

Reducing the Impact of Pharmaceuticals in the Great Lakes

Technical Study



POLLUTION PROBE
CLEAN AIR. CLEAN WATER.

CleanWater
Foundation

Prepared for Environment and Climate Change Canada



ABOUT

Reducing the Impact of Pharmaceuticals in the Great Lakes is a joint project of Pollution Probe and the Clean Water Foundation.



Pollution Probe is a Canadian charitable environmental organization (established in 1969) that is a leading agent of change at the intersection of communities, health and environment. Its approach is to define environmental problems through research, to promote understanding through education and to press for practical solutions through advocacy. Pollution Probe seeks to improve the health and well-being of Canadians by advancing policy that achieves positive and tangible environmental change.



The Clean Water Foundation is a Canadian not-for-profit organization dedicated to engaging individuals in actions that preserve, protect and improve our water. It works in partnership with public, private and charitable interests to create policies and programs that encourage water friendly behaviour. The foundation focuses on issues where individual action is both the cause and the solution to water challenges.

ACKNOWLEDGEMENTS

Pollution Probe and the Clean Water Foundation thank the study participants for their time and effort on this project. The information provided during interviews as well as comments made on draft study material were invaluable to producing a comprehensive report.

We are grateful to Environment and Climate Change Canada for providing financial assistance. We would also like to thank Tricia Mitchell, Lisa Sealock and Sara Varty from Environment and Climate Change Canada for their time and contributions to this project, including providing feedback on the drafts of this document, and sharing important resources and data to support the study.

Special thanks to Ken Ogilvie for generously contributing his time, expertise and editing skills to this project.

Copyright © 2019 Pollution Probe and Clean Water Foundation. All rights reserved. No part of this publication may be reproduced in any form whatsoever without the prior written permission of the publisher.



EXECUTIVE SUMMARY

The Great Lakes are a unique resource of immense value to Canada and the United States, especially to the Province of Ontario and the eight bordering Great Lakes States. They face many threats, including wetland losses, invasive species, eutrophication, toxic substances and climate change. Over the past decade, pharmaceuticals have received increased attention as contaminants in the lakes, with concerns related to adverse impacts on aquatic ecosystems and potentially on human health.

This study by Pollution Probe and the Clean Water Foundation examines the sources, pathways and impacts of pharmaceuticals in the Great Lakes. It provides an overview of actions taken within Canada to address this emerging issue, and compares them to research, monitoring and mitigation actions taken by other jurisdictions, especially the United States and the European Union. Drawing on an extensive literature review and input from study participants, this report identifies knowledge gaps and proposes further actions that Canada could take to better understand and manage pharmaceuticals.

Overview of Study Findings

Findings include the following:

1. Pharmaceuticals have been measured throughout the Great Lakes, in all aquatic media (water column, sediment and biota).
2. The main types of pharmaceuticals found include pain killers, hormones and endocrine disrupting compounds, antibiotics and psychiatric drugs. The presence of these pharmaceuticals varies by lake and location.
3. The sources of pharmaceutical pollution in the Great Lakes are multiple and include municipal wastewater (from homes, hospitals and healthcare facilities, landfill leachate and pharmaceutical manufacturers), agriculture and aquaculture.
4. The main pathway for pharmaceuticals entering the Great Lakes is from municipal wastewater treatment plants. Other pathways, such as run-off from agricultural sources, are secondary. Agriculture is a major user of antimicrobials and could be an important source of these compounds in the lakes.
5. The consistent use and continuous discharge of pharmaceuticals into the environment implies that some of these products can be considered as pseudo-persistent pollutants.
6. Pharmaceuticals in the Great Lakes are currently not a human health risk and are typically found below “environmentally relevant concentrations.” The highest concentrations are usually found close to wastewater treatment plants (WWTPs). Pharmaceuticals are found at environmentally relevant concentrations in proximity to areas of higher population density and/or intensive agriculture (particularly in Hamilton Harbour).
7. Instances of higher mortality rates and alterations to fish reproductive biology, reproductive behaviour and community behaviour coincide with areas in which environmentally relevant concentrations of pharmaceuticals have been observed.
8. Significant knowledge gaps exist:
 - a. The amount of an ingested pharmaceutical that leaves the human body unaltered or in metabolized form is not well understood.
 - b. Estimates of the relative contribution of excreted pharmaceuticals versus waste pharmaceuticals vary greatly.
 - c. Ecotoxicology data are severely lacking for active pharmaceutical ingredients (API) and mixtures of active pharmaceutical ingredients (APIs).
9. Canadian jurisdictions have a variety of legislative, regulatory and policy tools available to manage pharmaceutical pollution in the Great Lakes.
10. There is no Canadian strategy to facilitate a coordinated approach to research, analysis and action on pharmaceutical pollution in the Great Lakes.
11. Information generated through environmental impact assessments and the Canadian Integrated Program for Antimicrobial Resistance (CIPARs) is either not publicly available or is not made available in a timely and comprehensive manner.
12. There is no systematic sampling and reporting program in the Great Lakes that provides timely and publicly accessible information on the presence and impacts of pharmaceuticals.
13. Federal and Ontario wastewater regulations have no specific requirements pertaining to managing pharmaceutical pollutants.
14. Government departments and ministries are not providing consistent information on the safe disposal of unused and expired pharmaceuticals.

