Pharmaceuticals and Personal Care Products in the Canadian Environment: Research and Policy Directions

Workshop Proceedings

Queen’s Landing Inn ■ Niagara-on-the-Lake ■ Ontario ■ Canada ■ March 5th to 7th 2007
Pharmaceuticals and Personal Care Products in the Canadian Environment: Research and Policy Directions

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Workshop Proceedings

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Walkerton Clean Water Centre
Canadian Water Network

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This document includes abstracts from all presentations and a summary report of the breakout group discussions. For detailed proceedings please refer to the Workshop Summary document prepared by Lura Consulting Inc., available from all members of the organizing committee.

The recommendations and opinions expressed in this document are those of the participants and not necessarily representative of the sponsoring organizations or committee members.
**List of Commonly Used Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>3BC</td>
<td>3-benzylidene camphor</td>
</tr>
<tr>
<td>ACR</td>
<td>Acute to chronic ratio</td>
</tr>
<tr>
<td>AENV</td>
<td>Alberta Environment</td>
</tr>
<tr>
<td>APCI</td>
<td>Atmospheric pressure chemical ionization</td>
</tr>
<tr>
<td>AwwaRF</td>
<td>American Water Works Association Research Foundation</td>
</tr>
<tr>
<td>BMPs</td>
<td>Best management practices</td>
</tr>
<tr>
<td>CAEAL</td>
<td>Canadian Association of Environmental Analytical Laboratories</td>
</tr>
<tr>
<td>CAS</td>
<td>Chemical Abstracts Service</td>
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<tr>
<td>CEPA</td>
<td>Canadian Environmental Protection Act</td>
</tr>
<tr>
<td>CMP</td>
<td>Chemicals Management Plan</td>
</tr>
<tr>
<td>CRM</td>
<td>Certified reference materials</td>
</tr>
<tr>
<td>DSL</td>
<td>Domestic Substances List</td>
</tr>
<tr>
<td>EAU</td>
<td>Environmental Assessment Unit</td>
</tr>
<tr>
<td>EC50</td>
<td>Effective concentration – 50%</td>
</tr>
<tr>
<td>EDCs</td>
<td>Endocrine-disrupting compounds</td>
</tr>
<tr>
<td>EMEA</td>
<td>European Agency for the Evaluation of Medicinal Products</td>
</tr>
<tr>
<td>ERAPharm</td>
<td>Environmental risk assessment of pharmaceuticals</td>
</tr>
<tr>
<td>ESI</td>
<td>Electrospray ionization</td>
</tr>
<tr>
<td>EU</td>
<td>European Union</td>
</tr>
<tr>
<td>F&amp;D</td>
<td>Food and Drug Act</td>
</tr>
<tr>
<td>GUDI</td>
<td>Groundwater under the direct influence of surface water</td>
</tr>
<tr>
<td>GVRD</td>
<td>Greater Vancouver Regional District</td>
</tr>
<tr>
<td>ICL</td>
<td>In-commerce list</td>
</tr>
<tr>
<td>LC-MS/MS</td>
<td>Liquid chromatography – tandem mass spectrometry</td>
</tr>
<tr>
<td>LMB</td>
<td>Liquid municipal biosolids</td>
</tr>
<tr>
<td>LOEC</td>
<td>Lowest observed effective concentration</td>
</tr>
<tr>
<td>MBBR</td>
<td>Moving Bed Biofilm Reactor</td>
</tr>
<tr>
<td>MOE</td>
<td>Ministry of Environment (Ontario)</td>
</tr>
<tr>
<td>MWWE</td>
<td>Municipal wastewater effluent</td>
</tr>
<tr>
<td>NSACB</td>
<td>New Substances Assessment and Control Bureau</td>
</tr>
<tr>
<td>NSNR</td>
<td>New Substances Notification Regulations</td>
</tr>
<tr>
<td>OWC</td>
<td>Organic wastewater contaminants</td>
</tr>
<tr>
<td>PhACT</td>
<td>Pharmaceutical Assessment and Characterization Tool</td>
</tr>
<tr>
<td>PhATE</td>
<td>Pharmaceutical Assessment and Transport Evaluation</td>
</tr>
<tr>
<td>PhRMA</td>
<td>Pharmaceutical Research and Manufacturers of America</td>
</tr>
<tr>
<td>PNEC</td>
<td>Predicted no-effect concentration</td>
</tr>
<tr>
<td>PP</td>
<td>Peroxisomal proliferator</td>
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<tr>
<td>PPAR</td>
<td>Peroxisomal proliferator activated receptor</td>
</tr>
<tr>
<td>PPCPs</td>
<td>Pharmaceuticals and personal care products</td>
</tr>
<tr>
<td>QA/QC</td>
<td>Quality assurance/quality control</td>
</tr>
<tr>
<td>RXR</td>
<td>Retinoic acid X receptor</td>
</tr>
<tr>
<td>SRM</td>
<td>Standard reference materials</td>
</tr>
<tr>
<td>SRT</td>
<td>Solids (sludge) retention time</td>
</tr>
<tr>
<td>SSRI</td>
<td>Selective serotonin reuptake inhibitors</td>
</tr>
<tr>
<td>TSRI</td>
<td>Toxic Substances Research Initiative</td>
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<tr>
<td>USEPA</td>
<td>United States Environmental Protection Agency</td>
</tr>
<tr>
<td>USGS</td>
<td>United States Geological Survey</td>
</tr>
<tr>
<td>UV</td>
<td>Ultraviolet</td>
</tr>
<tr>
<td>VICH</td>
<td>International Cooperation of Harmonization of Technical Requirements for Registration of Veterinary Products</td>
</tr>
<tr>
<td>WAS</td>
<td>Waste activated sludge</td>
</tr>
<tr>
<td>WET</td>
<td>Whole effluent toxicity</td>
</tr>
<tr>
<td>WWTPs</td>
<td>Wastewater treatment plants</td>
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</tbody>
</table>
# Table of Contents

1.0 Workshop Summary

2.0 Introduction and Workshop Purpose
   2.1 Workshop Objectives
   2.2 Workshop Organization

3.0 Overview of the State of the Science
   3.1 Environmental Exposure and Monitoring Activities
   3.2 Effects of PPCPs on Aquatic Ecosystems
   3.3 Reduction of Human and Environmental Exposure to PPCPs
   3.4 Environmental Risk Assessment
   3.5 International and Industry Activities
   3.6 Provincial and Municipal Activities

4.0 Research and Policy Directions for PPCPs in the Canadian Environment
   4.1 Effects of PPCPs on the Canadian Environment
   4.2 Risk Management Approaches
   4.3 Developing a Monitoring Network
   4.4 Developing an Inventory of Information and Activities
   4.5 Developing a Consistent Framework for Chemical Analysis

5.0 Overview of Policy and Management Issues
   5.1 Wastewater Treatment
   5.2 Drinking Water Treatment
   5.3 Source Control, Prudent Use, and Source Separation
   5.4 Biosolids Management and Agricultural Best Management Practices (BMPs)

6.0 Workshop Conclusions

7.0 References and Recommended Reading

Appendix A: Workshop Agenda
Appendix B: Participants List
Appendix C: Poster Abstracts
1.0 Workshop Summary

It has been known for over 20 years that pharmaceuticals and personal care products (PPCPs) are released into the environment, however only in the last 10 years have analytical methods become sufficiently sensitive to identify and quantify their presence in wastewater treatment plant (WWTP) effluents, surface waters, drinking water, ground water, biosolids, agricultural manures, and biota. The presence of PPCPs in the environment has emerged as a societal issue, but the science with respect to exposure and impacts is still rudimentary.

Environment Canada and Health Canada hosted a multi-stakeholder workshop in 2002, entitled “Assessment and Management of PPCPs in the Canadian Environment”, to identify the major research and risk management needs. This workshop identified an initial set of research priorities as well as new policy thrusts, most notably the implementation of a “National Science Agenda” focused on the emerging issue of PPCPs in the environment. A second multi-stakeholder workshop, sponsored by Environment Canada, Health Canada, the Ontario Ministry of Environment, Agriculture and Agri-Food Canada, and the Canadian Water Network, was convened in 2004. This workshop, entitled “Toward a Monitoring Network: a Technical Workshop for PPCPs in the Environment”, examined in greater detail three areas of PPCPs research (analytical methods, sampling, and effects) and recommended strategies to achieve the 2002 research agenda. The recommendations from this workshop emphasized the importance of strengthening domestic and international partnerships and improving the transfer of knowledge as a whole.

These workshops catalyzed Canadian research on the occurrence and effects of PPCPs in the Canadian environment, and there has been considerable effort to determine whether PPCPs pose an ecological or human health risk. Little is known about the effects of these substances on non-target organisms, many of which differ from mammals in their receptor sensitivity, and in the roles various metabolic pathways play in their development and reproduction. Endpoints, such as neurobehavioral changes, can be very subtle but nonetheless lead to unanticipated, profound outcomes on non-target populations. Research continues to demonstrate the effects of single compounds on various aquatic organisms under laboratory conditions at environmentally relevant concentrations; however it is not known how these results translate into the complexity of mixtures and environmental conditions. Analytical methods have been developed for a wide variety of compounds and labeled standards have become commercially available in the last 5 years; however large-scale method comparison and validation exercises to improve the accuracy and precision of quantitative measurements have not yet been conducted. Options to reduce environmental exposure to PPCPs, particularly through wastewater discharges and land application of biosolids and manures, are being examined; however risk management strategies and Best Management Practices (BMPs) are not fully developed. Environmental effects, accurate quantitation, and risk management alternatives are all necessary facets of a comprehensive ecological risk assessment.

The subject of the current report was based on a third National Workshop entitled “Pharmaceuticals and Personal Care Products (PPCPs) in the Canadian Environment: Research and Policy Directions” took place March 5th to 7th, 2007 in Niagara-on-the-Lake, Ontario. The workshop was hosted by the Ontario Ministry of the Environment, Environment Canada, Health Canada, Agriculture and Agri-Food Canada, the Ontario Ministry of Agriculture, Food, and Rural Affairs, the Canadian Water Network, and the Walkerton Clean Water Centre, and was attended by over 150 scientists and regulators from across Canada. This workshop differed from the past two in that it was open to all those interested in PPCPs in the Canadian environment. Attendees represented a diverse group of interested parties, including municipalities, provincial regulators, federal risk assessors, pharmaceutical and fragrance industry associations, environmental consultants, United States Environmental Protection Agency and Non-Government Organizations, as well as government and university researchers.

This Workshop assessed the current state of Canada’s research on PPCPs in the environment in government, academia and industry sectors. Invited speakers provided overviews on environmental exposure and monitoring, effects of PPCPs on aquatic ecosystems, alternatives for
reduction of human and environmental exposure to PPCPs, risk assessment process and needs, international, industry activities, provincial and municipal activities.

A principal focus of the workshop was setting priorities for research, monitoring, and regulation of PPCPs. Facilitated discussion workgroups covered 5 topics:

1. Effects of PPCPs on the Canadian Environment
2. Risk Management Approaches
3. Developing a Monitoring Network
4. Developing an Inventory of Information and Activities
5. Developing a Consistent Framework for Analysis

These workgroups created a list of priorities and key actions to guide future PPCPs research and Canada’s path forward in this emerging field, and a synopsis of the recurring themes is provided below. In addition the report provides an overview of policy and management issues.

This workshop report is intended to strengthen communication in this important field. The proceedings provide a common understanding of the state of the science, thereby helping researchers prioritize needs and better identify collaborative opportunities to address knowledge gaps. This report will also make funding organizations aware of the research priorities in this field, and give managers a better appreciation of existing research challenges and broader potential policy issues.

**Recommendations and Priorities**

1. **Effects of PPCPs on the Canadian Environment**
   - The use of more relevant (chronic) endpoints and exposure scenarios are required for impact assessment.
   - Consideration should be given to synergistic and cumulative effects including the evaluation of mode of action.
   - There is a need to evaluate potential effects at environmentally relevant concentrations.
   - There is a need to examine potential seasonal/reproductive cycle sensitivity of different species.
   - Expanded analytical capability in terms of both laboratory capacity and field studies for a wider variety of parent compounds and transformation products needs to be developed.
   - Prioritization needs to be given to substances to monitor in the environment and to the identification of sentinel species (e.g. mussels, bivalves, frogs, insects).
   - Further studies focusing on development of promising bioindicators of individual, population, and ecosystem effects.
   - There is a need to define impairment, adversity and impact.
   - Effects studies need to include terrestrial ecosystems.
   - There is a need to assess the uncertainty regarding the development of antibiotic microbial resistance in the environment.
   - Communication needs to be expanded to explain to the public what the environmental effects are and what it means to them. This involves improving the dissemination of information, especially the grey literature, such as regulatory and unpublished information.
   - Pharmaceutically active compounds and personal care products should be evaluated as independent groups of compounds due to their different chemical characteristics and use patterns.
2 **Risk Management Approaches**

- There is a need for a nationally coordinated research program to support a regulated categorization program.
- Quantifying loadings and concentrations of PPCPs to determine which sources are the most important.
- Determining the cost-effectiveness of both conventional and advanced drinking water, wastewater, and sludge treatment technologies.
- Developing BMPs for land application of manures and biosolids to mitigate off-site contamination and exposure to both aquatic and terrestrial ecosystems, including detailed dissipation information for the compounds.
- Critical control points for environmental exposure should be evaluated and more efficient use of existing infrastructure for the collection of unwanted PPCPs needs to be investigated.
- Education of the health care profession, and the public to encourage judicious use of PPCPs including the consideration of alternative formulations for pharmaceuticals.
- Modifications to the current regulations so that PPCPs with low sales volumes must pass the risk assessment process.

3 **Developing a Monitoring Network**

A monitoring network should include a website sub-divided into the following subject areas: sources, loads and watershed mass balances; fate through WWTPs; fate through water treatment plants; concentrations in environmental matrices: sediment, groundwater, surface water, biota, etc.; ecological risk assessment and reports of field studies on effects; human health risk assessment; and analytical methods.

The purpose of the website would be to archive existing data, aid in the formation of hypotheses, support risk assessment exercises, and to help coordinate scientific research planning. Such an information source would identify collaboration opportunities, help to prevent duplication of efforts, and provide baseline data. The information generated from the monitoring should be available to scientists through portals on the website. Interpreted and peer reviewed results could be made available to the public. The next steps identified were:

- Nominating champions from each region and investigate what networks currently exist and examine different website models.
- Establishing a Technical Steering Committee to help guide the process (Federal lead).

4 **Developing an Inventory of Information and Activities**

An inventory would be useful to compile technical information (such as toxicological properties, compound fate, and Chemical Management Plan (CMP) and media specific information), assist in risk assessment, and identify knowledge gaps. Centralization of information could be accomplished by developing a specialized national database to capture: (1) transport and fate data (2) research projects, participants, and results (3) links to other PPCP groups and websites (4) all predicted no-effect concentrations (PNECs), and (5) publications. The next step would be to establish a Technical Steering Committee to guide the process (Provincial lead).

5 **Developing a Consistent Framework for Chemical Analysis**

The need for accurate, precise analytical methods that cover a wide range of PPCP parent compounds and metabolites in surface water, groundwater, wastewater, drinking water, sediment, sludge, biosolids, manures, and biota, and the need for increased laboratory capacity across Canada were identified in all discussions. Discussions at this workshop recommended a framework designed to accomplish the following:
A method compendium that is matrix dependent.

A mechanism to communicate methods with their respective method validation and QA/QC data.

A data quality objective statement to characterize the method of QA/QC and the validation data requirements.

Performance criteria to ensure consistent data quality for conducting routine sample analysis.

Conclusion
The National workshop on “Pharmaceuticals and Personal Care Products in the Canadian Environment: Research and Policy Directions” was very successful based on the number and diversity of participants, the animated discussions, and the positive feedback. The common theme in all discussion areas was the importance of communication between researchers, risk assessors, regulators, wastewater managers, and the public. The formation of a central “clearinghouse” for research and management data was recommended to enhance communication and exchange of information. To maintain momentum on this issue and strengthen relationships between interested parties, it is also recommended that a follow-up workshop be convened in February 2009.
2.0 Introduction and Workshop Purpose

It has been known for over 20 years that pharmaceuticals and personal care products (PPCPs) can enter the environment, however only in the last 10 years have analytical methods become sufficiently sensitive to identify and quantify their presence in wastewater treatment plant (WWTP) effluents, surface waters, drinking water, ground water, biosolids, agricultural manures, and biota. The issue of PPCPs in the environment has become established with the public, but the science is still emerging.

