Endocrine Disrupting Chemicals – 2012.*Retrieved from http://www.who.int/iris/bitstream/10665/78101/1/9789241505031_eng.pdf?ua=1.

Appendix A: Definitions

Absorption – the uptake of substances into or across tissues.

Acute – severe and of relatively short duration.

Ammonia – a compound of nitrogen and hydrogen (NH_3) that contributes significantly to the growth and survival of terrestrial and aquatic organisms.

Antagonistic – lower effect than the sum of each part, nullified action.

Antimicrobials – agents that kill microorganisms or inhibits their growth.

Bioaccumulative/Bioaccumulation – the accumulation of substances, such as pesticides or other chemicals, in an organism.

Biochemical oxygen demand (BOD) – amount of dissolved oxygen needed by aerobic biological organisms in a body of water to break down organic material present in a given water sample at a certain temperature over a specific time period.

Chronic – a state that continues for a long time or recurs frequently.

Cumulative – total effects with each part added.

Endocrine disruptor – a chemical that, at a certain dose, can interfere with the hormone system in mammals. These disruptions can cause cancer, birth defects or other development disorders.

Estradiol – specific estrogen and powerful female sex hormone.

Estrogen – female sex hormone secreted by the ovaries.

Drug – a broad term used to describe chemical substances that have known biological effects on humans or other animals. Otherwise defined as a chemical substance used in treatment, cure, or prevention.

Effluent – an outflowing of water or gas from a natural body of water, or from a human-made structure.

Emerging compounds of concern (ECC) – chemicals that have been recently discovered, or are being discovered in water that previously had not been detected. Some of these chemicals have been shown to pose a risk to human health and the environment. More research is required on many of these compounds.

Ethinyl estradiol (EE2) – a bioactive estrogen used in many formulations of combined oral contraceptive pills (i.e. the birth control pill).

Hormones – a class of signalling molecules produced by glands in multicellular organisms that are transported by the circulatory system to target distant organs to regulate physiology and behaviour.

Metabolic action – the chemical process occurring within a living cell or organism that is necessary for the maintenance of life.

Nanoparticles – particles between 1 and 100 nanometres in size. They are used in industry, consumer and medical applications because of their unique physico-chemical properties.

Nitrification – the process by which ammonia is converted to nitrites (NO_2) and then nitrates (NO_3). This process naturally occurs in the environment, where specialized bacteria carry it out.

Non-conventional contaminants (NCCs) – a diverse collection of thousands of chemical substances used by individuals, industry or agribusiness. Many of these substances are poorly understood, with their human and/or environmental health effects just beginning to be understood.

Organic nitrogen – a nitrogen compound that had its origin in living material. Organic nitrogen can enter wastewater systems as bodily wastes, discarded food material or as components of cleaning products.

Progesterone – female sex hormone released by the ovaries.

Sewage treatment – the process of removing contaminants from wastewater, including household sewage and runoff (effluents). It includes physical, chemical, and biological processes to remove physical, chemical and biological contaminants.

Synergistic – greater effect than the sum of each part.

Total ammonia nitrogen – a measure of the amount of ammonia in a given volume of wastewater or effluent.

Appendix B: Endocrine Disrupting Compounds

Common potential EDCs compiled from the 12 initial Stockholm Convention persistent organic pollutants, the Ontario Drinking-Water Systems Regulation O. Reg. 170/03, and the Rotterdam Convention.