15. Ontario's extended producer responsibility regulation for waste pharmaceuticals has achieved measurable diversions of unused and expired pharmaceuticals from going to landfill and municipal wastewater systems.
16. Outreach and engagement efforts by not-for-profit organizations have increased awareness and participation in pharmaceutical take-back programs and initiatives.
7. Increase the transparency of health and environmental risk assessments of pharmaceuticals to help Canadians understand potential threats as well as the mitigation measures that are being implemented.
8. Ensure that governments communicate up-to-date information on best practices for the management of unused and expired medications.
9. Conduct feasibility studies on increasing the use of advanced and alternative wastewater treatment technologies in the Great Lakes basin.

Overview of Study Recommendations

The following recommendations are provided for all the Great Lakes:

1. Develop a list of priority APIs requiring further investigation, based on existing Great Lakes research as well as US and European experience.
2. Implement monitoring programs in waters identified through Great Lakes research as having environmentally relevant concentrations of pharmaceuticals, particularly in embayments surrounded by dense urban populations, and report on changing concentrations of priority substances.
3. Measure and report on concentrations of priority APIs in effluents discharging directly or indirectly to the Great Lakes.
4. Conduct research on the presence and impacts of pharmaceuticals in multiple media, especially in locations where adverse impacts are more likely to occur (for example, near high population density areas and large animal husbandry operations).
5. Encourage citizen involvement in basin-wide water quality monitoring to enable a more complete dataset on the presence of pharmaceuticals in Great Lakes water, sediment and biota.
6. Publish the results of pharmaceuticals research in a timely, accessible and understandable form to advance knowledge and facilitate better decision-making.
10. Monitor discharges from pharmaceutical manufacturers to determine whether they are significant sources of APIs.
11. Monitor wastewaters from healthcare facilities, especially for antimicrobials and cancer-fighting medications, and explore the feasibility of requiring pre-treatment before discharging effluents to WWTPs.
12. Support take-back program outreach and engagement activities to prevent unused and expired pharmaceuticals from entering the Great Lakes.

These Additional Recommendations are Lake-Specific:

Ontario and Erie:

Given the high population densities and the significant concentration of agricultural operations in these lake basins:

13. Study the costs and benefits of WWTP upgrades to include advanced and alternative treatments.
14. Evaluate the efficacy of voluntary training and unused pharmaceutical collection programs in the agricultural sector and explore additional actions that may be required.



Huron:

Given the large number of aquaculture operations in Lake Huron:

15. Monitor the concentrations of pharmaceuticals in areas surrounding these operations.
16. Evaluate aquaculture medication application processes to determine if changes are required.

Superior:

Given the lack of data for Lake Superior:

17. Mobilize citizen scientists to collect samples and compile data on pharmaceuticals in water, focusing on priority substances.

Implementing the Recommendations

The recommendations are directed mainly at federal, provincial and municipal governments, as well as at hospitals and healthcare facilities, pharmaceutical manufacturers, pharmacies, agricultural operations and aquaculture. In addition, citizen scientists have a key role to play, as do consumers who can ensure that unused pharmaceuticals are returned to take-back facilities. Not-for-profit organizations can increase public awareness of the adverse impacts of waste pharmaceuticals and thus enhance the effectiveness of take-back programs.