Environment Canada and Health Canada hosted a multi-stakeholder workshop in 2002, entitled “Assessment and Management of PPCPs in the Canadian Environment”, to identify the major research and risk management needs. This workshop brought together invited scientists and policy specialists from Canadian, American, and European government and non-government organizations. It resulted in the identification of an initial set of research priorities as well as new policy thrusts, most notably the implementation of a “National Science Agenda” focused on the emerging issue of PPCPs in the environment.

A second multi-stakeholder workshop, sponsored by Environment Canada, Health Canada, the Ontario Ministry of Environment, Agriculture and Agri-Food Canada, and the Canadian Water Network, was convened in 2004. This workshop, entitled “Toward a Monitoring Network: a Technical Workshop for PPCPs in the Environment”, examined in greater detail three areas of PPCPs research (analytical methods, sampling, and effects) and recommended strategies to achieve the 2002 research agenda. The recommendations from this workshop emphasized the importance of strengthening domestic and international partnerships and improving the transfer of knowledge as a whole.

These workshops catalyzed Canadian research on the occurrence and effects of PPCPs in the Canadian environment, and there has been considerable effort to determine whether PPCPs pose an ecological or human health risk. Little is known about the effects of these substances on non-target organisms, many of which differ from mammals in their receptor sensitivity, and in the roles various metabolic pathways play in their development and reproduction. Endpoints, such as neurobehavioral changes, can be very subtle but nonetheless lead to unanticipated, profound outcomes on non-target populations. Research continues to demonstrate the effects of single compounds on various aquatic organisms under laboratory conditions at environmentally relevant concentrations; however it is not known how these results translate into the complexity of mixtures and environmental conditions. Analytical methods have been developed for a wide variety of compounds and labeled standards have become commercially available in the last 5 years; however large-scale method comparison and validation exercises to improve the accuracy and precision of quantitative measurements have not yet been conducted. Options to reduce environmental exposure to PPCPs, particularly through wastewater discharges and land application of biosolids and manures, are being examined; however risk management strategies and Best Management Practices (BMPs) are not fully developed. Environmental effects, accurate quantitation, and risk management alternatives are all necessary facets of comprehensive ecological risk assessment. The 2007 workshop was convened to explore the current state of both the science and policy aspects of PPCPs in the Canadian environment.

2.1 Workshop Objectives

The purpose of this three-day workshop, entitled “Pharmaceuticals and Personal Care Products in the Canadian Environment: Research and Policy Directions”, was to continue national discussions on research priorities, risk assessment and risk management approaches for PPCPs in the Canadian environment. Specifically, the goals of the workshop were to:

1. Develop a compendium of the state of the science;
2. Identify a list of research priorities, policy issues, and action items;
3. Identify potential partnership opportunities to address knowledge gaps.
Invited speakers provided a series of presentations on the state of PPCP science and research in Canada, the latest information on environmental and health effects assessment, and risk management approaches for PPCPs. Abstracts from these presentations are included in the section, “Overview of the State of the Science”. Additionally all attendees were invited to display posters to communicate the details of their research activities; abstracts and contact information from these posters are included in Appendix C. The path forward for PPCPs from a research and policy development perspective was discussed in breakout sessions. This document provides a compendium of the state of the science as presented by the invited speakers, and a summary of the discussions on scientific research and policy development issues.

2.2 Workshop Organization

The workshop was sponsored by the Ontario Ministry of the Environment, Environment Canada, Health Canada, Agriculture and Agri-Food Canada, the Ontario Ministry of Agriculture, Food, and Rural Affairs, the Canadian Water Network, and the Walkerton Clean Water Centre.

The workshop was organized by a planning committee of the following individuals:

- Sonya Kleywegt Standards Development Branch, Ontario Ministry of the Environment
- Shirley Anne Smyth Water Science and Technology Directorate, Environment Canada
- Andrew Beck New Substances Assessment and Control Bureau, Health Canada
- Edward Topp Environmental Health National Program, Agriculture and Agri-Food Canada
- Michael Payne Nutrient Management Branch, Ontario Ministry of Agriculture, Food and Rural Affairs
- Joanne Parrott Water Science and Technology Directorate, Environment Canada
- Karl Schaefer Science and Technology Liaison, Environment Canada
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- Shahram Tabe Standards Development Branch, Ontario Ministry of the Environment
- Alison McLaughlin New Substances Assessment and Control Bureau, Health Canada
- Jenn Dykeman Water Science and Technology Directorate, Environment Canada
- Rodney McInnis Water Science and Technology Directorate, Environment Canada

The workshop was held March 5th to 7th, 2007, at the Queen’s Landing Inn, Niagara-on-the-Lake, Ontario, Canada. It was attended by over 150 scientists and regulators from across Canada.

The program consisted of invited speakers, poster sessions and facilitated breakout sessions with opportunity for open discussion and questions.
3.0 Overview of the State of the Science

A series of invited speakers provided the current state of science and research for PPCPs in the Canadian environment.

3.1 Environmental Exposure and Monitoring Activities

Determining exposure of environmental ecosystems to PPCPs requires analytical methods to quantify concentrations in environmental matrices and sufficient monitoring data, in terms of compounds, matrices, and geographic locations, to determine the extent and relative severity of exposure. Analytical methods have expanded considerably in the past five years, both in sensitivity and accuracy and in the numbers of compounds and matrices for which methods have been developed. National monitoring programs have been expanded to include PPCPs to gain a better understanding of their distribution and persistence. However these activities are far from mature. The presentations about the current state of environmental and monitoring activities provided background information to guide discussions on future needs and priorities in this area.

Dr. Mark Servos, Scientific Director of the Canadian Water Network, spoke about the presence of PPCPs in the Canadian environment, the progress that has been made since the 2002 workshop, and his recommendations for future research directions.

Over the last five years there has been considerable effort across Canada to address the environmental exposure of PPCPs. This group of emerging chemicals of concern have become of interest because of developments in analytical chemistry, identification of potential subtle effects at very low concentrations and the recognition of their potential to be widespread environmental contaminants. Many acidic and neutral pharmaceuticals, antibiotics and personal care products (such as synthetic musk fragrances) are widespread in Canadian municipal treatment plant effluents, surface waters and drinking water. In addition, many veterinary medicines and animal care products have been detected in agricultural watersheds. Treatment processes have an impact on removal of most PPCPs in both wastewater and drinking water, but many compounds such as carbamazepine, are extremely persistent and have been found in finished water and wastewaters. Advanced oxidation (e.g. ozone) and filtration (nanofiltration) are capable of removing many of these compounds but are not widely applied. In pilot scale and full scale studies there is evidence that advanced treatment can remove or reduce many of these compounds. Despite considerable efforts the potential risk and significance of these compounds in the environment has not been fully addressed.

Sean Backus of the Ontario Water Quality Monitoring Section of Environment Canada, provided an overview of Environment Canada’s monitoring activities for PPCPs in the environment.

Environment Canada, through its Science and Technology Branch, conducts science activities to provide high-quality knowledge, information and data that enable decision makers to enhance the health and safety of Canadians, protect the quality of the natural environment, and advance Canada’s long-term competitiveness.

Pharmaceuticals and Personal Care Products (PPCPs), a large class of organic chemicals, have been designated as emerging contaminants because they are disposed or discharged to the environment on a continual basis from domestic and industrial wastewater including septic tank wastewater, landfills, and wet weather runoff.

The Department conducts a variety of environmental studies pertaining to PPCPs. They include science and risk assessments under the Canadian Environmental Protection Act (CEPA), including the NSNR; strategic science and technology planning and priority setting; atmospheric process studies; wildlife and landscape studies; and water quality monitoring and research.

Given that the main routes of entry to the environment of PPCPs are wastewater and domestic wastes such as municipal waste water treatment plants (WWTPs) and septic fields, disposal via municipal refuse in landfills that leach to groundwater, and storm water overflow from residential...
sources much of the science conducted by the Department has occurred with respect to water quality monitoring and research. This has included surveillance studies on the distribution of acidic and neutral pharmaceuticals and veterinary drugs in the Great Lakes Basin, the Fraser River Basin, prairie watersheds, fluvial systems (St. Lawrence River) and in marine/coastal watersheds of Eastern Canada. Scientific studies have also investigated the fate and effects of WWTP effluents using gene expression in fish, environmental transport and persistence of antibiotics in swine production, effects of antibiotics on algae and bacteria in prairie wetlands, reproductive health of fish downstream of WWTPs, effects of selected PPCPs on *Hyalella azteca* and lifecycle exposures using fathead minnows, to name a few. Future work and challenges will be to continue to develop an integrated environmental monitoring and predictive capability to address the issue of PPCPs in the environment.

Dr. Chris Metcalfe, a professor in Environmental and Resource Studies at Trent University, spoke about the current state of analytical methods for PPCPs in environmental matrices. PPCPs that are not rapidly degraded in WWTPs may remain dissolved in the aqueous phase of wastewater effluents, or they may bind to biosolids. The most direct route of release of PPCPs into the environment is through the discharge of WWTP effluents into surface waters. Biosolids containing PPCPs may be placed in landfills or spread on agricultural land for soil amendment, where these compounds may be transported by runoff into the surrounding surface water or may leach into underlying groundwater. The most widely used method for analyzing PPCPs in environmental matrices is liquid chromatography with tandem mass spectrometry (LC-MS/MS). However, there are several analytical challenges associated with the use of LC-MS/MS instrumentation, including “matrix effects” that either reduce or enhance the signal as a result of co-extractives in the sample matrix. The electrospray (ESI) ion source is susceptible to ion suppression and our recent studies have shown that atmospheric pressure chemical ionization (i.e. APCI) is most susceptible to signal enhancement. Analytical solutions to these challenges include effective clean-up of extracts, use of low injection volumes, and calibration using “standard additions” methods or stable isotope surrogates. These methods have been applied to the analysis of PPCPs in complex environmental matrices, including the analysis of serotonin reuptake inhibitors in fish tissues and the analysis of beta-blocker drugs in both municipal wastewater and biosolids.

3.2 Effects of PPCPs on Aquatic Ecosystems

The primary driver for the issue of PPCPs in the Canadian environment is the concern that long-term exposure to low levels of PPCPs residues could have adverse effects on aquatic and terrestrial ecosystems and/or human health. Effects research spans a wide range of activities, from observations at the molecular level about up- and down-regulation of genes to observations on growth and reproduction of a fish species as a result of exposure to a compound under controlled conditions. The presentations about the current state of PPCP effects research provided background information to guide discussions on future needs and priorities in this area.

Dr. Karl Fent, a professor at the University of Applied Sciences in Muttenz, Switzerland, provided the keynote address on the subject of “Pharmaceuticals and ultraviolet absorbing compounds (UV filters) effects in the aquatic environment”

The chronic toxicity and potential subtle effects of pharmaceuticals are only marginally known. In my presentation, I critically review the current knowledge about human pharmaceuticals in the environment and address several key questions (Fent et al. 2006a). What kind of pharmaceuticals and what concentrations occur in the aquatic environment? What are the modes of action of these compounds in humans and are there similar targets in lower animals? What acute and chronic ecotoxicological effects are there elicited by pharmaceuticals and by mixtures of pharmaceuticals? What are the effect concentrations and how do they relate to environmental levels? I show that only very little is known about long-term effects of pharmaceuticals to aquatic organisms, in particular with respect to biological targets. For most human medicines analyzed, acute effects to aquatic organisms are unlikely to occur, except for spills. For investigated pharmaceuticals
chronic lowest observed effect concentrations (LOEC) in standard laboratory organisms are about two orders of magnitude higher than maximal concentrations in WWTP effluents. However, for diclofenac, the LOEC for fish toxicity was in the range of wastewater concentrations, whereas the LOEC of propranolol and fluoxetine for zooplankton and benthic organisms were near to maximal measured WWTP effluent concentrations. Targeted ecotoxicological studies are lacking almost entirely and such investigations are needed for better and comprehensive risk assessments of pharmaceuticals. Using recombinant yeast systems, we show that some pharmaceuticals show estrogenic activity in vitro (Fent et al. 2006b). We evaluate the cytotoxicity in vitro of 34 pharmaceuticals from different classes and modes of action. Cytotoxicity was found for 21 pharmaceuticals with EC50-values ranging from 2.1 µM (doxorubicin) to 8.66 mM (salicylic acid). A good correlation with log Dow and between the in vitro data and in vivo data was found for Daphnia. We show that in vitro assays using cell lines are well suited for the first screening of the acute in vivo toxicity of pharmaceuticals (Caminada et al. 2006). In addition, we show that lipid lowering agents do not reduce Daphnia reproduction at reasonable concentrations. Currently, we analyze biochemical effect parameters in fish cell systems and in fish besides classical toxicity endpoints.

UV filters have been detected in surface water, wastewater and fish, and some of them are estrogenic in fish. At present, little is known about their additional hormonal activities in different hormonal receptor systems. We systematically analyzed the estrogenic, antiestrogenic, androgenic, and antiandrogenic activity of 18 UV filters and one metabolite in vitro at non-cytotoxic concentrations with recombinant yeast systems carrying either a human estrogen (hER) or androgen receptor (hAR). All 19 compounds elicited hormonal activities, surprisingly most of them multiple activities. We found 10 UV-filters having agonistic effects towards the hER. Surprisingly, 6 UV filters showed androgenic activities and many of them having pronounced antiestrogenic and antiandrogenic activities. (Kunz and Fent, 2006). Mixtures of UV filters show in most cases synergistic interactions (Kunz and Fent 2006b). The UV filter 3-benzylidene camphor (3BC) has been shown in vitro and in vivo in fish to be estrogenic (Kunz et al. 2006a). After a pre-exposure period of 21 days, reproductively mature fathead minnows were exposed to increasing concentrations of 3BC for 21 days in a static-renewal procedure. 3BC affected reproduction in a dose-dependent manner with weak effects on fecundity at 3 µg/L, a significant decrease at 74 µg/L and a cessation of reproduction at 285 µg/L. 3BC was accumulated in fish with an average bioconcentration factor of 313. Dose-dependent demasculinisation in secondary sex characteristics of male fish and dose-dependent induction of plasma vitellogenin occurred, which was significant at 74 µg/L. 3BC had a profound and dose-dependent effect on the histology of gonads of males and female fish at 3 µg/L and higher. At 74 and 285 µg/L, oocyte and spermatocyte development was inhibited in male and female gonads. Our studies show estrogenic activity of UV filters and significant effects of the common UV filter 3BC on fertility, gonadal development and reproduction of fish after short-term exposure that may have negative consequences on the population level (Kunz et al. 2006b).

There have been some measurements of UV filter chemicals, such as benzophenone, in treated wastewater in Switzerland and California. A study on municipal sewage sludge showed concentrations of some UV filters occurring in ranges of 1 to 6 mg/kg of dry matter. Concentrations have also been found in fish, including some bioconcentration factors in the range of 300 – 500 and other compounds concentrated higher.

Dr. François Gagné of the Aquatic Ecosystem Protection Research Division of Environment Canada provided a review of current and new strategies to assess the toxicological effects of PPCPs on aquatic species.

Pharmaceutical, personal care and veterinary products, which have been found in wastewater and surface water, are likely to contaminate the aquatic environment, including groundwater. Aquatic sentinel species that bioaccumulate some of these drugs remain to be identified, but studies with mussels and plants have shown that some antibiotics significantly accumulate in tissues. Laboratory tests have been conducted with some success on several aquatic species, including bacteria, plants, invertebrates (molluscs and arthropods) and fish, with commonly found drugs both individually and in mixtures. These toxicity tests generally indicate that acute lethal effects
are not likely to occur in the environment but that chronic or long-term effects are possible. In an attempt to measure the effects of pharmaceuticals and personal care products, two types of biomarkers are proposed. The first class, known as integrative biomarkers, consists of measuring ecologically relevant biomarkers that encompass the effects of drugs, such as oxidative stress or DNA damage. Biomarkers that have been shown to predict changes at both the individual and population levels, and that respond to these products, are particularly useful for taking into account the final effects of pollution on feral aquatic organisms. The second class of biomarkers, known as drug target-specific biomarkers, measures the state/integrity of drug targets likely to impede the organism’s health and reproduction. For example, prostaglandin synthase produces prostaglandins necessary to assist spawning in bivalves, and its activity could be blocked by non-steroidal anti-inflammatory drugs such as acetylsalicylate and ibuprofen.