Chemical	Common use	Possible or confirmed EDC	Additional Information
1,2 Dichlorobenzene	Solvent, degreaser	confirmed	A pale yellow liquid used to make herbicides (PubChem 2016).
1,4 Dichlorobenzene	Insecticide - controls moths, mildew and mold	possible	A colorless or white solid with a strong, pungent odor. When exposed to air, it slowly changes to a vapor (PubChem 2016).
1,2 Dichloroethane	Manufacturing, degreaser	possible	Inhalation of vapor can induce effects on the human nervous system, liver, and kidneys, as well as respiratory distress, cardiac arrhythmia, nausea, and vomiting (PubChem 2016).
1,1 Dichloroethane	Chemical synthesis, solvent, degreaser, fumigant	possible	Studies in animals have reported effects on the kidneys. No information is available on the chronic (long-term), reproductive, developmental, or carcinogenic effects of ethylidene dichloride in humans (PubChem 2016).
2,4 Dichlorophenol	Herbicide component	confirmed	An irritant effect on the eye and the gastrointestinal system (PubChem 2016).
Alachlor	Pesticide	highly possible	A herbicide that is associated with thyroid follicular tumours in rats, and is believed to be an endocrine disruptor (Lyons 1999).
Aldicarb	Pesticide	highly possible	An extremely toxic systemic carbamate insecticide that is suspected of being an endocrine disruptor. When given to female pregnant rats at low levels of 1-100 mg/kg, it has been shown to depress acetylcholinesterase activity more in the fetus than in the mother. It has also been suggested that there may be a link between low-level exposure and effects on the immune system (Lyons 1999).
Aldrin	Pesticide	confirmed	In humans, the fatal dose for an adult male is estimated to be about 5 g. Humans are mostly exposed to aldrin through dairy products and animal meats (Stockholm Convention 2008).

Chemical	Common use	Possible or confirmed EDC	Additional Information
Azinphos-methyl	Insecticide	confirmed (on EU list)	It is toxic by inhalation, skin absorption, and/or ingestion (Lyons 1999).
Bisphenol-A (BPA) and Bisphenol-S	Used in plastics	confirmed (EPA)	An estrogenic plastic by-product used in the manufacture of polycarbonate plastics; can leach into food or drinks from the plastic containers holding them. BPA and BPS display relatively similar estrogenicity and anti-androgenicity (Conley et al. 2015).
Chlordane	Pesticide	confirmed (sex hormone disruptor)	Mainly used to control termites and on home lawns and gardens. Due to atmospheric transport, Inuit women tend to have a diet highly contaminated with chlordane (Lyons 1999). The acute effects of chlordane in humans consist of gastrointestinal distress and neurological symptoms, such as tremors and convulsions. Chronic inhalation exposure of humans to chlordane results in effects on the nervous system (PubChem 2016).
DDT and metabolites	Insecticide	confirmed	Banned in all countries for use in agriculture. Still used in disease vector control (e.g. Malaria) (Lyons 1999). Exposure to DDT mainly affects the nervous system resulting in tremors, dizziness, nausea, lack of coordination, convulsions, and seizures. This substance is reasonably anticipated to be a human carcinogen (PubChem 2016).
Diclofop-methyl	Herbicide	possible	Some studies have indicated that Diclofop-methyl is a possible endocrine disruptor and carcinogen, with some in vivo and in vitro studies revealing that Diclofop-methyl and its phenolic metabolites are possible estrogen-receptor ligands (Cai et al. 2007).
Dieldrin	Pesticide	confirmed (World Wildlife Fund)	Has been used as a sheep dip and in wood treatment. Dieldrin has been found in breast milk, and is still found in some UK samples, although levels have declined since usage was banned (Lyons 1999).

Chemical	Common use	Possible or confirmed EDC	Additional Information
Dimethoate	Insecticide	confirmed	This material is a contact and systemic organophosphate insecticide effective against a broad range of insects and mites when applied on a wide range of crops (PubChem 2016).
Dinoseb	Herbicide	confirmed	Used as a plant growth regulator; insecticide and herbicide (PubChem 2016).
Diquat	Herbicide	confirmed	It is a liquid that can easily penetrate the soil and contaminate groundwater and nearby streams. It can cause illness by inhalation, skin absorption, and/or ingestion (PubChem 2016).
Dioxin	Herbicide, result of waste incineration, cigarettes	confirmed (EPA)	Dioxins are highly toxic and can cause cancer, reproductive and developmental problems, damage to the immune system, and can interfere with hormones (EPA 2016c).
Diuron	Herbicide	confirmed	It can cause illness by inhalation, skin absorption, and/or ingestion (PubChem 2016).
Glyphosate	Herbicide	confirmed	It is a widely used herbicide used to kill both broadleaf plants and grasses. Exposure has been linked to developmental and reproductive effects at high doses that were administered to rats repeatedly during pregnancy (NPIC).
Heptachlor	Insecticide	confirmed (World Wildlife Fund)	Very limited information is available on the health effects of heptachlor in humans. Acute inhalation exposure to heptachlor may result in nervous system effects, with oral studies showing gastrointestinal effects. Human studies are inconclusive regarding heptachlor and cancer. Animal oral studies have reported liver tumors. EPA has classified heptachlor as a Group B2, probable human carcinogen (PubChem 2016).