TABLE OF CONTENTS

About	2
Acknowledgements.....	2
Executive Summary	3
Abbreviations and Acronyms	8
Select Definitions	9
Section 1: Introduction	10
Section 2: Methodology	11
Section 3: Analytical Framework	12
Section 4: Key Findings.....	13
4.1 Spatial and Temporal Distribution of Studies.....	13
4.2 Occurrence of Pharmaceuticals in the Great Lakes	14
4.3 Sources and Pathways	15
4.3.1 Municipal Wastewater Systems.....	16
4.3.2 Animal/Agricultural Industry.....	18
4.3.3 Aquaculture.....	19
4.3.4 Landfill Leachate.....	20
4.3.5 Pharmaceutical Manufacturing Industry.....	20
4.3.6 Hospital and Healthcare Institutions	21
4.4 Impacts on Aquatic Systems and Human Health.....	22
4.4.1 Impacts on Aquatic Ecosystems	22
4.4.2 Impacts on Human Health	23
4.5 Measures and Actions.....	24
4.5.1 Research, Surveillance and Monitoring Activities.....	24
4.5.2 Treaties, Legislation, Regulations and Policies ...	26
4.5.3 Waste/Wastewater Management	36
4.5.4 Animal Husbandry Practices.....	38
4.5.5 Stakeholder and Consumer Education and Engagement Programs	40
4.6 Gap Analysis Summary	43
Section 5: Conclusions.....	45
Section 6: Recommendations.....	47
References	49
Appendix A. Participants in the Pharmaceuticals in the Great Lakes study.....	62
Appendix B. Comparative Analysis.....	63
Appendix C. Occurrence of Pharmaceuticals in the Great Lakes Basins.	72
Appendix D. Distribution of Wastewater Treatment Plants in the Great Lakes Basin	85
Appendix E. Impacts of Pharmaceuticals on Selected Species	86

ABBREVIATIONS AND ACRONYMS

AOP – advanced oxidation process	EC – European Commission	NEPA – <i>National Environmental Policy Act (US)</i>
AMR – antimicrobial resistance	ECCC – Environment and Climate Change Canada	NMA – <i>Nutrient Management Act (Ontario)</i>
AMU – antimicrobial use	EDCs – endocrine disrupting compounds	NPDES – National Pollutant Discharge Elimination System (US)
APIs – active pharmaceutical ingredients	EFP – Environmental Farm Plan	OCWA – Ontario Clean Water Agency
BMP – beneficial management practices	EFPIA – European Federation of Pharmaceutical Industries and Associations	OMRP – Ontario Medications Return Program
CAAP – Concentrated Aquatic Animal Production	EII – Environmental Impact Initiative	OTC – over the counter
CAFO – confined animal feeding operation	EPA – <i>Environmental Protection Act (Ontario)</i>	PPCPs – pharmaceuticals and personal care products
CAHI – Canadian Animal Health Institute	ERA – Environmental Risk Assessment	RCRA – <i>Resource Conservation and Recovery Act (US)</i>
CCL – Contaminant Candidate List	EPR – extended producer responsibility	REACH – <i>Registration, Evaluation, Authorisation and Restriction of Chemicals (EU)</i>
CDC – Centers for Disease Control and Prevention (CDC)	FDA – <i>Food and Drug Administration (US)</i>	RMM – Risk Mitigation measures
CECs – Contaminants of Emerging Concern	FFDCA – Federal Food, Drug and Cosmetic Act (US)	USDA – U.S. Department of Agriculture
CEPA – <i>Canadian Environmental Protection Act (1999)</i>	GHS – Green Hospital Scorecard	USEPA – United States Environmental Protection Agency
CIPARS – Canadian Integrated Program for Antimicrobial Resistance Surveillance	GLFMSP – Great Lakes Fish Monitoring and Surveillance Program	USGS – U.S. Geological Survey
CMC – Chemicals of Mutual Concern	GLNPO – Great Lakes National Program Office (USEPA)	UWWTD – Urban Wastewater Treatment Directive (EU)
CMP – Chemicals Management Plan (Canada)	GLWQA – Great Lakes Water Quality Agreement (Canada and US)	WWTPs – wastewater treatment plants
COA – Canada-Ontario Agreement on Great lakes Water Quality and Ecosystem Health	HPSA – Health Products Stewardship Association	
CVMA – Canadian Veterinary Medical Association	IUPAC – International Union of Pure and Applied Chemistry	
CWA – <i>Clean Water Act (US)</i>	KNAPPE – Knowledge and Need Assessment on Pharmaceutical Products in Environmental Waters	
DEA – <i>Drug Enforcement Administration (US)</i>	MA – Marketing Authorisation	
DPD – Drug Product Database	MECP – Ministry of the Environment, Conservation and Parks (Ontario)	
DSL – Domestic Substances List (Canada)		

SELECT DEFINITIONS

The following definitions and explanations are provided to help readers who are not familiar with the terminology used in this report.