Finally, two case studies are presented to exemplify the use of biomarkers to assess drug target specific interactions and tissue damage in aquatic species. In the first case study, primary cultures of rainbow trout hepatocytes were used to assess the cytotoxicity of carbamazepine, a drug commonly found in municipal wastewater, at µg/L range, after exposure for 48 h at 18°C. Results showed that carbamazepine induced the activity of cytochromes P4503A4 and 2B6 (benzyloxyresoruﬁn as the substrate), known biotransformation enzymes for this drug class (iminostillbene), and was highly correlated with lipid peroxidation and cell viability at environmentally relevant concentrations. Lipid peroxidation and cell viability are considered integrative biomarkers, while cytochrome P4503A4/2B6 activity is a target-specific biomarker. The second case study concerns feral carp that had survived for four years in an aerated lagoon that treats domestic municipal effluent. Results showed that cytochrome P3A4 activity, as determined by dibenzyloxyfluorescein (another substrate speciﬁc for cytochromes P450 3A4, 3A5 and 2C9), was readily induced in the post-mitochondrial supernatant of liver homogenates. ATP-dependent dopamine transport activity in synaptosome preparations of brain tissues was shown to be signiﬁcantly reduced. Increased cytochrome P450-related activities and reduced dopamine uptake suggest the pharmacological effects of opiate-like substances. Preliminary ﬁndings thus indicate that some aquatic species are likely to accumulate some drugs and that they are likely to produce harmful effects on fish. Further research is needed to validate such biomarkers and to relate changes in drug targets with their residual levels in tissues.

Dr. Thomas W. Moon, a professor in the Department of Biology and Centre for Advanced Research in Environmental Genomics at the University of Ottawa, discussed environmental effects in freshwater ecosystems.

This presentation addresses changes in the knowledge base and methods used for effects assessment of pharmaceuticals in the environment over the past five years. Although a number of PPCPs are studied by academic researchers, this paper deals primarily with the fibrates and the selective-serotonin re-uptake inhibitor (SSRI) fluoxetine, compounds commonly found in waste-water efﬂuents and surface waters. Studies have indicated both groups act in fish as endocrine disruptors affecting the production of both sex (testosterone, estradiol) and stress (cortisol) steroids. Given that steroid synthesis shares common pathways but generally different tissues, tools for their study are similar. Fibrates are peroxisomal proliferators (PPPs) and as such act through a nuclear receptor, the peroxisomal-proliferator activated receptor (PPAR) which heterodimerizes with the
RXR (retinoic acid X receptor, also a nuclear receptor) to bind to response elements in the promoter regions of PP-sensitive genes.

It has been demonstrated in goldfish that a fibrate drug, gemfibrozil, bioconcentrates in blood by more than 400-fold at environmental concentrations and reduces testosterone levels by 50%. To understand the mechanism(s) responsible for such dramatic changes, PPAR transcript levels and other components within the steroidogenic pathway were examined. Strong seasonal effects were found in all parameters studied which is probably (although not conclusively) related to the seasonal reproductive behavior of this species. We have also examined ACTH-induced cortisol release using a dispersed rainbow trout head-kidney cell preparation as a model that may be less seasonally-dependent. Using this system we have isolated the effects of fibrate drugs to specific enzymes within the cortisol synthetic pathway. What is intriguing about these results is that using a similar preparation, others have shown that salicylate and ibuprofen do not act on enzymes of the pathway but rather at the level of cholesterol entry.

We have also developed a very sensitive rainbow trout gill cell reporter-gene assay that responds to environmental concentrations of fibrate drugs. And finally, using a goldfish-carp cDNA array, it is demonstrated that fluoxetine not only up- and down-regulates a number of critical genes, but specifically down-regulates isotocin, a neuropeptide that modulates spawning and social behaviors in fish. Using similar designs, fluoxetine is shown to reduce the number of eggs produced and aromatase expression in zebrafish. These results demonstrate that we know much more about the mechanisms by which PPCPs act on fish, but at the same time we have huge gaps in our understanding of differential sensitivities of species, the seasonal responses that are seen and whether these can be linked specifically to seasonal reproductive cycles, and the role of mixtures of chemicals including PPCPs and their impacts. Clearly more studies using environmentally-relevant PPCPs concentrations, a toxicokinetic approach with parent compounds and metabolites, and a multi-generational approach but at defined time periods and chronic exposure, are required before we are able to demonstrate the full impact of PPCPs on aquatic organisms, including fish.

Dr Katsuji Haya, from the Marine Environmental Sciences Division of Fisheries and Oceans Canada, discussed the environmental effects of PPCPs on marine ecosystems.

Research in Canada concerned with the biological effects of PPCPs on marine organisms is limited. Overviews of active research on the exposure to municipal and industrial effluents during seaward migration of salmon; laboratory and field exposure to municipal waste water effluents; and environmental effects of salmon aquaculture wastes is presented.

Under laboratory conditions juvenile Atlantic salmon were exposed to sublethal concentrations of nonylphenol, estradiol, or methyl testosterone in fresh water for one to two weeks in May. The salmon were then acclimated to ambient sea water and held until October. Salmon exposed to the chemicals had a greater proportion of small fish compared to the controls. Similarly juvenile salmon caged in the Miramichi Estuary, New Brunswick, for one week had a greater proportion of small fish compared to those held in the less impacted Tabusintac Estuary. Juvenile salmon were exposed to nonylphenol, tagged and released in the Burrishoole River, Ireland in 2003 and 2004, and returning adults are being monitored.

Early life stages and underyearlings of rainbow trout, Coho salmon and Chinook salmon were exposed to both end of pipe and environmentally relevant concentrations of municipal wastewater in fresh water and saltwater. Chemical analyses for “emerging chemicals” were tailored to those previously identified as being of paramount concern with respect to biological effects. Gene array analysis of chemicals indicated significant up and down
regulation of key genes; changes in immune-related and metabolism-based genes predominated the response to wastewater effluent; and individual analytical chemistry results did not correlate with biological effect(s).

Blue mussels were caged in various locations in Pictou Harbour, New Brunswick and Burrard Inlet, British Columbia and the potential toxicity of wastewater effluents on the immune system and disease resistance were determined. Results suggest that treated and untreated wastewater can modulate the immune system of blue mussels and that most immunological endpoints measured were sensitive to the exposure and not different than results observed from experiments under laboratory conditions.

Antibiotics are used in salmon aquaculture operations and administration is by feed fortified with the antibiotic. Oxytetracycline has been the antibiotic of choice for salmon aquaculture in Atlantic Canada. The presence of oxytetracycline has been observed in sediment samples collected from under salmon cages and along a transect 100 m from under the cage presumably due to excess feed wastes and excretory products from cultured salmon. Also antibiotic resistant bacteria have been observed in the sediments. There was no correlation between oxytetracycline concentrations and the occurrence of antibiotic resistant bacteria.

Dr. Tom Edge, of the Aquatic Ecosystem Protection Research Division of Environment Canada, provided an overview of antibiotic resistance as an environmental effect of PPCPs.

The spread of enteric bacteria with antibiotic resistance is a growing public health concern. While hospital settings and the retail food supply are increasingly recognized as important sources of these bacteria, the significance of waterborne sources is less understood. Large quantities of enteric bacteria from human and animal fecal wastes can be released into rivers and lakes that serve as sources of water for drinking, recreation or irrigation. A better understanding is needed of the prevalence of antibiotic resistance in these enteric bacteria, and the significance of their occurrence in aquatic ecosystems. The potential of antibiotic resistance analyses for microbial source tracking of fecal pollution also needs further investigation. Escherichia coli is a useful enteric bacterium for studying antibiotic resistance because it is adapted to diverse human and warm-blooded animal gastrointestinal tracts, and is readily exposed to a variety of medical and veterinary antibiotic treatments. It is also the basis of many microbial water quality decisions across Canada. We have found that E. coli from municipal wastewater sources generally have higher levels of antibiotic resistance than those from pet or wildlife fecal droppings. In some cases, these results can be used for microbial source tracking purposes to determine the source of fecal pollution in aquatic ecosystems. Antibiotic resistance analysis for source tracking seems to work because the effects of antibiotics occur largely at the point of use in intestinal tracts rather than from exposure to low levels of antibiotics in aquatic ecosystems. We have detected E. coli in Lake Ontario recreational waters that are resistant to antibiotics at clinical breakpoints, although they do not appear to be common from preliminary observations. Further research will be required to ascertain the significance of antibiotic resistant bacteria in untreated waters used for drinking (e.g. wellwater), recreation or irrigation of food crops.

3.3 Reduction of Environmental And Human Exposure To PPCPs

Dr. Saad Jasim is the Chief Executive Officer of the Walkerton Clean Water Centre. He discussed the presence of PPCPs and pesticides in source water supplies, and the effectiveness of removal technologies in drinking water treatment.

Reports by different scientific groups indicate concern about traces of drugs that could make their way into tap water. The occurrence and fate of PPCPs in surface waters originating from urban sources is one of the leading emerging issues in environmental chemistry. At least 80 PPCPs (e.g., analgesics, antibiotics, antiepileptics, antidepressants, and blood lipid regulators) have been identified in outflows from WWTPs and surface waters worldwide. However, many PPCPs remain unidentified. Moreover, little is known regarding the fate, characterization and quantification at drinking water intakes. In wastewater effluent discharges, PPCPs and endocrine disrupting
compounds (EDCs) may be present as a result of incomplete removal during treatment, from combined wastewater and storm water overflows, illicit connections, or leaking septic systems. Other point source contamination can result from pharmaceutical manufacturers. Agricultural practices can constitute a significant contribution to non-point sources of PPCPs and EDCs. Veterinary antibiotics were detected in surface water supplies in proximity to large-scale hog confinement operation in Iowa. Some pharmaceuticals have also been shown to leach through subsoil and into groundwater.

Since medical drugs are designed with a specific mode of action, it is expected that they will have a variety of effects on non-target receptors and can possibly cause adverse effects in a target organism. Antibiotic resistance is the issue receiving the most attention, especially since a large portion of antibiotics leave the body and end up in receiving waters. It is not known what threshold levels are toxic, especially in complex mixtures. It is speculated that EDCs may be responsible for declining sperm counts and decreased sperm motility and function in the human population. EDCs may cause adverse effects including hormone dependent cancers, reproductive tract disorders, and reduction in reproductive fitness. Studies indicate that activated carbon and ozone are promising treatment methods to remove traces of pharmaceuticals and pesticides.

A study was conducted to evaluate the occurrence of pharmaceuticals and endocrine disrupting chemicals in the Detroit River, and the effectiveness of ozone in degrading these compounds. The analysis indicated that trace levels of compounds such as carbamazepine, caffeine, cotinine, and atrazine were detected in raw water and that treatment with ozone resulted in a greater degradation versus conventional treatment. The study provides a unique and advanced level of information for water supply and treatment for the Great Lakes Region. These findings concur with current research applied in different locations in North America and Europe, which has shown that ozone treatment alone or coupled with other treatments remove a wide range of contaminants from water. The experiments provided useful information about the presence of these compounds in Detroit River raw water, and the seasonal variations in their concentrations. The findings of this study provide information to other communities about the presence of these compounds in water supplies, and the treatment processes that are capable of removing them.

Dr. Lori Lishman, of the Aquatic Ecosystem Management Research Division of Environment Canada, discussed the capabilities and limitations of wastewater treatment in reducing environmental and human exposure to PPCPs.

This presentation summarized research in the area of wastewater treatment efficacy for PPCPs reduction. Current research focuses on reduction mechanisms rather than removal mechanisms because analytical chemical methods to characterize transformation products are still in development. In a WWTP, there are four sinks for PPCPs: enmeshment/sorption to the primary sludge or waste activated sludge (WAS); loss to the atmosphere through biological mineralization (e.g. degradation to carbon dioxide and water); volatilization from process tanks; and release with final effluent. A compound’s physical and chemical characteristics play a major role in defining its removal mechanism.

During primary clarification, settable solids are removed from the raw wastewater stream by physical settling. Primary sludge, the settable organic solids, is periodically removed from the clarifier for further stabilization. PPCPs enmeshed with or sorbed to the organic material will leave the wastewater stream with the primary sludge. Traditionally the octanol/water distribution coefficient (K_{ow}) has been used to identify the likelihood of a compound partitioning to organic material. General guidelines for predicting whether the compound will be associated with the liquid or organic phase have been developed.
for uncharged compounds. However, many pharmaceuticals are ionizable with the charge being a function of the compound’s pKₐ and the solution pH, and K_{OW} is inadequate to predict sorption in this more complicated solution. Regression equations have been developed to incorporate the influence of more variables than K_{OW}; however these equations were developed using a very limited database. Further research is required to validate and possibly improve these equations. The same questions exist when predicting whether PPCPs will sorb to activated sludge and leave the wastewater stream with the WAS. Primary sludge and WAS are stabilized by aerobic or anaerobic digestion, and the digested biosolids are applied to agricultural land in some jurisdictions.

Secondary biological treatment removes organics and suspended solids from wastewater through microbial metabolism in the activated sludge. Reduction of PPCPs through biological treatment is an attractive option due to the possibility that the compounds of interest can be mineralized to carbon dioxide and water. Realistically, a WWTP will not be built to remove any specific trace contaminant or class of trace contaminants. Any design changes would be based on overall capacity to remove trace contaminants, and will not trespass on the plant’s capacity to remove aggregate organics and in some cases nitrogen and phosphorus. Consequently, research quantifying the reduction of specific PPCPs contributes to a database which can be used to make design decisions based on the weight of evidence.

Biological treatment of wastewater can be enhanced by increasing the solids retention time (SRT) and/or making use of different electron acceptors in the microbial population. Many WWTPs in Europe use longer SRT and different electron acceptors to achieve organic and nitrogen removal. Nitrogen removal is the net effect of nitrification and denitrification. Nitrification, the conversion of ammonia to nitrate, is achieved by slow growing autotrophic organisms whose maintenance in the system requires a longer SRT. Denitrification, the conversion of nitrate to nitrogen gas, occurs under anoxic conditions (i.e. growth using nitrate for cell respiration) and requires bacteria to switch from aerobic to anoxic respiration. Only a percentage of the bacterial population is capable of switching between respiration modes. When there are stringent limits on both effluent nitrogen and phosphorus, biological nutrient removal may be utilized. This treatment regime incorporates aerobic, anoxic and anaerobic zones. The presence of these different zones increases the diversity of the microbial population which enhances the possibility of mineralization of PPCPs; thus there are many reports of attempts to correlate treatment parameters with PPCPs reduction. Consistent correlations between SRT or treatment zones and PPCPs reduction remain elusive due to the large variability in wastewater characteristics, treatment systems, and results of PPCPs analysis. More study of controlled treatment systems is needed to elucidate the relationship between wastewater treatment parameters and reduction of PPCPs.

Advanced treatment of wastewater effluents using either ozonation or granulated activated carbon appears to be effective in removing/degrading PPCPs, based on a very limited dataset. To date, most studies have used pure compounds in a simple matrix. Further work with these technologies using final effluents will provide a better assessment of their capabilities. Other outstanding research questions include the possible inhibitory effect of antibiotics on current activated sludge performance, and the integration of research results with treatment plant models such as ToxChem™. The current state of research on the effects of PPCPs on aquatic ecosystems indicates that, at present, there is insufficient evidence of effects to justify the increased operating and capital costs associated with treatment technologies capable of removing PPCPs from wastewater.

Dr. Edward Topp, from the Southern Crop Protection and Food Research Centre of Agriculture and Agri-Food Canada, discussed technologies and practices for the land application of biosolids/manure as they related to reducing exposure to PPCPs.