Chemical	Common use	Possible or confirmed EDC	Additional Information
Hexachlorobenzene (HCB)	Fungicide and industrial chemical	confirmed (World Wildlife Fund)	In high doses, HCB is lethal to some animals and, at lower levels, adversely affects their reproductive success. HCB has been found in food of all types. A study of Spanish meat found HCB present in all samples (Stockholm Convention 2008).
Lindane	Pesticide	confirmed (World Wildlife Fund)	Lindane is used as an insecticide for hardwood logs, lumber, and crops. Lindane is also used as a topical treatment for lice due to its neurotoxic effects. Inhalation exposure to this substance causes severe irritation of the nose and throat, causes anemia, and affects the liver, nervous, cardiovascular, and immune systems. Lindane is reasonably anticipated to be a human carcinogen. As of 2015, Lindane was still approved for use in Canada (PubChem 2016).
Malathion	Insecticide	confirmed	Malathion is an irreversible cholinesterase inhibitor and has low human toxicity. Malathion is used to kill insects on farm crops and in gardens, to treat lice on humans, and to treat fleas on pets. Malathion is also used to kill mosquitoes (PubChem 2016).
Methoxychlor	Insecticide	confirmed	Methoxychlor has estrogenic effects in mammals, among other effects (Pubchem 2016).
Metolachlor	Herbicide	confirmed	A selective herbicide, absorbed predominantly by the hypocotyls and shoots. Is carcinogenic (PubChem 2016).
Metribuzin	Herbicide	confirmed	It is widely used in agriculture and has been found to contaminate groundwater (PubChem 2016).
Monochlorobenzene	Solvent, degreaser	possible	Long-term exposure of humans to chlorobenzene affects the central nervous system (PubChem 2016).
Parabens	Wide range of products, including deodorants	possible	Parabens mimic estrogen (Precision Nutrition Inc. 2016).

Chemical	Common use	Possible or confirmed EDC	Additional Information
Paraquat	Pesticide	confirmed	It is quick-acting and non-selective, killing green plant tissue on contact. It is also toxic to human beings and animals. It is linked to the development of Parkinson's disease (PubChem 2016).
Parathion	Pesticide	confirmed (World Wildlife Fund)	Parathion is a highly toxic cholinesterase inhibitor that is used as an acaricide and as an insecticide. The central nervous system, blood, respiratory system, eyes and skin are the organs most affected by acute exposure of humans to parathion. Chronic inhalation and oral exposure of humans and animals to parathion have been observed to result in depressed red blood cell cholinesterase activity, nausea, and headaches. No information is available on reproductive, developmental, or carcinogenic effects of parathion in humans (PubChem 2016).
Pentachlorophenol	Pesticide	confirmed (World Wildlife Fund)	Pentachlorophenol is a widespread environmental pollutant. Both chronic and acute pentachlorophenol poisoning are medical concerns. The range of its biological actions is still being actively explored, but it is clearly a potent enzyme inhibitor and has been used as such as an experimental tool (PubChem 2016).
Phthalates	Plastics, packaging, cosmetics, cleaning agents	confirmed	If a product has "fragrance" or "perfume" it probably has phthalates (Precision Nutrition Inc. 2016).
Phorate	Insecticide	confirmed	It is among the most poisonous chemicals commonly used for pest control (PubChem 2016).
Phytoestrogens	Soy and other foods	confirmed	Naturally-occurring non-steroidal compounds that connect to and stimulate estrogen receptors (Precision Nutrition Inc. 2016).
Picloram	Herbicide	confirmed	Picloram is of moderate toxicity to the eyes and only mildly toxic on the skin.