Citizen science – This is the practice whereby members of the public (typically volunteers) participate and contribute to monitoring programs and scientific research by assisting researchers with the collection and processing of environmental data.^{1,2}

Endocrine Disrupting Compounds (EDCs) – These are substances in the environment, food and consumer products that may interfere with the body's hormone systems. They can mimic or block naturally occurring hormones, and affect the production, transport and removal of hormones in other ways.³ EDCs have been linked to adverse health effects in people and animals, such as changes in reproductive function, increased cases of breast cancer, changes in immune function and others.⁴

Environmental media – Refers to part of the environment that can contain pollutants. In this study, the term refers to water, sediment and living organisms.

Environmentally Relevant Concentrations (ERCs) – Defined by the International Union of Pure and Applied Chemistry (IUPAC) as concentrations of environmental contaminants that are likely to affect a determinable ecological characteristic of an exposed system.⁵ In other words, certain adverse effects are likely to occur at concentration levels of chemicals that are found in the environment. For example, antidepressants were found to have diverse negative impacts on multiple aquatic animals at environmentally relevant concentrations, which are reported to be below 100 ng/L in a number of studies (such as those reviewed by Ford and Fong, 2016).⁶

Intersex – This is the simultaneous presence of both male and female characteristics in a single organism.

Pharmaceuticals (also commonly known as drugs or medicines) – These are substances that are used to detect, treat, or prevent a variety of diseases and improve the quality of life in humans and animals. Pharmaceuticals are referred to in different ways by various researchers and others, but for purposes of readability and understanding, this report will use the following terms: pharmaceuticals, pharmaceutical substances and active pharmaceutical substances (APIs).

Pseudo-persistent – Refers to pharmaceuticals that tend to behave as persistent compounds in the environment because they are continuously introduced into the environment (for example, via release from wastewater treatment plants). The removal and transformation of these pollutants by environmental processes such as biodegradation (among others) is offset by their replenishment, leading to a permanent presence in the environment.^{7,8}

Study participants – Subject matter experts and stakeholders who participated in interviews conducted as part of this study, and reviewed drafts of this document.

¹ Millar, E. E.; Hazell, E. C.; Melles, S. J. (2018). The 'Cottage Effect' in Citizen Science? Spatial Bias in Aquatic Monitoring Programs. *International Journal of Geographical Information Science*, 1–21. <https://www.tandfonline.com/doi/abs/10.1080/13658816.2018.1423686>

² National Geographic. (n.d.). *Citizen Science*. <https://www.nationalgeographic.org/encyclopedia/citizen-science/>

³ Pollution Probe. (2012). *Primer on Toxic Substances*. <http://www.pollutionprobe.org/publications/primer-on-toxic-substances/>

⁴ Monneret, C. (2017). What is an endocrine disruptor? *Comptes Rendus Biologies*, Vol. 340 (9–10), pp. 403–405. <https://www.sciencedirect.com/science/article/pii/S1631069117301257>

⁵ International Union of Pure and Applied Chemistry (IUPAC) (2007). *Glossary of Terms Used in Toxicology*, 2nd Ed. (IUPAC Recommendations 2007). <http://media.iupac.org/publications/pac/2007/pdf/7907x1153.pdf>

⁶ Ford, A. T. and Fong, P. P. (2016). The Effects of Antidepressants Appear to be Rapid and at Environmentally Relevant Concentrations. *Environmental Toxicology and Chemistry*, Vol. 35 (4), pp. 794–798. <https://setac.onlinelibrary.wiley.com/doi/epdf/10.1002/etc.3087>