Liquid municipal biosolids (LMB) are a source of nutrients for crop production. The application of this material to soil must be managed to minimize the risk of contamination of adjacent water resources with chemical or microbial agents that are of public or environmental health concern. This presentation gave a general overview of the control of environmental exposure to agricultural inputs, background information on the PPCPs content in human waste, research characterizing the off-site movement of PPCPs from fields receiving biosolids, and a preliminary analysis of the
relative contributions of agricultural use of biosolids and of wastewater effluents as a source of aquatic exposure to selected PPCPs in Ontario, Canada. In field studies, we applied LMB at a commercial rate using the recommended practices of either subsurface injection, or broadcast application followed by incorporation. The concentrations of PPCPs in surface runoff following broadcast incorporation of biosolids were generally low (i.e. ng/L), and could be effectively eliminated by injecting LMB below the soil surface. In field experiments, generally less mass of PPCPs moved to tile water draining field plots receiving biosolids applied with an AirWay device than from fields that received biosolids that were broadcast incorporated. Estimates of the total mass of the model PPCPs potentially released into aquatic environments in runoff from agricultural fields amended with biosolids in the province of Ontario were orders of magnitude lower than the total mass of these compounds estimated to be released in the effluent of Ontario WWTPs. A key knowledge gap remaining with respect to an exposure assessment of PPCPs from agriculture include detailed dissipation information on a wider range of chemicals, including antibiotics entrained in animal waste.

3.4 Environmental Risk Assessment

CEPA is jointly administered by the ministers of the Environment and Health and serves to protect the Canadian environment and health of Canadians. CEPA provides the legislative framework to carry out necessary functions such as information gathering, risk assessment, risk management, implementation of remedial measures, and compliance and enforcement for any new or existing substance in Canada. This group of presentations by Health Canada representatives provided the link between research and regulation for PPCPs in the Canadian Environment.

Gordon Stringer is the manager of the Environmental Impact Initiative Division of Health Canada. This group is tasked with the development of appropriate environmental assessment regulations for new substances contained in products regulated under the Food and Drug Act (F&DA), as well as developing best management practices, guidelines, or environmental stewardship plans to target specific routes of entry into the environment for F&DA products.

There is no abstract available for this presentation; Mr. Stringer’s contact information is included in Appendix B.

Andrew Beck, head of the Environmental Assessment Unit (EAU), NSACB at Health Canada provided an overview of the risk assessment process for substances that fall under the NSNR. Substances in F&DA products, including human pharmaceuticals and veterinary drugs, have been subject to the notification requirements of the New Substance Notification Regulations (NSNR) of CEPA since September 2001. This presentation reviews why these substances are subject to NSNR and why Health Canada is responsible for conducting the environmental risk assessments for these substances. An overview of the notification process is provided – including data requirements, assessment timelines and a brief introduction to the assessment tools used by evaluators at Health Canada. Since September 2001 the EAU of the NSACB within Health Canada has received approximately 400 new substance notifications (NSNs) for substances in F&DA products. Cosmetic ingredients have been the most common type of substance notified to date, consisting of 62% of all notifications received. Pharmaceutical substances consist of 21% of all substances notified. The majority of these submissions however, have been notified at the first notification level – a level that does not require the generation of environmental fate, distribution or effects data. This lack of experimental data is only one of the many challenges facing Health Canada in determining the risks these substances might pose to the environment. Other limitations or issues that need to be considered include the appropriateness of current notification trigger quantities, the types of fate and effects data that should be generated and the high degree of uncertainty associated with the use of existing fate/effects models and generic release scenarios. As a result, the research priorities for the EAU have and will continue to focus on filling these information gaps. Specifically, the need for additional environmental data on "classes" of substances would be beneficial, the suitability of existing physical, chemical, fate and effects models must be more closely investigated and, the significance of subtle chronic effects and how they are incorporated into the risk assessment process should be considered.

Pharmaceuticals and Personal Care Products in the Canadian Environment: Research and Policy Directions
Dr. Neil Tolson, head of the In-Commerce Substances Unit, New Substances Assessment and Control Bureau at Health Canada, provided an overview of challenges, approaches, and research needs for hazard and risk determination of In-Commerce substances.

The In Commerce List (ICL) contains approximately 9,000 substances in products regulated under the F&DA. The list contains a maximum of three pieces of information for each substance: CAS Name; CAS Registration Number; and, an alternate name. There is no information on use patterns, chemical structures, or estimated annual volumes.

Health Canada established the In Commerce Substances Unit to determine the potential human health and environmental impacts resulting from exposure to these substances in the environment and to recommend risk management measures, where required. The first task is to obtain a definitive identification of each substance and basic information needed for determination of potential hazards of these substances.

There is a need to develop appropriate procedures and tools for this work. The approach taken will utilize experience gained by Health Canada and Environment Canada in the categorization of the Domestic Substances List (DSL), taking into account the types of substances on the ICL and their life cycle. Consideration will be given to the use of predictive models, exposure scenarios, the use of empirical data vs. surrogate data, and combination of tools, and weight of evidence. Special attention will be given to mixtures of variable and unknown composition. These substances comprise an estimated 50% of the ICL substances. Consultations are being held within government and with industry, academia, and other regulatory jurisdictions to examine these issues.

The following areas of research were identified as being beneficial to work on the ICL: predictive models for fate and effects; expanded environmental studies on environmental concentrations; laboratory and field studies on chronic effects; Acute to Chronic Ratio (ACR); population effects; improved exposure scenarios; and effect of mixtures on aquatic and terrestrial species. There is also a need to consider best practices, e.g., new technologies for wastewater treatment plants, good veterinary and agricultural practices, good manufacturing practices, and disposal programs. Research partners include government laboratories, universities, and industry.

### 3.5 International and Industry Activities

Dr. Joanne Parrott of the Aquatic Ecosystem Protection Research Division of Environment Canada provided a summary of environmental risk assessment of pharmaceuticals (ERAPharm) in the European Union (EU).

ERAPharm is an EU funded project comprised of over forty scientists from 13 research institutions in 8 countries. The group is collaborating on a 3-year multi-million dollar research project to determine the data needs to assess the environmental risks of pharmaceuticals. The objectives of the project are to contribute to the improvement of knowledge and procedures for the environmental risk assessment of human and veterinary pharmaceuticals. ERAPharm will assess two model compounds, the human pharmaceutical atenolol (beta-blocker drug used to reduce heart rate) and the veterinary pharmaceutical ivermectin (an anti-parasitic drug used in cattle, horses, and sheep, as well as in aquacultures).

The scientists are assessing the biological fate, exposure pathways and ecotoxicological effects of the selected pharmaceuticals. Data from ERAPharm researchers will be used to fill out the current proposed environmental risk assessment frameworks (from the European Agency for the Evaluation of Medicinal Products (EMEA) and the International Cooperation on Harmonization of Pharmaceuticals and Personal Care Products in the Canadian Environment: Research and Policy Directions
Technical Requirements for the Registration of Veterinary Medicinal Products (VICH) in Europe, which will predict the potential environmental risks of these compounds under the current guidelines. Then, additional data will be generated in the ERAPharm project under the categories of ‘exposure assessment’ (fate processes and exposure modeling) and ‘effects assessment’ (bioanalytical tests, and bioassays with microorganisms, aquatic and terrestrial invertebrates, and fish) that may better predict the potential environmental risks of these compounds. The goal is to provide a more complete picture of the risk assessment for these chemicals, and to recommend tools for exposure assessment and effects assessment that will enhance our ability to predict environmental effects of these pharmaceuticals. Unique sets of data will be generated in the ERAPharm Project, and assembled to form complete example environmental risk assessments for these model pharmaceuticals.

The ultimate aim of ERAPharm is to develop improved guidance on the environmental risk assessment of pharmaceuticals. Tools generated in the project will include a web database containing information on fate and effects of pharmaceuticals, and a web screening-level risk assessment tool. Recommendations from the project will be used to refine the environmental risk assessment of human and veterinary pharmaceuticals, and will be of use to regulators, industry and the scientific community.

Dr. Mary Buzby, director of Global Safety and Environmental Technology for Merck Co. Inc., provided a summary of research and risk assessment activities by the Pharmaceutical Research and Manufacturers of America (PhRMA).

Improved analytical testing technology has made it possible to detect trace amounts of pharmaceuticals and other compounds in water at low concentrations. The pharmaceutical industry is using a science based approach to understand and address concerns resulting from detection of pharmaceutical compounds in the environment.

The PhATE (Pharmaceutical Assessment and Transport Evaluation) model was developed as a tool to estimate concentrations of active pharmaceutical ingredients (APIs) in United States surface waters that result from patient use (or consumption) of medicines. PhATE uses a mass balance approach to model predicted environmental concentrations (PECs) in 11 watersheds selected to be representative of most hydrologic regions of the United States. PhRMA has also developed the PhACT (Pharmaceutical Assessment and Characterization Tool) database to compile all of the peer-reviewed literature about aquatic effects, treatment, and environmental depletion of APIs. This information will be used to understand the potential for effects of APIs on aquatic organisms.

3.6 Provincial and Municipal Activities

Provincial and municipal jurisdictions do not generally undertake extensive research projects; however they contribute toward federal and university research activities and may also conduct monitoring programs geared to their local conditions and priorities. These presentations summarized activities in Alberta, Ontario, Quebec, and the Greater Vancouver Regional District.

Thorsten Hebben, a limnologist and water quality specialist in the Environmental Assurance Division of Alberta Environment, provided an overview of PPCPs and other organic wastewater contaminants in the province of Alberta.

In 2002-2003, Alberta Environment (AENV) undertook a preliminary survey of PPCPs and other organic wastewater contaminants (OWCs) in five rivers and seven WWTP outflows situated throughout the province. Of 105 studied compounds, several were detected at trace concentrations in both media. The results of this work led to the initiation of a quarterly monitoring program in 2004. Focused on a set of nine sampling sites located on five major rivers in Alberta, this project currently assesses surface water concentrations of 58 OWCs upstream and downstream of four major urban centres. To date, upstream detections of the sampled compounds have been relatively rare, while downstream detections are limited to 5 or 6 compounds that occur with some degree of regularity. In general, non-steroidal anti-inflammatory drugs and synthetic fragrances (musk) are detected most frequently and at the highest concentrations. More recently, AENV has
begun to examine a similar suite of OWCs in riverine sediments and fishes from several sites throughout the province. Although fish data are still pending, sediment analyses suggest that several compounds not detected in water samples, including some anti-depressants and antibiotics, tend to adsorb to sediment particles. Future efforts for AENV will include a focus on polybrominated diphenyl ethers (flame retardants) and perfluorinated compounds (surfactants) in major rivers, riverine sediments, and aquatic biota of the province.

Aside from AENV, a wide variety of groups and agencies in Alberta are currently working on the issue of emerging contaminants in surface-, drinking-, and wastewaters. Among these are Alberta Agriculture and Food (veterinary pharmaceuticals), the Universities of Alberta, Calgary, and Lethbridge, the City of Calgary, EPCOR (drinking water utility, Edmonton), and the Alberta Research Council (Vegreville). Most of these organizations are faced with similar knowledge gaps and challenges in dealing with the topic at hand. Among these is a paucity of information regarding various aspects of PPCPs and other OWCs, including fate, persistence, partitioning to sediments and biota, compound interactions, metabolites, isomers, human health considerations, and so forth. These issues are further complicated by a general lack of communication and collaboration, both on a provincial and national scale. Efforts to establish a provincial emerging contaminants network as a means of bridging these gaps are currently underway. Ultimately, it is hoped that this network will facilitate contact, discussion, and partnerships between the various groups and serve as a central repository of relevant information for those wishing to do related work in Alberta.

Dr. Sonya Kleywegt, a scientist with the Standards Development Branch of the Ontario Ministry of Environment, provided an overview of activities in the province of Ontario.

The Ontario Ministry of the Environment (MOE) encourages and contributes to investigations and research to identify and determine levels and fate of emerging contaminants in the environment, inclusive of pharmaceuticals and personal care products (PPCPs). The ministry has been actively involved in this research initiative for over 5 years. To address the issue of PPCPs in Ontario, the ministry is working towards building a database of the concentrations of PPCPs in all media to support setting scientifically defensible policies (standards or guidelines) if warranted.

To date the ministry has focused its research initiatives and support in three main areas which are;

1. Develop working analytical methods;
2. Quantify PPCP concentrations in different media and;
3. Minimize / eliminate PPCP discharges to the environment.

The ministry has developed a LC/MS-MS method to analyze for a suite of over 51 PPCPs in different environmental matrices.

The ministry has monitored for PPCPs in drinking water, surface waters and wastewater. In particular, we have collaborated with the; (1) University of Waterloo to conduct monitoring studies in drinking water plants and GUDI wells (2) Awwa Research Foundation to study the occurrence of PPCPs in the Detroit River and the efficiency of ozonation in removing these compounds (3) University of Ottawa and the Walkerton Clean Water Centre to investigate and assess a novel membrane technology to remove PPCPs from source water and, (4) University of Toronto to study various membranes and operating conditions for PPCP removal. The MOE has recently completed
a provincial wide survey to characterize the levels of PPCPs in raw and finished waters, their removal efficiencies associated with different treatment processes and seasonal variations.

In collaboration with Environment Canada, Agriculture and Agri-Food Canada, and Ontario universities, we have evaluated; (1) different treatment technologies and treatment processes for PPCP removal from wastewater (2) new Moving Bed BioReactor technology versus conventional treatment and PPCP removal at different stages of wastewater treatment (3) the removal/partitioning of these compounds during to the aerobic and anaerobic digestion processes (4) the impact of wastewater operating conditions on their removal (5) Tier 1 screening assays (for endocrine disruption) on fish exposed to wastewater and (6) incorporated passive water samplers for PPCPs into the Great Lakes Monitoring network.

Lastly, the ministry is working with the provincial and federal agriculture governments to develop best management practices to control the activities and quantities of biosolids and manure used in agricultural settings.

The most pressing challenges and issues facing the MOE are the limited analytical capacity and the difficulty to assess the long-term effects to humans or aquatic ecosystems from chronic, low-level, exposure to mixtures. Current risk assessment procedures do not address the implications of adversity and impairment at environmentally relevant concentrations nor do they consider chronic data. It should also be noted that pharmaceuticals and personal care products need to be assessed separately. There is a need to assess the uncertainty regarding the development of antibiotic microbial resistance and to consolidate research activities.

Caroline Robert, a scientist with the Water Policy group of the Ministry of Sustainable Development, Environment, and Parks, provided an overview of activities in the province of Quebec.

Québec’s Ministère du Développement durable, de l’Environnement et des Parcs started monitoring PPCPs in 2003. So far, samples have been periodically collected at six WWTP effluents, as well as at raw and treated water of eight water treatment plants. A total of five hormones and 34 PPCPs are analyzed, selected mainly from a list of substances detected by similar studies. Publication of a report summarizing the results and main findings is expected in 2007.

Andrew Marr, a senior engineer with the Utility Analysis and Environmental Management group of the Greater Vancouver Regional District (GVRD), summarized the PPCPs research activities of this large municipality.

Residues and metabolites of PPCPs can and do reach the receiving environment via municipal wastewater, whether they are used as directed, disposed of through the sewer system, or discarded with regular garbage. Local governments are tasked with the treatment of municipal wastewater, and held responsible for the environmental impacts of the discharge of treated effluent. However, that wastewater can often include inputs from sources which no local governments can completely control, and from substances that local governments can neither realistically prevent nor treat at end of pipe. For example, stormwater and urban run-off can at times contribute significantly to municipal wastewater through inflow & infiltration or through combined sewer overflows. Similarly, there are banned substances no longer in use or in production that are persistent and ubiquitous in the environment, and inevitably pass through municipal primary or secondary WWTPs which cannot effectively remove or treat them. Most of the effective tools for minimizing the amounts of PPCPs entering municipal wastewater are in the jurisdiction of senior governments. These include: regulation of product formulations, new Extended Producer Responsibility programs that make the manufacturing industries responsible for the collection and proper disposal of unused PPCPs, and increasing the effectiveness of existing industry PPCPs collection infrastructure.
4.0 Research and Policy Directions for PPCPs in the Canadian Environment

A major objective of this workshop was to identify research priorities, policy issues and action items based on the current state of knowledge and research on PPCPs in the Canadian environment. Participants from different sectors and disciplines were divided into small groups to facilitate discussion on specific issues or to develop actions plans arising from needs identified in the 2004 Workshop. The discussion groups included:

4.1 The state of PPCPs effects research in Canada;
4.2 Potential risk management approaches;
4.3 Developing a monitoring network for PPCPs;
4.4 Developing an inventory of PPCPs information/activities; and
4.5 Developing a consistent framework for PPCPs analysis.