Chemical	Common use	Possible or confirmed EDC	Additional Information
Polychlorinated Biphenyls (PCB)	Industrial chemicals	confirmed	PCBs are used in industry as heat exchange fluids, in electric transformers and capacitors, and as additives in paint, carbonless copy paper, and plastics. Of the 209 different types of PCBs, 13 exhibit a dioxin-like toxicity. PCBs are toxic to fish, killing them at higher doses and causing spawning failures at lower doses. Research also links PCBs to reproductive failure and suppression of the immune system in various wild animals, such as seals and mink (Stockholm Convention 2008).
Prometryn	Herbicide	confirmed	Prometryn is a triazine used as a selective pre- and post-emergence herbicide. Developmental toxicity studies with rats show maternal and developmental toxicity (PubChem 2016).
Simazine	Pesticide	confirmed	Simazine is highly toxic if inhaled, moderately toxic if ingested, and slightly toxic via dermal exposure.
THM (trihalomethanes)	Solvent, refrigerant	confirmed	Acute chloroform toxicity results in impaired liver function, cardiac arrhythmia, nausea, and central nervous system dysfunction (PubChem 2016).
Temephos	Insecticide	confirmed	Temephos inhibits the action of the group of enzymes called cholinesterases.
Terbufos	Insecticide, nematicide	confirmed	Terbufos is used as a soil insecticide. The substance can be absorbed into the body in hazardous amounts by ingestion, by inhalation and through the skin (PubChem 2016).
Tetrachloroethylene (PERC)	Degreaser, cleaner	confirmed	Exposure irritates the upper respiratory tract and eyes and causes neurological effects as well as kidney and liver damage. Tetrachloroethylene is anticipated to be a human carcinogen (PubChem 2016).
Tetrabromobisphenol A	Flame-retardant	confirmed	This can disrupt thyroid balance. Found in plastics, paint, furniture, electronics, food (Precision Nutrition Inc. 2016).
2,3,4,6 tetrachlorophenol	Preservative, pesticide	confirmed	This substance is very toxic to aquatic organisms. Bioaccumulation of this chemical may occur in fish. It is possibly carcinogenic to humans.

Chemical	Common use	Possible or confirmed EDC	Additional Information
Toxaphene	Insecticide	confirmed (World Wildlife Fund)	For humans, the most likely source of toxaphene is exposure is food. While the toxicity to humans of direct exposure is not high, toxaphene has been listed as a possible human carcinogen due to its effects on laboratory animals. It is highly toxic to fish; brook trout exposed to toxaphene for 90 days experienced a 46% reduction in weight and reduced egg viability, and long-term exposure to levels of 0.5 micrograms per litre of water reduced egg viability to zero (Stockholm Convention 2008).
Triallate	Herbicide	confirmed	Toxic by inhalation, ingestion or skin absorption (PubChem 2016).
Trichloroethylene	Degreaser, solvent, in surgical procedures	confirmed	Prolonged exposure to high concentrations of the vapor can lead to cardiotoxicity and neurological impairment (PubChem 2016).
2,4,6 trichlorophenol	Pesticide	confirmed	This substance is very toxic to aquatic organisms. Bioaccumulation occurs, specifically in fish. It may have effects on the liver, resulting in impaired functions and is possibly carcinogenic to humans.
2,4,5 trichlorophenoxy acetic acid	Herbicide	confirmed	Animal tests show that this substance possibly causes toxicity to human reproduction or development.
Triclosan	Personal care products, anti-microbial products	possible	May influence how thyroid hormones act in the body (Precision Nutrition Inc. 2016).
Trifluralin	Herbicide	confirmed	Has long-term, reproductive, developmental, or carcinogenic effects in humans (PubChem 2016).
UV Filters	Sunscreens, cosmetics	possible	These products exhibit estrogenic activity (Precision Nutrition Inc. 2016).
Vinyl chloride	PVC, plastic	confirmed	Exposure to this substance affects the central and peripheral nervous system and causes liver damage (PubChem 2016).