⁷ Ebele, A. J., Abdallah, M., A-E., Harrad, S. (2017). Pharmaceuticals and Personal Care Products (PPCPs) in the Freshwater Aquatic Environment, *Emerging Contaminants*, Vol 3(10), pp. 1–16. <https://www.sciencedirect.com/science/article/pii/S2405665016300488>

⁸ Li, W. (2014). Occurrence, Sources, and Fate of Pharmaceuticals in Aquatic Environment and Soil. *Environmental Pollution*, 187, 193–201. <https://doi.org/10.1016/j.envpol.2014.01.015>

01

Section 1:

Introduction

The Great Lakes form the largest freshwater system on Earth. They contain almost one-fifth of the world's surface freshwater supply⁹ and support more than 3,500 plant and animal species, some of which are only found in the region.¹⁰ In addition to supplying drinking water to more than 40 million people, the Great Lakes basin encompasses a wide range of economic activities, including manufacturing, transportation, farming, tourism, recreation and energy production.¹¹

The lakes have faced and continue to face many threats, including wetland losses, invasive species, eutrophication, toxic substances and climate change. While some progress has been made in dealing with these threats, pharmaceuticals in Great Lakes water, sediment and biota have become an emerging issue over the past decade because of concerns related to adverse impacts on aquatic ecosystems and potentially on human health.

Pharmaceuticals provide many benefits. Particularly, they are used to treat disease and improve the quality of life for humans and animals. Commonly used pharmaceuticals include the following: pain killers, such as acetaminophen and ibuprofen; birth control pills containing synthetic hormones, such as ethinylestradiol; antidepressant drugs, such as fluoxetine; and, antimicrobial drugs, such as sulfonamides.

Study Objectives

This study seeks to better understand and report on the issue of pharmaceuticals in the Great Lakes. The objectives are as follows:

- to analyze what is known about pharmaceuticals in the Great Lakes from human and veterinary sources, as well as their pathways and impacts on Great Lakes aquatic systems and human health;
- to examine measures and actions that have been taken to address the issue and their effectiveness in Canada and international jurisdictions, such as the US and Europe; and,
- to identify knowledge gaps and propose actions that could be taken to address the issues.

PHARMACEUTICALS IN GREAT LAKES WATER, SEDIMENT AND BIOTA HAVE BECOME AN EMERGING ISSUE OVER THE PAST DECADE BECAUSE OF CONCERNS RELATED TO ADVERSE IMPACTS ON AQUATIC ECOSYSTEMS AND POTENTIALLY ON HUMAN HEALTH.

⁹ Pollution Probe. (2013). *Great Lakes Fact Sheets*. <http://www.pollutionprobe.org/publications/great-lakes-fact-sheets/>

¹⁰ Pollution Probe. (2013). *Great Lakes Fact Sheets: Biodiversity*. <http://www.pollutionprobe.org/publications/great-lakes-fact-sheet-8-biodiversity/>

¹¹ Environment and Climate Change Canada and the U.S. Environmental Protection Agency. (2017). *State of the Great Lakes 2017 Technical Report*. Cat No. En161-3/1E-PDF. EPA 905-R-17-001. https://binational.net/wp-content/uploads/2017/09/SOGL_2017_Technical_Report-EN.pdf

Methodology

An extensive literature review was conducted in conjunction with subject matter expert interviews to collect information on:

- Sources, pathways and impacts of pharmaceuticals in the Great Lakes
- Measures and actions that have been taken to prevent and reduce pharmaceutical pollution in Canada and internationally

The literature review examined the presence of pharmaceuticals in the Great Lakes and their impacts on aquatic ecosystems and human health. Internet and academic databases (including Web of Science) searches were conducted using questions and keywords on the state of knowledge and action on pharmaceuticals in the aquatic environment. Additional information sources were identified by staff of Environment and Climate Change Canada (ECCC) and through contacts made with a range of organizations, including academic departments and research institutes, provincial governments, industry and not-for-profit organizations. Study participants were asked to recommend high quality information sources and identify subject matter experts who should be interviewed.

Experiences with monitoring and managing pharmaceuticals in the United States, Europe and Asia were reviewed to position Canadian findings within an international context and to identify best management practices. Researchers conducted 11 telephone interviews (10 of the study participants are based in Ontario, while one is in Quebec). Eight of the participants were academics conducting research on pharmaceuticals in the Great Lakes. In addition, individuals working in communications and on stakeholder engagement in water issues were interviewed. A list of participants is included in Appendix A.