Groups 1 and 2 were asked to identify the most pressing challenges, priority actions needed, and agencies that should be involved in these PPCP issues. Groups 3a, 3b, and 3c were asked to discuss action items arising from the previous PPCPs workshops: what each initiative should be designed to accomplish, who should be involved, next steps, and other topic-specific questions.

Group presentations to the plenary session, as well as invited presentations, generated questions and comments. Additionally each invited speaker was asked to provide their opinions on the challenges, gaps, and issues, the priority actions, and the partnership needs to clarify the research and policy directions for PPCPs in the Canadian environment. The following summary provides a synthesis of all these contributions to the discussion.

4.1 Effects of PPCPs on the Canadian Environment

The primary driver for the issue of PPCPs in the Canadian environment is the concern that long-term exposure to low levels of PPCPs residues could have adverse effects on aquatic and terrestrial ecosystems and/or human health. Individual PPCPs have been associated with adverse effects on growth and reproduction of selected aquatic organisms under controlled laboratory conditions. However “effects research” still has many unexplored facets in terms of species to investigate, endpoints to elucidate, combinations of compounds, etc. Group discussions identified four areas of effects research that they considered to be the most pressing:

1. Effects of PPCPs mixtures at the population and ecosystem levels;
2. Standardization of effects research;
3. Focusing on worst-case scenarios or model ecosystems; and
4. Enhancing communication.

Effects of Mixtures on Populations

PPCPs in the environment are always present in mixtures, which include pharmaceutical parent compounds, metabolites, and transformation products in addition to the already present organic
and metal compounds. Aquatic ecosystems are also mixtures of trophic levels in water and sediment matrices. Most laboratory studies to date have focused on one or two parent compounds and species of organisms at a time. New research from Europe, as presented by Dr. Karl Fent, has indicated the presence of synergistic or antagonistic effects with certain mixtures of PPCPs. There is a need to expand our capacity to characterize environmental mixtures and identify the effects of chronic exposure on populations; thus more accurately characterizing real environmental conditions at environmentally relevant concentrations.

The priority actions for improving our understanding of PPCPs in mixtures in ecosystems include:

- The use of Whole Effluent Toxicity (WET) studies, using more relevant (chronic) endpoints and exposure scenarios are required. Consideration should be given to synergistic and cumulative effects including the evaluation of a compounds mode of action;
- The use of both laboratory and field studies;
- Expanded analytical capability in terms of both laboratory capacity and methods for a wider variety of parent compounds and transformation products;
- Further studies on promising and developing bioindicators of population and ecosystem effects, particularly related to “genotoxicology” and metabolomics;
- Development of indicators of adversity and impairment to ecosystems;
- Improved (chronic) exposure scenarios;
- Multi-year funding to expand capabilities for long-term chronic effects studies at the ecosystem level.

These actions require the involvement of funding bodies, researchers, and municipalities to provide access to WWTP effluents.

**Standardized Effects Research**

Standardizing effects research would allow clearer comparison and confirmation of results between research laboratories. This type of research approach would require a consensus among researchers as to which substances should be tested on which organisms; the use of similar and environmentally-relevant end-points; the use of laboratory species rather than resident species; and the examination of multi-trophic effects.

The priority actions for standardizing effects research include:

- Determining those PPCPs that are most likely to be a problem and prioritizing substances to monitor (indicator compounds or mechanistic comparison);
- Determining which populations in an ecosystem most likely to be sensitive or vulnerable (e.g. mussels, bivalves, frogs, insects);
- Characterizing environmentally relevant exposure to chemicals;
- Evaluating potential effects at environmentally relevant concentrations and examining seasonal/reproductive cycle sensitivity of different species;
- Laboratory and field studies on chronic effects and Acute to Chronic Ratio (ACR) need to be considered;
- Effects studies need to include terrestrial ecosystems;
- Use of a top-down (directed by research consensus) rather than a bottom-up (directed by individuals) approach to drive additional research; and
- Ensuring that analytical methods are available for use on the selected priority substances.

Government and academic researchers, regulators, and funding bodies would need to be involved in decisions on research directions.
Focusing on Worst-case Scenarios or Model Ecosystems

Focusing on the worst case scenarios, in terms of both ecosystem vulnerability and PPCPs potency, involves looking at chronic effects rather than acute effects; conducting field environmental effects monitoring in areas where the most serious problems have been observed to occur or would most likely occur; and accounting for complicating factors such as seasonality and reproductive status. This approach would encourage multi-faceted studies in the selected areas (e.g. watersheds), which could then serve as model ecosystems for prediction of effects in other areas.

The priority action for this “worst-case” or model approach include:

- Identification of high-risk Canadian sites/ecosystems through the use of a monitoring network;
- Development of field sites useable by a diverse group of researchers, that are monitored and that demonstrate a gradient of environmental degradation;
- Design of focused studies with multiple partners on the identified high-risk sites;
- Identification of those PPCPs with higher potency or persistence;
- Predictive models for fate and effects;
- Adequate long-term funding in order to design and operate a comprehensive research program.

This approach to PPCP effects research would need the involvement of government and university researchers, municipalities, and perhaps PPCP industries.

Enhancing Communications

Enhancing communications regarding the issue of PPCPs in the Canadian environment includes:

- Communicating to the public the environmental effects and what it means for them;
- Improving the transfer of information among researchers and stakeholder organizations, and to decision-makers, to stay current on research activities and policy issues;
- Developing interactions between the scientists responsible for monitoring and assessment, and those with the opportunity to do research on biomarkers, bioindicators, and mechanisms;
- Improving communications across borders both within Canada and internationally; and
- Improving the dissemination of information, especially “Grey” literature, such as regulatory and unpublished information.

The priority action for enhancing communication would be the establishment of a coordinating network to monitor and disseminate PPCP research information. This could be done through one of the existing National Centres for Excellence, e.g. the Canadian Water Network. The federal government’s Domestic Substances List could be used as a starting point for cataloguing information.

Additional Concerns: Effects Research

In addition to the four priorities discussed above, workshop participants identified other concerns and needs in the area of effects research:

- Pharmaceutically active compounds and personal care products should be evaluated as independent groups of compounds due to their different chemical characteristics and use patterns. Pharmaceuticals are designed to have a biochemical effect on the target organism, and tend to be more water-soluble. Personal care products are designed for external use and tend to be more lipid-soluble. Restrictions on the use of problematic ingredients in personal care products are also easier to justify than restrictions on the use of pharmaceuticals.
UV filters must be better analyzed for hormonal effects on fish and other aquatic organisms. 

Assessment of the potential for PPCPs to affect human health. PhRMA and the Dutch government have both issued statements that the presence of PPCPs in the environment does not pose a human health risk. PhRMA is working with the USEPA to issue a similar statement.

4.2 Risk Management Approaches

Effects research to date continues to indicate that there may be cause for concern about adverse effects on environmental health due to the presence of PPCPs in environmental matrices. Wastewater effluent discharges and land application of biosolids and manures have been identified as important sources of PPCPs to the environment. If PPCPs discharges to the environment represent a risk to the health of the environment, management alternatives need to be identified to reduce or eliminate this risk. Group discussions identified three principal research needs to guide future risk management approaches:

- Continuing uncertainty of the issue and risk assessment needs;
- Identification of the most important sources of PPCPs to the environment;
- Source control and life cycle management programs.

Uncertainty of the Issue/Risk Assessment

The issue of PPCPs in the environment is not yet sufficiently understood. More study, quantifying environmental concentrations and observed effects at environmentally relevant concentrations, is needed in order to verify the assumption that there is a risk to be managed. Risk management follows risk assessment.

The priority actions to address this uncertainty include:

- Nationally coordinated research to support a regulated categorization program. Substances could be categorized, possibly by class or substance or on the predicted risk.
- More study of the presence of antibiotic resistance within WWTP activated sludge;
- Modifications to the current regulations so that PPCPs with low sales volumes, such as ethinylestradiol, must pass the risk assessment process (100 kg trigger value is inappropriate);
- Better coordination of the F&DA and the CEPA in the labeling and registration of new products;
- Investigation of the suitability of existing physical, chemical, fate and effects models;
- Incorporation of chronic effects data into the risk assessment process;
- More effects studies.

All levels of government (Health Canada, Environment Canada, provincial governments and municipalities), the pharmaceutical and personal care product industries, and academia need to be involved to create a coordinated research program.

Identification of Major Sources of PPCPs to the Environment

The current understanding of routes of PPCPs into the environment include wastewater effluent discharges, land application of biosolids and manures, and disposal of unused PPCPs to municipal wastewater and/or landfill leachate. There is insufficient information available to date to determine which of these sources are more important than others.

The priority actions to address this gap included:

- Quantifying loadings and concentrations of PPCPs to determine which sources are the most important (e.g. agricultural, WWTPs, landfill leachate or rural sources);
Determining the cost-effectiveness of both conventional and advanced drinking water, wastewater, and sludge treatment technologies;

Developing BMPs for land application of manures and biosolids.

All levels of government would be needed for this work: Health Canada, Environment Canada, provincial governments, and municipalities. If a research coordination entity is formed, that entity should include expertise to represent the practice as well as the theory of municipal wastewater management.

Source Control and Life Cycle Management Programs

Since it is anticipated that end-of-pipe treatment of PPCPs at WWTPs would be very costly, it is important to include source control and life cycle management programs as alternatives to reduce PPCPs discharges. This would include communicating the PPCPs issue to the public in plain language and raising public awareness of the consequences of the presence of PPCPs in the environment.

The priority actions needed to move forward with source control include:

- Collaboration by all stakeholders;
- Identification of critical control points;
- Increased and more efficient use of existing infrastructure for the collection of unwanted PPCPs;
- Education of the medical profession, and the public to encourage judicious use of PPCPs;
- Consideration of alternative formulations for pharmaceuticals.

Again, all levels of government would be needed for this initiative, with the addition of the pharmaceutical industry, pharmacist associations, the media, and the education system.

4.3 Developing a Monitoring Network

At the 2004 workshop “Towards a Monitoring Network”, participants identified the need to develop a monitoring network to increase the understanding of the presence and potential risks of PPCPs in the environment. It was proposed that a monitoring network could include concentrations of PPCPs in a variety of matrices and population dynamics of selected “sentinel” species. Group discussions focused on the elements of an action plan to initiate a monitoring network.

A monitoring network should include a website sub-divided into the following subject areas:

- Sources, loads and watershed mass balances;
- Fate through WWTPs;
- Fate through water treatment plants;
- Concentrations in environmental matrices: sediment, groundwater, surface water, biota, etc.;
- Ecological risk assessment and reports of field studies on effects;
- Human health risk assessment; and
- Analytical methods.
The purpose of the website would be to archive existing data, aid in the formation of hypotheses, support risk assessment exercises, and to help coordinate scientific research planning. Such an information source would identify collaboration opportunities, help to prevent duplication of efforts, and provide baseline data.

A monitoring network should be led at the national level and include champions from Environment Canada and Health Canada. The model for this network could be based on previous experience with the Toxic Substances Research Initiative (TSRI) or the Sustainable Forestry Management Network.

The monitoring should include compounds that are indicators of each major source of PPCPs to the environment (e.g., carbamazepine as a tracer for WWTP effluents) and compounds in high use. There are 10 to 15 compounds with various chemical and physical properties previously identified through categorization.

Strategic watersheds across Canada could be selected for intense and seasonal study. The watershed should be large, such as the Georgia Basin ecosystem or the St. Lawrence River basin.

The information generated from the monitoring should be available to scientists through portals on the website. Interpreted and peer reviewed results could be made available to the public.

A number of next steps were identified for implementing the monitoring network:

- Nominating champions from each region (the Water Quality Monitoring and Surveillance Directorate of Environment Canada is preparing a research project to rationalize water monitoring activities; research on human health effects from drinking water would be led by Health Canada);
- Establishing a Technical Steering Committee to help guide the process;
- Investigating what networks currently exist and examine different models (for example, wef.org, cwaa.org, weao.org; or owwa.org);
- Identifying who has resources to contribute;
- Identifying who is able to take the lead role;
- Investigating Quality Assurance/Quality Control (QA/QC) methods and developing inter-laboratory comparisons; and
- Prioritizing the compounds currently being monitored.

### 4.4 Developing an Inventory of Information and Activities

At the 2004 workshop “Towards a Monitoring Network” participants recommended that information on PPCPs and the environment should be available from some central location. Centralization of information could be accomplished by developing a specialized national database to capture:

- Transport and fate data;
- Research projects, participants, and results;
- Links to other PPCPs groups and websites;
- All predicted no-effect concentrations (PNECs), and
- Publications.

An inventory would be useful to compile technical information (such as toxicological properties, compound fate, and Chemical Management Plan (CMP) and media specific information), assist in risk assessment, and identify gaps in knowledge. It could also be used as a tool to assist research collaboration and target resources. The inventory should cover national and international information.

Development of an inventory would require the participation of federal and provincial governments to provide the necessary start-up and maintenance resources. The estimated costs for the network were approximately $200,000 to set up and $75,000 per year to maintain. Cooperation
from municipal governments, academia, and industry stakeholders would also be required to ensure a comprehensive product. Inventory entries would need to be filtered through peer-reviewed QA/QC standards to provide a context for the reported results. Access to the information should be restricted to stakeholders and to those who entered data or provided resources. The impact of Access to Information legislation would also have to be considered in this area.

The next steps identified for this action item include:

- Learn from the experience of others, such as the USEPA Endocrine Disrupting Chemicals program;
- Establish a lead on this (Ontario Ministry of Environment provisionally) with a Technical Steering Committee; and
- Commit resources.

4.5 Developing a Consistent Framework for Chemical Analysis

Analytical chemistry methods that quantify PPCPs in environmental matrices establish environmentally relevant concentrations that guide effects research and enable monitoring programs. The need for accurate, precise analytical methods that cover a wide range of PPCPs parent compounds and metabolites in surface water, groundwater, wastewater, drinking water, sediment, sludge, biosolids, manures, and biota, and the need for increased laboratory capacity across Canada were identified in all discussions.

The 2004 workshop “Towards a Monitoring Network” identified the need for collaboration between analytical laboratories, both domestic and international, to validate and compare methods for accuracy and precision, improve the exchange of knowledge, and reduce duplication in method development and research efforts. Discussions at this workshop recommended a framework designed to accomplish the following:

- A method compendium that is matrix dependent (acknowledging that matrices can vary);
- A mechanism to communicate methods with their respective method validation and QA/QC data;
- A data quality objective statement to characterize the method of QA/QC and the validation data requirements; and
- Performance criteria to ensure consistent data quality for conducting routine sample analysis.

All workshop participants are stakeholders for this action item. It was recommended that a national entity be formed, with international collaboration with organizations such as ERApharm, the USEPA, or the United States Geological Survey (USGS). The Ontario Ministry of the Environment Laboratory Services Branch, the Information and Quality Management group of Environment Canada, or the Canadian Association of Environmental Analytical Laboratories (CAEAL) have the experience to begin forming such a framework.
The next steps identified for this action item include:

- Interested laboratories need to take the initiative to coordinate and establish effective communication channels;
- These communication channels should ensure the sharing of validated methods, associated performance indicators (such as operation QC/QA data), and matrix effects and details;
- Gather knowledge on the current state of analytical science;
- Identify a group of target compounds from sources such as existing occurrence data, usage data, market data, toxicity data, risk assessment indicators, and the available analytical method of participant laboratories;
- Create Standard/Certified Reference Materials (SRM, CRM), and start an inter-laboratory round robin to obtain data and compare results;
- Expand the collaboration to make the most cost-effective use of resources in the development of new methods and acquisition of standards; and
- Establish long-term funding sources.
5.0 Overview of Policy and Management Issues

Clearly, the state of the science in Canada and beyond is not yet sufficiently evolved to compare potential policy options or even begin to develop a risk management strategy. However, with this 3rd Canadian workshop, organizers wanted to begin to explore policy and management issues more generally, the rationale being that there is a growing body of research not only on the possible risks of PPCPs in the environment, but also on the removal efficiencies of various wastewater treatment technologies and a growing recognition for the potential role of other preventative options for source water protection. Further, although the science continues to emerge, public awareness of this issue is growing rapidly, and it seems prudent to start to identify a suite of potential options for responding to this issue, and to better communicate those options to decision-makers.