**THE RESEARCH
METHODOLOGY COMBINED
A LITERATURE REVIEW
WITH SUBJECT MATTER
EXPERT INTERVIEWS TO
COLLECT INFORMATION
ON SOURCES, PATHWAYS
AND IMPACTS OF
PHARMACEUTICALS
IN THE GREAT
LAKES, AND ACTIONS
TAKEN TO ADDRESS
PHARMACEUTICAL
POLLUTION IN CANADA
AND INTERNATIONALLY.**

03

Section 3

Analytical Framework

Information was gathered and analyzed on the sources, pathways and impacts of pharmaceuticals in the Great Lakes, as well as on the effectiveness of measures taken to monitor and mitigate pharmaceutical pollution in waters in Canada and internationally. The significant volume of information acquired required a robust analytical framework to ensure comparability, as per Table 1. Detailed comparative tables are contained in Appendix B.

Table 1: Questions comprising the analytical framework of this study

Section	Questions/Topics
1. What do we know about sources, pathways and impacts of pharmaceuticals in the Great Lakes?	<ul style="list-style-type: none">• Can we quantify how much passes through the body into wastewater systems versus how much is from unused medications that get flushed down the drain?• Have pharmaceuticals that were improperly disposed in landfills contaminated waterways?• What is known about pathways and volumes from the animal industry?• What are the impacts of pharmaceuticals on aquatic ecosystems? What is the level of concern?• What are the impacts of pharmaceuticals on human health? What is the level of concern?• What classes of (or specific) pharmaceuticals are of greatest concern? Why?
2. What measures/actions have been taken to address the issue and what impacts have those actions had?	<ul style="list-style-type: none">• What waste/wastewater management practices exist, including infrastructure and new developments?• What animal husbandry practices are in place?• Are any medication take-back programs in place?• Have there been any attempts at consumer education?
3. International experience and best practices	<ul style="list-style-type: none">• What could be learned from key international jurisdictions on the issue of pharmaceuticals and key management approaches?
4. Identification of knowledge/action gaps	<ul style="list-style-type: none">• What knowledge gaps remain with respect to the sources, pathways, and impacts of pharmaceuticals in the Great Lakes?• What further actions could be taken to address the issue?

THE SIGNIFICANT VOLUME OF INFORMATION ACQUIRED AS PART OF THIS STUDY REQUIRED A ROBUST ANALYTICAL FRAMEWORK TO ENSURE COMPARABILITY

Key Findings

4.1 Spatial and Temporal Distribution of Studies

Information from 192 sources, including peer-reviewed articles, government reports and key stakeholder interviews, was reviewed as part of this study, as shown in Table 2.

Table 2: Data Collection Summary

Data Source	Number of Sources Reviewed
Peer-reviewed articles	58
Government reports and policy documents	84
Key stakeholder interviews	11
Other (news articles, websites, etc.)	39
Total	192

Figure 1 shows the spatial and temporal distribution of Great Lakes peer-reviewed studies examined for this report. Lake Ontario was the most studied basin on pharmaceuticals, comprising 37% of the studies. Less research has been conducted in Lake Erie (19%), with Lakes Superior and Huron being the least studied. The majority (56%) of the studies examined were relatively recent, taking place between 2013 and 2018.

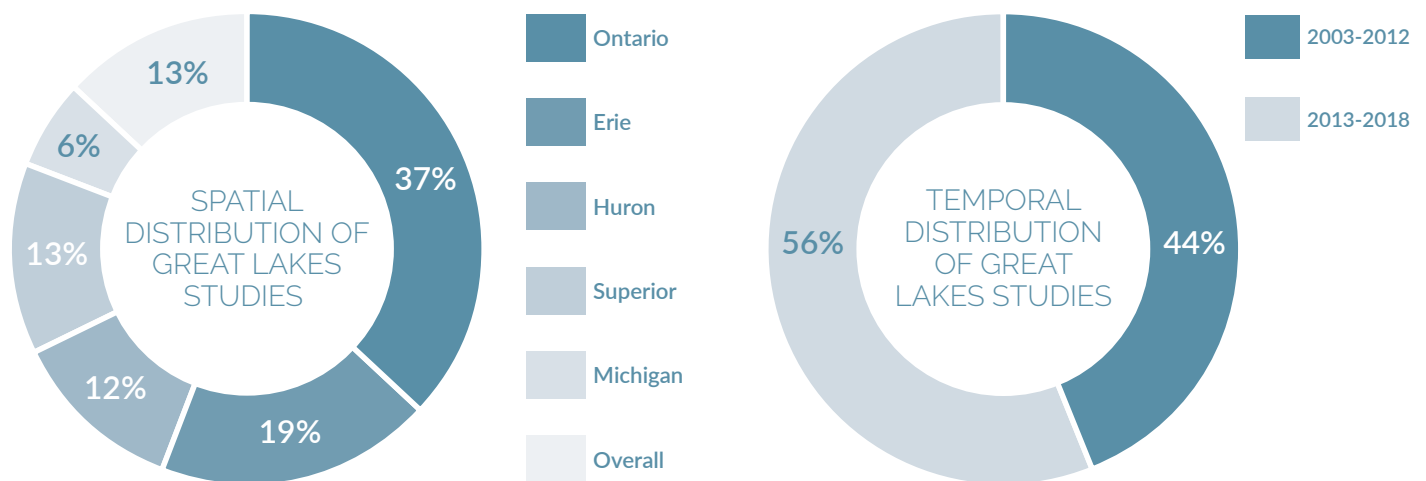


Figure 1: The spatial and temporal distribution of studies examined. ¹²

¹² Note: The number of studies included in this figure exceeds the total number of studies listed in Table 1 because some studies covered multiple regions.

4.2 Occurrence of Pharmaceuticals in the Great Lakes

Highlights:

- A variety of pharmaceuticals have been detected in surface water, WWTP effluent and fish tissue.
- Concentrations of pharmaceuticals are highest near WWTP outfalls.
- Hamilton Harbour is the most contaminated study area in the Great Lakes basin.
- Lake Ontario is the most studied area, while Lake Superior is the least studied.
- Pharmaceuticals can bind to sediments, fish, etc., leading to water column concentrations being misleadingly low.
- Surface water concentrations of pharmaceuticals in the Great Lakes are similar to those found in international jurisdictions (US and Europe).

A variety of pharmaceuticals have been detected in the Great Lakes basin, including the following: analgesics, antibiotics, antidepressants, antidiabetics, antiepileptics, antihistamines, anti-inflammatories, beta blockers, hormones, lipid regulators and stimulants (see Appendices B and C).

Pharmaceuticals have been found in all the Great Lakes, typically in wastewater effluents and surface waters downstream from WWTPs (see Appendix C). Pharmaceuticals have been measured in fish tissue in Lakes Ontario and Huron. Wu et al.'s (2009) study on agricultural area in the Lake Erie basin detected a range of pharmaceuticals in surface water, but not in sediment samples.¹³ Carrara et al. (2008) observed elevated concentrations of several pharmaceutical compounds in groundwater in Long Point Provincial Park on the north

shore of Lake Erie.¹⁴ Lake Michigan was found to have pharmaceuticals in its sediment and in nearshore waters, with numerous pharmaceuticals, such as sulfamethoxazole and codeine, detected up to 3.2 km from the shoreline of Lake Michigan (Blair et al., 2013a).¹⁵

Several compounds have also been detected in open water, fish tissue and drinking water treatment plants. Concentrations found in some fish brain tissues exceed environmentally relevant concentrations (i.e., about 30-500µg/L, depending on pH).¹⁶ Concentrations of pharmaceuticals vary greatly among sites, most likely due to dilution as the contaminants move away from discharge sources.

In conclusion, pharmaceuticals are present in more than just WWTP effluents and surface waters, which have been the most studied areas.

A study by Uslu et al. (2013) demonstrated that concentrations of many APIs discharged into Great Lakes waters are below environmentally relevant levels, but this does not account for API concentrations in specific media, such as sediments, fish and other organisms.¹⁷ Study participants suggested that a large proportion of APIs are not present in the water column as they are absorbed by other media, such as suspended particles, organic matter and biological organisms. Future research should expand knowledge on the presence of pharmaceuticals in sediment and organisms.