Information for this section is derived from the Workshop speakers, from the discussions that ensued at the Workshop, and from related publications. This section does not deal with the regulatory risk assessment process per se; that is, the assessment and evaluation of specific substances, towards eventual potential regulation of their use. For more information on the risk assessment process in Canada, the reader is directed to Section 3.4 of this report.

Options for Managing Environmental Exposure to PPCPs

5.1 Wastewater Treatment

Although WWTPs are designed to remove solids, nutrients, and biodegradable organic matter, through their normal operation, these plants will also remove many types of PPCPs. Published research indicates that the most common sequence of treatment – primary settling followed by biological treatment, secondary clarification and disinfection – can remove over 90% of endocrine disrupting compounds from wastewater through degradation and/or partitioning (WERF, 2005).

Sewers are generally viewed as the dominant disposal path for PPCPs consumed by households, hospitals and industry. With thousands of different PPCPs in the market for human use in Canada, centralized WWTPs represent a major potential PPCP point source to the aquatic environment, and a major opportunity for centralized removal processes.

This, in combination with increased therapeutic drug use – Canadian drug expenditures grew by an average annual rate of 12.2% between 1985 to 1992 (CIHI, 2004) – rationalizes, to a large extent, the considerable research effort underway to explore PPCP removal mechanisms at centralized WWTPs.

In Europe for example, the EU project POSEIDON, funded between 2001 and 2004 as a major research priority of and supported by the EU’s 5th Framework Programme for Research, was aimed at assessing the optimal treatment technologies for both wastewater treatment and drinking water treatment processes. In the U.S., the Water Environment Research Foundation (WERF), American Water and Wastewater Association’s Research Foundation (AWWARF), WaterReuse Foundation and a range of research institutes and urban water agencies are developing a growing compendium of research results on the removal of PPCPs through wastewater treatment processes. In Canada, Environment Canada, the Ontario Ministry of Environment and several academics are engaged in PPCP and wastewater treatment research.

Summarizing research results in this area is not simple. The reader is directed to section 3.3 and 7.0 for additional information. Individual PPCPs have distinct chemical and physical properties that suggest potentially different mechanisms and locations for removal/reduction in a WWTP. Reduction measurements are further complicated by biological transformations, the effects of mixtures, hydraulic and temperature variations, analytical limitations and the combination of treatment processes in a WWTP. Advanced treatment such as ozonation, activated carbon, and tight membrane filtration are receiving considerable attention, while research into a better understanding of removal in conventional treatment (primary, secondary and tertiary) remains active. Understanding removal in conventional treatment is particularly important in the
Canadian context since the additional cost of advanced treatment tends to be incurred only where wastewater reuse is necessary, such as in parts of Europe and the southern U.S., and the need for wastewater reuse in Canada is minimal at present. Although the current lack of evidence on widespread environmental effects makes it premature to justify increased operating and capital costs, most researchers conclude that centralized municipal wastewater treatment has the potential to make a significant contribution to reducing the load of PPCPs to the aquatic environment. If and when toxicological effects evidence is sufficient to warrant additional treatment, it is practicable that abatement design will not be tailored to an individual compound but based rather on overall capacity to remove trace contaminants. Until then, research in this area remains of fundamental importance.

5.2 Drinking Water Treatment

Although existing research and new analytical capabilities have detected certain PPCPs in raw drinking water sources, they have generally been found in orders of magnitude below any daily therapeutic dose. Concerns have, however, arisen over potential health effects related to the consumption of drinking water including antibiotic resistance and unknown potential long term chronic effects caused by the intake of mixtures of PPCPs in low concentrations to individuals during sensitive life stages.

Generally where research is underway in this area in Europe and the U.S., it is frequently in the context of better understanding the removal of EDCs during centralized water reclamation/reuse processes. In the Great Lakes, a number of partners have assessed, and continue to investigate, the occurrence of pharmaceuticals and endocrine disrupting chemicals in the Detroit River, and the effectiveness of ozone in degrading these compounds (see Jasim summary in section 3.3).

Reviews of the science are less plentiful here though von Gunten et al. (2006) provide a recent summary of the state of knowledge on the removal of PPCPs during drinking water treatment:

- The raw water of waterworks using surface water is likely to be contaminated by many pharmaceuticals whereas the presence of pharmaceuticals in groundwater is rather unlikely. Depending on the water treatment, finished drinking water might contain pharmaceuticals at very low concentrations;
- Ozonation, activated carbon, and nanofiltration are very efficient treatment processes for the removal of PPCPs. Treatment trains using these advanced techniques are effective to prevent drinking water contamination by most pharmaceuticals;
- Waterworks that treat groundwater have short treatment lines if any, frequently consisting only of disinfection with e.g. chlorine or UV; these processes are inadequate to eliminate most polar pharmaceuticals;
- Iodinated contrast media are among the compounds found most often in drinking water, since they generally persist after activated carbon treatment as well as oxidation processes such as ozonation. The only options to guarantee a complete elimination are nanofiltration, reverse osmosis and activated carbon filtration with frequent renewal or regeneration;
- Only in a very few cases do the concentrations of pharmaceuticals in drinking water exceed the maximum European concentration level of 0.1 µg/L required for individual pesticides;
Even if the highest concentration of individual pharmaceuticals reported for drinking water is considered for the assessment of effects on humans, based on the current knowledge, adverse effects via the consumption of drinking water are very unlikely.

5.3 Source Control, Prudent Use, and Source Separation

Another general category of management options that received discussion at this workshop and has garnered more attention in other publications, is that of preventing PPCPs from entering the wastewater stream in the first place. The potentially high cost of advanced centralized treatment options for PPCPS has also generated more interest in reductions at the source. Consequently, at this time, source control and source separation options are seen as a complement to end-of-pipe treatment, though it remains to be tested whether source control / source separation options represent the most cost, energy and removal efficient approach.

Source control generally refers to managing which compounds and how much of them enter the water system. Essentially, effective source control reduces the consumed quantities as well as the ecological exposure of selected compounds. Existing literature suggests several options here:

- **Ecolabelling** – Eco-labelling aims to provide consumers with trustworthy information on the ecological soundness of products, allowing them to opt for more environmental friendly products. Schemes to assess specific product groups within personal care products already exist. The Nordic European countries have set up criteria for ecolabel awards for shampoo, body shampoo, liquid and solid soaps. Strategies for ecolabelling of pharmaceuticals are also being developed in Europe (Joss et al., 2006b).

- **Product take-back programs** – Pharmaceutical producers have been particularly active in setting up programs allowing consumers to return (at no charge) their residual medications to pharmacies. The pharmaceutical industry of British Columbia, for example, voluntarily established the Medications Return Program in 1996. As of 2004, over 90 per cent of pharmacies in the province participate in it (BC MOE, 2007), though more research is needed to assess the cost-effectiveness of these programs (e.g. types and amounts of medicine being collected, the participation rates, regulatory compliance issues, programs costs, funding sources and final disposal). In Canada, the Post Consumer Pharmaceutical Stewardship Association’s (PCPSA) website provides updates on various province-wide and municipal take-back programs (www.medicationsreturn.ca).

- **Reducing medical consumption** – Clearly many medications are essential and for some drugs, no substitute exists to date. However in some cases, it is possible to opt for alternate therapeutic choices and supporting complementary strategies (e.g. improved sanitation, nutrition and access to general health care). Sweden is developing an environmental classification of pharmaceuticals which will help health care workers choose less persistent and bio-accumulative drugs when deciding on a prescribed therapy.

- **Education** – Education campaigns and programs aimed at providing information on the effects of PPCPs in the environment and on available solutions are a critical component of increasing the uptake of other source control alternatives. The actions taken by the public will inevitably impact all other initiatives and can make a major contribution towards reducing PPCP residuals entering the environment.

- **Fostering a product stewardship culture** – Often called extended producer responsibility or life cycle management, this option involves the process of managing the entire life cycle of a product from its conception, through design and manufacture, to service and disposal programs. It means improved product stewardship by extending the responsibility of industry and services sectors towards the effects of their product on the environment. Various measures, voluntary or legislated, can induce a shift to more environmentally friendly products and can influence the pace at which new solutions enter the market. Enhanced attention to life cycle management programs is one key need identified from this workshop.
Prudent use of veterinary drugs in agriculture – Conventional livestock production systems typically use antibiotics therapeutically, prophylactically, and to enhance feed conversion. Although the role of agricultural use in promoting the resistance of bacteria to antibiotics generally is difficult to define, the consensus in the scientific community is that the widest approach is to adopt a practice of “prudent use”. This consists essentially of implementing various management practices to minimize the use of antibiotics consumed for all purposes, and avoiding the veterinary use of drugs that are employed in human medicine. Some livestock systems (e.g. organic) characteristically use fewer pharmaceuticals.

Source control initiatives involve a variety of stakeholders from consumers to physicians to industry. Consequently, significant changes will require concerted action from all parties. Some initiatives like ecolabelling and education are synergistic: they can initiate the public discourse necessary to trigger voluntary product stewardship from the industry, and the demand for eco-labelled products will drive the supply. Many voluntary programs have been quite successful to date, however, back-up by legislation can achieve broader compliance.

Source separation is a specific form of source control, involving separating and treating concentrated PPCP waste streams before discharging into the wastewater collection system, where they will mix with and affect the quality of all wastewater. Options include:

- **On-site treatment** – treating industrial, hospital and nursing home wastewaters before discharge will prevent waters with high concentrations of specific compounds from “contaminating” waters with much lower PPCP concentrations. More aggressively, local authorities can regulate the composition of wastewaters entering the sewers through sewer use by-laws. With respect to health care facilities specifically, the American not-for-profit organization Hospitals for a Healthy Environment has developed a blueprint for managing/minimizing pharmaceutical waste at health care facilities (Pines, 2006).

- **Disposal of unused pharmaceuticals** – Complementing the take-back programs, developing predetermined pathways for disposal of unused pharmaceuticals to prevent disposal in sewers or dump sites represents another understudied area. Conveyance to incineration, however, may not be viewed as a sustainable option here, and more research on suitable pathways is needed.

- **Urine separation** – Urine separation upon excretion is one of the most efficient domestic measures of source separation. Since a large proportion of ingested pharmaceuticals are excreted via urine, separation of this waste stream allows collection of a significant amount of the total pharmaceutical consumption at a concentration about 100 times higher than that in municipal wastewater (IWA, 2006). This remains an active research area.

### 5.4 Biosolids Management and Agricultural Best Management Practices (BMPs)

Sludge consists of the solid portion of municipal wastewater plus the solids generated during wastewater treatment. This sludge is stabilized and reduced in volume through aerobic or anaerobic digestion producing biosolids. Biosolids at the plant can be treated according to different standards, depending on the end use. Jones-Lepp and Stevens (2007) provide an overview of pathogens- and pollutant-based regulatory standards currently in place in the US and EU. In Canada, biosolids are generally applied to agricultural land if they meet provincial regulations for heavy metals content. Biosolids which do not meet land application requirements can be disposed of in landfills, or incinerated. Land application is the preferred method of biosolids from the perspective of recycling nutrients and organic matter back into the soil for crop production.
Sorptive PPCPs will partition from the aqueous phase into solids during wastewater treatment, and land application of biosolids may be a more important route of environmental exposure than sewage outflows. (Kinney et al. 2006; Jones-Lepp & Stevens 2007; NAS 2002). Generally, knowledge is still limited on the fate and transport of PPCPs in land application and studies have detected only very low levels of PPCPs in the runoff from agricultural fields (WERF, 2005; Xia et al. 2005). Biosolids better management practices (BMPs) are intended to minimize the transport of biosolids components including PPCPs from the point of application to adjacent water. Current research is investigating the effectiveness of surface versus injection applications; buffer zones between application areas and watercourses; and application before or after rain events.

Other considerations in land application of biosolids include the potential effects of PPCPs on soil organisms; uptake by crops; and the dissipation kinetics and pathways in soil. Research on management options for land applied biosolids falls into two categories: 1. improved treatment of sludge prior to its application; and 2. use of BMPs during their application on land. Work on BMPs indicates that the greatest exposure risk is at or shortly after the time of biosolids application (see Topp summary in this proceedings). The risk of transportation through runoff or leaching is greatest before PPCPs residuals can bind to soil particles. Mixing the biosolids with soil at application could reduce the risk of runoff.
6.0 Workshop Conclusions

The National workshop on “Pharmaceuticals and Personal Care Products in the Canadian Environment: Research and Policy Directions” was very successful based on the number and diversity of participants, the animated discussions, and the positive feedback.

Participants strongly supported the need to develop frameworks and models for furthering and communicating our knowledge of PPCPs in the Canadian environment. All levels of government and industry have expressed an interest in taking action. What is needed now is a lead to be identified and for funding to be provided to initiate the activities that have been identified in all three workshops.

The results of this workshop provide additional direction for actions that could be taken to gain a better understanding of the impacts of PPCPs on the environment health. In particular, the participants identified major gaps in the knowledge base, and the need for standardized monitoring and environmental effects monitoring. They identified the need to communicate with each other in a more effective way as well as with the general public.

While risk management approaches were considered, there are still several issues to be resolved. There is still much uncertainty associated with PPCPs in the environment and problems in understanding how chemicals work in combination. In addition, the most important sources of PPCPs have yet to be determined, and, when applicable, source control approaches need to be established and/or enhanced.

Participants supported the need for a monitoring network, an inventory of activities, and a consistent framework for PPCPs analysis, and provided specific advice on how to create and maintain these activities. Overall, they felt that the issue of PPCPs should be addressed on a large scale watershed basis.

A common theme in all discussion areas was the importance of communication between researchers, risk assessors, regulators, wastewater managers, and the public. The formation of a central “clearinghouse” for research and management data was recommended to enhance communication and exchange of information. To maintain momentum on this issue and strengthen relationships between interested parties, it is also recommended that a follow-up workshop be convened in February 2009.
7.0 References and Recommended Reading


Caminada D., Escher C., Fent K. 2006. Cytotoxicity of pharmaceuticals found in aquatic systems: comparison of PLHC-1 and RTG-2 fish cell lines. *Aquatic Toxicology* 79: 114-123.


APPENDIX A: Workshop Agenda

Purpose:
Build on the success of the 2 previous Niagara-on-the-Lake workshops (2002 and 2004) to maintain momentum on PPCPs research in Canada and explore policy implications.

Format:
- Overview presentations on the current state of research and policy.
- One-half day of open discussion guided by a professional facilitator.
- Concurrent poster session to display research details.

Deliverables:
1. Compendium of the state of the science
2. Limited list of priorities, identification of policy issues and action items
3. Development of research partnerships to address gaps identified
4. Abstracts from research posters

Day 1: Monday March 5

<table>
<thead>
<tr>
<th>Time</th>
<th>Topic</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:30 - 5:00</td>
<td>Arrival, Hotel and Workshop sign-in</td>
<td>Atrium / Grand Georgian Ballroom</td>
</tr>
<tr>
<td>3:00 - 7:00</td>
<td>Poster Session</td>
<td>Grand Georgian Ballroom</td>
</tr>
<tr>
<td>6:00</td>
<td>Welcome and Introductions</td>
<td>Organizing Committee</td>
</tr>
<tr>
<td>6:00</td>
<td>Opening remarks</td>
<td>John Carey, Environment Canada</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Andrew Beck, Health Canada</td>
</tr>
<tr>
<td>6:15 – 7:00</td>
<td>Keynote speaker: “Pharmaceuticals and UV absorbing compounds (UV filters): Effects in the aquatic environment”</td>
<td>Karl Fent, University of Applied Sciences, Muttenz, Switzerland</td>
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<tr>
<td>7:00 – 10:00</td>
<td>Adjourn and Dinner</td>
<td>Tiara Dining Room, Sponsored by the Canadian Water Network</td>
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Day 2: Tuesday March 6

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<tr>
<th>Time</th>
<th>Topic</th>
<th>Speaker</th>
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<tbody>
<tr>
<td>7:30</td>
<td>Sign-In</td>
<td>Atrium / Grand Georgian Ballroom</td>
</tr>
<tr>
<td>7:30</td>
<td>Breakfast</td>
<td>Tiara Dining Room</td>
</tr>
<tr>
<td>8:45</td>
<td>Agenda Review</td>
<td>Lura Consulting</td>
</tr>
<tr>
<td>9:00</td>
<td>Exposure and monitoring: Then and now 2002 – 2006</td>
<td>Mark Servos, Canadian Water Network</td>
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<tr>
<td>9:30</td>
<td>Exposure and monitoring: Environment Canada mandate and activities</td>
<td>Sean Backus, Water Quality Monitoring and Surveillance, Environment Canada (EC)</td>
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<tr>
<td>9:45</td>
<td>Provincial activities: Alberta</td>
<td>Thorsten Hebben, Environmental Assurance Division, Alberta Environment</td>
</tr>
<tr>
<td>10:00</td>
<td>Provincial activities: Ontario</td>
<td>Sonya Kleywegt, Standards Development Branch, Ontario Ministry of Environment</td>
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<tr>
<td>10:15</td>
<td>Coffee Break, Atrium</td>
<td>Poster Session, Grand Georgian Ballroom</td>
</tr>
<tr>
<td>10:45</td>
<td>Environmental effects: Environment Canada research</td>
<td>François Gagné, EC Aquatic Ecosystem Protection Research Division</td>
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<tr>
<td>11:15</td>
<td>Environmental effects: Freshwater ecosystems</td>
<td>Tom Moon, Department of Biology, University of Ottawa</td>
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<tr>
<td>11:45</td>
<td>Environmental effects: Marine ecosystems</td>
<td>Katsuji Haya, Marine Environmental Sciences Division, Fisheries and Oceans Canada</td>
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### Day 3: Wednesday March 7

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<tr>
<td>7:30</td>
<td>Breakfast</td>
<td>Tiara Dining Room</td>
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<tr>
<td>8:30</td>
<td>Synopsis of Day 2</td>
<td>Lura Consulting</td>
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<tr>
<td>8:40</td>
<td>Health Canada: Environmental regulations under CEPA</td>
<td>Gordon Stringer, Policy Planning and International Affairs Directorate, Health Canada (HC)</td>
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<td>9:05</td>
<td>Health Canada: Risk assessment</td>
<td>Andrew Beck, HC New Substances Assessment &amp; Control Bureau</td>
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<tr>
<td>9:30</td>
<td>Health Canada: In-commerce substances</td>
<td>Neil Tolson, HC New Substances Assessment &amp; Control Bureau</td>
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<td>9:55</td>
<td>ERAPharm Project: Environmental Risk Assessments</td>
<td>Joanne Parrott, EC Aquatic Ecosystem Protection Research Division</td>
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<tr>
<td>10:15</td>
<td>Coffee Break, Atrium</td>
<td>Poster Session, Grand Georgian Ballroom</td>
</tr>
<tr>
<td>10:45</td>
<td>Municipal wastewater management: Vancouver</td>
<td>Andrew Marr, Utility Analysis and Environmental Management - Greater Vancouver District Regional District</td>
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<tr>
<td>11:00</td>
<td>Provincial activities: Québec</td>
<td>Caroline Robert, Quebec Ministry of Sustainable Development, Environment, and Parks</td>
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<td>11:15</td>
<td>Charge to attendees</td>
<td>Lura Consulting</td>
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<td>11:30</td>
<td>Lunch, Tiara Dining Room</td>
<td>Sponsored by the Walkerton Clean Water Centre</td>
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<td>12:30</td>
<td>Break out groups: Facilitator driven</td>
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<tr>
<td>2:00</td>
<td>Coffee Break, Atrium</td>
<td>Poster Session, Grand Georgian Ballroom</td>
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<tr>
<td>2:30</td>
<td>Synthesis and Open discussion</td>
<td>Lura Consulting</td>
</tr>
<tr>
<td>3:50</td>
<td>Closing Remarks</td>
<td>Organizing Committee</td>
</tr>
<tr>
<td>4:00</td>
<td>Adjourn</td>
<td></td>
</tr>
</tbody>
</table>
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APPENDIX C: Poster Abstracts

Acidic pharmaceuticals in surface waters of selected Ontario watersheds
Donald T. Bennie and John Struger*
Water Science and Technology Directorate, Environment Canada, Burlington, Ontario
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Pharmaceutical products are used to control human diseases and conditions as well as enhance animal health and increase food production efficiency. These substances enter the environment via WWTP effluent discharges, land application of sewage sludges and agricultural animal wastes. This study set out to determine the temporal occurrence of acidic pharmaceuticals in surface waters at 6 sites in Hamilton Harbour (HH) and 6 sites in the Grand River in southern Ontario. Both watersheds receive multiple inputs from WWTPs. Monthly samples were collected from these locations from May 2003 to May 2004 and were analyzed for 12 acidic pharmaceuticals. Preliminary data shows four pharmaceuticals were detected regularly at levels above analytical detection limits. Those substances were ibuprofen, gemfibrozil, naproxen and triclosan. The maximum concentrations found in the study were 1590, 103, 753 and 428 ng/L, respectively. Other detectable substances include clofibric acid, salicylic acid, diclofenac, indomethacin and fenofibrate. In HH, concentrations of pharmaceuticals decrease significantly in the gradient from the WWTPs to the Harbour to Lake Ontario. Distribution patterns on the Grand River are different due to the increased number of WWTP discharge contributions at periodic intervals to the River.

Lifecycle exposure to municipal wastewater effluent decreases egg production and male sex characteristics of fathead minnows.
Joanne Parrott*, Beverley Blunt, Cheryl Sullivan, and Don Bennie.
Water Science and Technology Directorate, Environment Canada, Burlington, Ontario
*Joanne.Parrott@ec.gc.ca
Assessing the effects of municipal wastewater effluents (MWWEs) on fish poses a challenge, as the effluents are complex mixtures of nutrients, metals, oils, with traces of hormones and pharmaceutical drugs and personal care products. Some pharmaceuticals discharged in MWWEs can have profound endocrine disrupting effects on fish. Assessment of the effects of very low concentrations (1-10 ng/L) of pure endocrine disrupting substances (estrogens and androgens) allows the development of sensitive and predictive fish tests that can assess the potential reproductive effects of complex mixed municipal effluents. Laboratory lifecycle exposure to an Ontario MWWF (100%) caused a decrease in egg production and decreases in male secondary sex characteristics of fathead minnows, although both male and female fish exposed to MWWF grew as well as or better than control fish. For assessing the endocrine disrupting potential of pharmaceuticals, long term fish tests of real MWWEs provide clues that will link to the health and reproductive performance of wild fish.

Presence and Seasonal Variability of Pharmaceuticals in Southern Ontario Drinking Water Supplies
Kormos, J.1, Yang, P.2, Hao, C.2, Kleywegt, S.3, Oakes, K.1, Cheung, P.4, Socha, A.5, Whitehead, B.4 and Servos, M.1*
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3 Standards Development Branch, Ontario Ministry of the Environment, Toronto, Ontario
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It has been well documented that pharmaceuticals are widespread environmental contaminants. These compounds have been detected in different matrices including wastewater treatment plant effluents, surface waters, sediments, soils, groundwater and to a lesser extent drinking water supplies. Few studies have investigated the presence of these contaminants in drinking water supplies, with most studies focusing on a limited number of compounds and utilizing a small sample size. The current project investigates the presence and seasonal variability of different therapeutic classes of pharmaceuticals in raw and treated water samples from two drinking water facilities in southern Ontario. Water samples were collected at monthly intervals for one year to help characterize the seasonal variability of these contaminants. A pilot study also investigated the presence of these compounds in raw water samples collected from groundwater wells, which were potentially under the influence of surface water (i.e. susceptible GUDI wells). All samples were extracted by solid-phase extraction techniques, separated by high performance liquid chromatography and detected using a triple quadrupole mass spectrometer. The concentrations found in the water samples have been in the low ng/L range, with higher concentrations detected in the raw water than the treated water. In general, human pharmaceuticals (i.e. gemfibrozil, ibuprofen and carbamazepine) were detected in raw and treated water samples. Seasonal variability was also observed in the concentrations and compounds detected, which might be explained by changes in surface water hydrology and point sources of contamination over each season. The results also show the impact water treatment processes have on the ability to reduce these contaminants during drinking water production.
Sorption and Partitioning Behaviour of Selected Trace Polycyclic Synthetic Musks in a Suspended Growth Aerobic Activated Sludge System

Vince Pileggi1,2, Lori A. Lishman2, Steven N. Liss1*

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The removal of polycyclic synthetic musks (PSMs), with respect to operating conditions in the activated sludge treatment process is of current interest due to the potential to reduce environmental impacts on aquatic organisms and impacts from the land utilization of sewage sludges, through process optimization. This study investigated the influence of solids retention time (SRT) and temperature (T) on selected activated sludge properties and how sludge properties influenced the sorption behaviour of selected trace polycyclic synthetic musks of environmental concern.

Bench scale sequencing batch reactors (SBRs) fed municipal wastewater were employed in the study. These reactors were operated under well-controlled conditions which permitted examination of the influence of T (10 and 20°C) and SRT (3.5 and 10.5 days) on sludge properties and behaviour of PSMs. The selected PSMs monitored included Cashmeran, Celestolide, Phantolide, Traseolide, Galaxolide and Tonalide. The reduction of PSMs from the aqueous phase ranged from 62 to 80%, and the total PSMs associated with sludge was found to be between 15 and 27 µg/g dry matter. Galaxolide and Tonalide were found to represent over 95% of the total PSMs in both the aqueous and solid phases. The lowest concentration of PSMs associated with solids was observed at a SRT of 10.5 days when operated at 20°C, conditions which resulted in nitrification. SRT was the dominant operational factor, followed by T and T×SRT which influenced selected sludge properties and the partitioning of the PSMs. For PSMs, Freundlich equilibrium sorption and desorption isotherms were determined using lyophilized sludge. The results showed significant SRT dependencies under sorption conditions.

The relative hydrophobicity (RH) and total extracellular polymeric substances (EPS) of sludge, showed a significant increase (p < 0.05) with an increase of SRT and strong linear positive correlation (r² = 0.7 and 0.8, respectively) with increased removal of PSMs from the aqueous phase. The log octanol-water partition coefficients (log KOW) of the PSMs showed a good linear correlation (r² = 0.9) with the solids-aqueous partition coefficients (log KP, KP=CS/CL (L/kg)). The mean log KP range was between 3.7 to 4.5 L/kg for all the PSMs with the exception of Cashmeran (2.1 to 2.5 L/kg) and the KP showed a significant difference (p < 0.05) between sludges for Celestolide, Phantolide and Galaxolide.

Occurrence of Bioactive Pharmaceutical and Endocrine Disrupting Compounds in Source and Finished Drinking Water in Ontario, Canada

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Drinking-water quality affects public health directly. The Drinking Water Surveillance Program (DWSP) of the Ministry of the Environment is a voluntary program operated by the ministry, and in cooperation with municipalities, to acquire monitoring data on drinking-water quality in Ontario. This presentation reports preliminary results of a DWSP study from September 2005 to November 2006, with an emphasis on the occurrence and environmental background concentrations of bioactive pharmaceutical and personal care products (PPCPs) and endocrine disrupting compounds (EDCs) in various selected locations in Ontario. The goal was to gain an initial understanding of this group of compounds, and to assess the PPCPs and EDC removal efficiency of different types of drinking-water treatment processes.

Forty-eight PPCPs and EDCs including antibiotics, acidic, neutral and basic drugs, hormones and veterinary drugs, were selected as target compounds. Samples were collected on a monthly schedule, pre-concentrated from 800-mL to 5 mL using a single solid phase extraction (SPE) to a final sample volume of 0.1 mL, and analyzed by three liquid chromatography/tandem mass spectrometry (LC-MS-MS) methods. Among these 48 targets, the most frequently detected were carbamazepine, gemfibrozil, ibuprofen, bisphenol A, lincomycin, naproxen, monensin, sulfamethoxazole, tylosin, trimethoprim, bezafibrate, and acetaminophen. Analytical results also indicated that the existing drinking-water treatment process can decrease levels of these targets except bisphenol A, which may come from the numerous plastic products used in the treatment plants.
Management Strategies for Human Pharmaceuticals in the Environment
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Over the past decade, pharmaceuticals (PhACs) have been detected in Canadian wastewater effluent, surface water, and occasionally groundwater and drinking water. Scientific studies suggest that they may represent a risk to aquatic organisms, and possibly even human health. The precautionary principle, outlined in the Canadian Environmental Protection Act (1999), states, “Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.” This principle suggests that management strategies and policies to mitigate the environmental impacts of pharmaceuticals should be developed and possibly implemented. Here, we present the results of a consultation of international stakeholders from government, academia, and the pharmaceutical industry, on management strategies for human pharmaceuticals. Furthermore, an analysis of management options within a Canadian context is conducted. We suggest that governments at various levels can act to minimize the release of PhACs to the environment through a combination of strategies including pharmaceutical returns programs, education, and improvements to wastewater treatment.

Veterinary Pharmaceuticals in the Fraser Valley, BC: Status of Investigation
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Management of animal wastes is a significant concern, especially in areas of intensive livestock production. In addition to the potential to overload soil nutrient levels in the field and aquatic ecosystems, animal waste may contain numerous veterinary pharmaceuticals. The public health implications of antimicrobial resistance have received much attention; however, little information is available on the environmental fate and impact of these compounds.

In British Columbia, Fraser Valley, the first steps in determining the environmental impact of those compounds have been made. Methodologies to detect veterinary pharmaceuticals used in the poultry and dairy industries have been developed and preliminary sampling has detected some of them in animal wastes and soil samples. For the veterinary pharmaceuticals detected, assessment of the possible biological impacts on soil dwelling organisms (e.g. isopods and worms) at environmentally meaningful concentrations is in the planning stage.

From Safe Products to Safe Environments: The Cosmetic Ingredient Hotlist.
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INTRODUCTION: The presence of chemical ingredients in pharmaceuticals and personal care products (i.e., cosmetics) as trace environmental pollutants, originating from consumer use and action, continues to become more firmly established. As more is learned about possible environmental hazards, there is a greater need for a range of control measures to minimize the environmental load of substances. The Cosmetic Ingredient Hotlist is one possible tool.

OBJECTIVE: A major objective of the investigation was to minimize public health risks from the use of a newly imported non-oxidative hair dye shampoo containing a colouring agent, p-phenylenediamine (PPD) and an anionic detergent, sodium lauryl sulphate (SLS). This is one example of how cosmetic risks are dealt with and how ingredients of concern are ultimately controlled on the Cosmetic Ingredient Hotlist. This can also serve as an example of a possible control/reduction measure to minimize the disposition of substances in cosmetics into the environment, thus also reducing indirect exposure to ingredients of concern.

DESIGN: We applied the HC Decision-Making Framework, which drives the decisions that affect the acceptability of cosmetic products and their ingredients. An in-depth investigation into the chemistry and safety of the hair dye shampoo provided the scientific information to be used in the decision-making process. The quantitative and qualitative analyses of the product were conducted using the GC-MS method.

OUTPUTS/RESULTS: We found that the use of the product caused injury from a combination of irritation and contact allergy from PPD and SLS. The elevated PPD level was due to the absence of an oxidizing agent,
which accelerates a polymerisation reaction of the dying process. Based on our findings, the product posed a health risk and was therefore in violation of section 16(a) of the Food and Drugs Act. We recommended that the product be either removed from sale and reformulated to meet Canadian safety standards for cosmetics.

IMPACTS/OUTCOMES/CONCLUSIONS: Our work resulted in changes to the Cosmetic Ingredient Hotlist with respect to PPD’s use in hair dyes and removal of the product of concern from sale. Limiting PPD to oxidative hair dyes and reducing exposure to SLS protect consumers from undue risks. At the same time, promoting safer products can minimize their potential to affect the environmental health.

Modeling Alkylphenol Ethoxylate Biotransformation in Municipal Wastewater Treatment
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Constituents in treated municipal wastewater effluents, such as synthetic hormones, pesticides and industrial chemicals in commercial products, can exert endocrine disrupting properties in receiving waters. One group of constituents that has been scrutinized intensively for their endocrine-disrupting potential is alkylphenol ethoxylates (APEs).

Wastewater surveys have identified the fate of the most stable metabolites (e.g. alkylphenols with one or two ethoxylate units, also designated APE1-2), different metabolic pathways under aerobic and anaerobic conditions, and the formation of ether carboxylates from these APE1-2. While this knowledge base is substantial, the ability to evaluate the factors governing the extent of secondary biodegradation of metabolites under different treatment plant operating conditions could not be attempted previously due to a lack of adequate modeling tools.

This poster will discuss the development of a dynamic model for predicting the fate of APEs and metabolites during municipal wastewater treatment. Anticipated use of the model will be to answer important questions such as:

- How would a shorter hydraulic retention time (HRT) affect the primary and ultimate degradation of the APEs?
- What effect does temperature have on treatment efficiency?
- What effect might a higher solids retention time (SRT) have on the fate of the APEs?
- If the dissolved oxygen level in wastewater treatment falls below a critical concentration (e.g., 0.5 mg/l) how will the biodegradation of APEs be affected?
- Will upgrading a plant for biological nutrient removal (BNR) have a positive or negative impact on biodegradation of APEs? Can choosing one BNR design over another aid in the management of APE release?
- What optimizing procedures can be used to promote the ultimate biodegradation of the APEs?
- Are there operating methods to reduce the levels of the alkylphenol in residual solids?

The wastewater treatment simulator will also provide the distribution of effluent concentrations of the APE metabolites, which can then be used in other environmental fate models which represent the receiving water, sediment and biota compartments.

Keywords: Alkylphenol ethoxylate, wastewater, model, biotransformation

Extraction of contaminants from complex matrices using molecularly imprinted polymers
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In the extraction of trace residues, sample pre-treatment is often both elaborate and time-consuming. One rapidly developing method that obviates the need for multiple clean-up and extraction steps, thereby simplifying the pre-treatment procedure, is solid-phase extraction phases based on molecularly imprinted polymers (MIPs). In addition to their simplicity, use of such phases allows a wide range of solvents and less or no need for additional sample pre-treatment steps, reduces the total sample handling time and thereby reduces the analysis time and significantly lowers the cost of sample preparation.

MIP sorbents are designed to contain artificial ‘receptor cavities’ that are complementary both in shape and chemical properties to desired target analytes. By targeting discreet chemical differences between molecules through the use of ‘smart’ templates, MIPs can be used for selective extraction of either single molecular species, or ‘classes’ of molecules containing the same functional or chemical motif.

In this work, we present examples of the extraction and separation of trace compounds from complex matrices that will illustrate the growing use of MIPs in trace analysis.

48 Pharmaceuticals and Personal Care Products in the Canadian Environment: Research and Policy Directions
MIP materials selective to classes of drugs have been developed. Extraction of Beta blockers (beta receptor antagonists) and of Beta agonists from wastewater and from urine is discussed. The MIP material developed for Triazine herbicides shows excellent selectivity towards triazines and triazine metabolites. The material allows fast and robust extraction from industrial wastewater, environmental samples of drinking and river water. The extraction results in high recoveries with, compared to conventional extraction methods, less ‘chemical noise’ obtained, allowing lower detection limits.

Other selective MIP materials are shown and simultaneous extraction of anti-depressants (paroxetine and fluoxetine) is discussed. MIP materials show high selectivity to the specified compounds and fast and sensitive methods for trace compound determinations have been developed. MIPs have been shown to be very valuable in clinical, veterinary and environmental monitoring and have been shown to simplify the extraction, quantitation and analysis of pharmacologically active compounds\textsuperscript{1}, carcinogenic compounds\textsuperscript{2} as well as banned compounds in foodstuffs\textsuperscript{3-5} and the environment\textsuperscript{6}.


The effects of 17α-ethynyl estradiol on goldfish (Carassius auratus) estrogen receptor subtypes, vitellogenin and aromatase B

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This study examined the gene expression profile of the three goldfish estrogen receptor (ER) subtypes simultaneously in multiple tissues, in relation to mRNA levels of liver vitellogenin (VTG) and brain aromatase following 17α-ethynyl estradiol (EE2) exposure. Male goldfish were exposed to waterborne ethanol (0.001% solvent control) and 100 ng/L EE2 for 24 h. A multiplex real-time RT-PCR system using TaqMan chemistry was used to determine relative mRNA levels of the three ER subtypes (α, β1, and β2) compared to the control gene (β-actin) in testes, liver, hypothalamus and telencephalon. In the liver, EE2 induced a significant increase in ERα transcript levels (~4 fold), but no significant changes in ERβ1 or ERβ2 levels were observed. The EE2 transcript levels were not affected in the testes or in the hypothalamus and telencephalon. The EE2 treatment did not alter transcript levels of brain aromatase, but did elevate liver vitellogenin levels (~7 fold). Previous studies in our lab have revealed that goldfish ER subtypes are differentially auto-regulated by 17β-estradiol \textit{in vivo}, and that this regulation depends on the tissue, dose and length of exposure. The present study suggests that EE2 also differentially affects ER subtype levels within the hypothalamic-pituitary-gonad axis of male goldfish. In addition, the increase in ERα transcripts concomitant with vitellogenin transcripts suggests that ERα may also be a sensitive biomarker of xenoestrogen exposure in this teleost model.

Key words: estrogen receptors, goldfish, vitellogenin, aromatase
In recent years, pharmaceutical and personal care products (PPCPs) have been found in diverse environments (including groundwater, river water, and municipal wastewater). While antibiotics can easily be detected using tandem LC-MS in pure water, more complicated matrices (such as natural waters and wastewater) generate confounding matrix effects. In this study, we report on our ongoing activities involving 18 antibiotics (belonging to the following classes: sulfonamides, fluoroquinolones, tetracyclines). We developed a sampling protocol after evaluating the effect of various sampling materials (e.g., LDPE, HDPE, PTFE, and glass) and of storage temperature on compound stability. Furthermore, we developed a Solid Phase Microextraction (SPME) technique using a Carbowax / Divinylbenzene fiber that was found to overcome matrix effects observed in the determination of antibiotics in ground water samples.

A number of recent studies have been suggestive of undesired effects of pharmaceuticals and personal care products (PPCPs) and endocrine disrupting compounds (EDCs) on human health, marine life, and the environment. While the environmental concentrations of these chemicals are much lower than the dosages required to directly affect human health, their indirect effects through manipulation of micro-organisms and marine life have attracted attentions from the environmental research community. Many of these substances are removed from water through natural or technical processes such as precipitation to the river bed and removal by conventional treatment processes. However, a number of them were found to persist through these processes and end up in drinking water. Further studies are thus required to evaluate and optimize the existing processes or develop novel technologies to remove these contaminants from raw water sources or transform them into harmless substances.

In collaboration with a host of research institutions, the Ontario Ministry of the Environment has initiated a project to optimize the design and operation of ozonation process to remove/transform PPCPs and EDCs present in water. The study, designed in bench-scale and pilot-plant stages, investigates the efficiency of ozonation processes in oxidizing a selection of target contaminants that were detected in the Detroit River Watershed through a 13 months occurrence study. The preliminary results from the bench-scale experiments indicated that a number of target chemicals were efficiently removed from water to levels below the instrument detection limit (IDL). Others were removed at efficiencies in the vicinity of 90%. Further experiments are underway to optimize the operating conditions for maximum removal efficiency. The results of the bench-scale experiments will be evaluated at pilot-plant level with further optimization trials. In this poster the experimental procedure as well as the results obtained thus far and the future plans will be presented and discussed.

Chlortetracycline, lincomycin and sulfamethazine are veterinary antibiotics used in livestock production to control or prevent disease and to enhance weight gain. Since a portion of the administered dose of each of these antibiotics may be excreted in the faeces and urine, the management practice of applying livestock manure to crop and pasture land as a plant nutrient source may result in their transport via surface runoff (rainfall, snow melt) into surface receiving waters. However, little is known about the persistence of these veterinary antibiotics in aquatic ecosystems such as prairie wetlands. In September 2004 and 2005, three wetlands, situated near Saskatoon, Saskatchewan, Canada were fortified with environmentally relevant concentrations of chlortetracycline (2 μg/L), lincomycin (1.5 μg/L) or sulfamethazine (8 μg/L). The wetland water volume varied from 622 to 1,015 m$^3$ and water pH varied from 7.5 to 8. The dissolved organic carbon concentration ranged from 12.4 to 29.4 mg/L$^{-1}$ and specific conductivity ranged from 400 to 1,910 μS/cm.
Water samples were collected on the day prior to fortification and, after fortification, until ice formation in October. Following ice melt in the spring, water samples were collected monthly until August. Lincomycin concentrations in the water column >0.1 µg/L and sulfamethazine concentrations >1.0 µg/L were monitored by direct injection of the water samples into the LC-MS-MS system. Water samples with lincomycin concentrations <0.1 µg/L, sulfamethazine concentrations <1.0 µg/L and all chlortetracycline were analyzed by solid-phase extraction followed by LC-MS-MS quantification. The persistence of the antibiotics in the wetlands is expressed as half-lives in the water column.

**Pharmaceuticals and Personal Care Products in Municipal Wastewater**

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Pharmaceuticals and personal care products (PPCPs) are considered an emerging issue in municipal wastewater treatment in Europe and North America. Their principal route into the environment is through discharges of municipal wastewater effluent and the land application of biosolids. In 2002 Environment Canada, the Ontario Ministry of Environment (MOE), and the City of Toronto embarked on a large-scale collaborative wastewater research study to generate information for development of risk management strategies to control the release of PPCPs into the Canadian environment. The poster provides an overview of the scope and results of each facet in this collaborative research study, and the following publications have been generated from the study.


**Investigation of the Stability of Chlortetracycline in Prairie Wetlands by LC-MS/MS**

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Chlortetracycline (CTC) undergoes a reversible epimerization at the C-4 position to produce the corresponding epimer, 4-epi-CTC. When dissolved in de-ionized water, CTC will epimerize over a 24-h period at room temperature until an approximate 1:1 equilibrium mixture of CTC and 4-epi-CTC is established. Epimerization results in a 50% reduction of the CTC originally present in the solution and this can lead to substantial quantification errors. CTC and 4-epi-CTC have different physical-chemical properties which allow them to be separated using an Xterra C18 stationary phase under isocratic operating conditions. Under identical mass spectrometric collision-induced dissociation conditions, CTC and 4-epi-CTC produce different ratios of the same product ions. For protonated CTC and 4-epi-CTC, the major fragment ions are: (1) m/z 462, due to the direct loss of NH\textsubscript{3}, (2) m/z 461, due to the direct loss of H\textsubscript{2}O, and (3) m/z 444, due to the combined loss of NH\textsubscript{3} and H\textsubscript{2}O.

**The Effects of Fluoxetine on the Reproductive Axis of Female Goldfish (Carassius auratus)**

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We investigated the effects of fluoxetine, the active ingredient of Prozac™, on neuroendocrine function and the reproductive axis in the goldfish. Fish were i.p. injected with fluoxetine twice a week for 14 days, resulting in five injections of 5 µg fluoxetine/g of body weight. We measured the concentrations of serotonin, 5-hydroxyindolacetic acid, dopamine, L-dopa, homovanillic acid, norepinephrine and 3-methoxy-4-hydroxyphenylglycol in the hypothalamus and telencephalon using HPLC. Homovanillic acid, a metabolite in the dopaminergic pathway, increased significantly in the hypothalamus. Plasma oestradiol levels were measured by RIA and were significantly reduced by approximately 5-fold after fluoxetine treatment. We found that fluoxetine also significantly reduced the expression of ER\textsubscript{}\textsubscript{a} mRNA by 4-fold in both the hypothalamus and telencephalon and ER\textsubscript{\alpha} mRNA in the telencephalon by 1.7-fold. Fluoxetine had no effect on the expression of ER\textsubscript{\beta} mRNA in the brain. Microarray analysis identified isotocin, a neuropeptide that stimulates reproductive behaviour in fish, as a candidate gene affected by fluoxetine treatment. Real-time RT-PCR verified that isotocin mRNA was down-regulated approximately 6-fold in the hypothalamus and 5-fold in the telencephalon. Our results indicate that fluoxetine has the potential to disrupt reproduction and modulate genes involved in reproductive function and behaviour in the brain of female goldfish. Supported by the Canadian Water Network and NSERC.

**Environmental Fate and Persistence of Two Antibiotics**

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Antibiotics administered to livestock can be excreted up to 80% in the feces and urine. Liquid manure, when applied to cropland as a nutrient source, is thus a possible source of antibiotics to nearby surface and ground waters through runoff and leaching, respectively. The environmental fate of these pharmaceuticals is of increasing concern to the Canadian public. Trace concentrations of veterinary antibiotics have been detected in surface and ground waters in Canada, the United States and Europe. In Saskatchewan, Canada, lincomycin and spectinomycin are two antibiotics that are administered together to swine for the prevention and control of post weaning diarrhea. An analytical method was developed to analyze simulated rainfall runoff, snow melt runoff and ground water samples collected from manure treated cropland for traces of these antibiotics. The method, which uses LC-MS/MS for quantitation and confirmation, allows for concurrent analysis of both lincomycin and spectinomycin with limits of detection being 8 and 400 ng/L, respectively. Lincomycin concentrations in simulated rainfall runoff samples collected immediately after manure application ranged from <8 to 3,800 ng/L, whereas those in snow melt runoff following fall manure application ranged from <8 to 4,000 ng/L. Lincomycin was also detected in ground water samples at levels <160 ng/L. Spectinomycin was not detected in any samples; this may be due to lower sensitivity and/or lower concentrations in the applied manure.
There is No “AWAY”: Pharmaceuticals, Personal Care Products, and Endocrine-Disrupting Substances: Emerging Contaminants Detected in Water
Carolyn Webb
Canadian Institute for Environmental Law and Policy
www.cielap.org

This poster provides a brief summary of CIELAP’s 2006 report that reviews the developing issue of emerging contaminants now being detected in water, including pharmaceuticals, personal care products (together abbreviated PPCPs) and endocrine-disrupting substances (EDSs). The poster also provides CIELAP’s recommendations on this issue.

Occurrence of Bioactive Pharmaceutical Compounds and Endocrine Disrupting Chemicals in the Detroit River Watershed
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We present in this poster results obtained from a 13 month field study of a new multi-residue method for the analysis of bioactive pharmaceutical compounds (PhCs) and endocrine disrupting compounds (EDCs) in environmental water matrices. The goal was to evaluate the ruggedness of the method with a rigorous quality control/quality assurance (QA/QC) protocol while obtaining occurrence and background concentration of PhCs and EDCs in the aquatic environment. A total of 66 field and 42 QA/QC samples were analyzed using a solid phase extraction (SPE) and liquid chromatography-tandem mass spectrometry (LC-MS-MS) analytical method.

The preliminary results, including seasonal occurrences of selected PhCs and EDCs in both raw and treated water samples collected from September 2005 to October 2006 at various locations along the Detroit River as well as from the confluence of the Little River and Detroit River, and QA/QC data obtained during this field study, are presented. Analytical results for 48 PhC and EDC target compounds revealed that bezafibrate, carbamazepine, erythromycin, ibuprofen, indomethacin, naproxen, sulfamethoxazole, trimethoprim were the most frequently detected target analytes in the effluent of the Little River waste water treatment plant, with the concentrations of these compounds decreased in the confluence of Little River and Detroit River. Further dilution was observed in the intake water before entering the drinking-water system. QA/QC data showed that matrix effect is a concern using an LC-MS-MS analysis and cannot be overcome easily. Possibility of using isotope-labeled compounds to correct for the matrix effect will be presented and discussed in details.