A study by Li et al. (2010) found that Hamilton Harbour had the highest concentration of every pharmaceutical examined compared to other study areas throughout Lake Ontario.¹⁸ In some instances, concentrations in the harbour were almost 10 times higher than in other areas. Hamilton Harbour receives effluent from three WWTPs at a rate of about 400 million litres per day,¹⁹ as well as receiving runoff from the cities of Hamilton and Burlington.

¹³ Wu, C.; Witter, J. D.; Spongberg, A. L.; Czajkowski, K. P. (2009). Occurrence of Selected Pharmaceuticals in an Agricultural Landscape, Western Lake Erie Basin. *Water Research*, 43 (14), 3407-3416. <https://doi.org/10.1016/j.watres.2009.05.014>

¹⁴ Carrara, C., Ptacek, C. J., Robertson W. D., Blowes, D. W., Moncur, M. C., Sverko, E., Backus, S. (2008). Fate of Pharmaceutical and Trace Organic Compounds in Three Septic System Plumes, Ontario, Canada. *Environmental Science & Technology*, 42:2805-2811. <https://pubs.acs.org/doi/abs/10.1021/es070344q>

¹⁵ Blair, B. D.; Crago, J. P.; Hedman, C. J.; Klaper, R. D. (2013a). Pharmaceuticals and Personal Care Products found in the Great Lakes above Concentrations of Environmental Concern. *Chemosphere*, 93 (9), 2116-2123. <https://doi.org/10.1016/j.chemosphere.2013.07.057>

¹⁶ Note: Environmentally Relevant Concentrations (ERCs) are defined by the International Union of Pure and Applied Chemistry (IUPAC) as concentrations of environmental contaminants that are likely to affect a determinable ecological characteristic of an exposed system. More than 4,000 pharmaceuticals are currently in use, and it is challenging to experimentally assess their environmentally relevant concentrations in a timely manner (Boxall et al., 2012). A more realistic approach would be to conduct ecotoxicology studies on specific pharmaceuticals that are most often detected in wastewater effluent.

¹⁷ Uslu, M. O.; Jasim, S.; Arvai, A.; Bewtra, J.; Biswas, N. (2013). A Survey of Occurrence and Risk Assessment of Pharmaceutical Substances in the Great Lakes Basin. *Ozone: Science & Engineering*, 35 (4), 249-262. <https://doi.org/10.1080/01919512.2013.793595>

¹⁸ Li, H.; Helm, P. A.; Metcalfe, C. D. (2010). Sampling in the Great Lakes for Pharmaceuticals, Personal Care Products, and Endocrine-disrupting Substances using the Passive Polar Organic Chemical Integrative Sampler. *Environmental Toxicology and Chemistry*, 29 (4), 751-762. <https://doi.org/10.1002/etc.104>

¹⁹ Hamilton Harbour: What's Good, What's not so Good? (2002). *The Hamilton Spectator* <https://www.thespec.com/news-story/2235878-hamilton-harbour-what-s-good-what-s-not-so-good/>

The harbour is largely separated from Lake Ontario by a sandbar,²⁰ which could cause contaminants to remain in the harbour and become concentrated, rather than flowing into Lake Ontario and becoming diluted. This suggests that other embayment areas should be checked for elevated pharmaceutical levels.

In Lake Ontario, most studies have analyzed the concentrations of pharmaceuticals in wastewater effluent as well as downstream of WWTPs. The most frequently detected APIs include antidepressants, anti-inflammatories, hormones, antibiotics and beta-blockers (see Appendix C).

The majority of studies on Lakes Erie and Huron examined the concentrations of pharmaceuticals in WWTP effluent, with the most frequently detected compounds in Lake Erie being anti-inflammatories and lipid regulators, and in Lake Huron being anti-inflammatories and hormones. The most frequently detected pharmaceuticals in Lake Superior include antibiotics, antidepressants, antimicrobials and anticoagulants.

Studies in other jurisdictions have measured a wide range of pharmaceuticals in aquatic environments. Germany has conducted one of the most comprehensive meta-studies on the subject to date, compiling 123,761 measurements of environmental concentrations of human and veterinary

pharmaceuticals worldwide in surface water, groundwater, tap/drinking water, manure, soil and other environmental media.²¹ Pharmaceuticals or their transformation products have been detected in the environments of 71 countries. In total, 631 different pharmaceuticals were found above the detection limits of the analytical methods employed. Li (2014) conducted a meta-study demonstrating the occurrence of the most commonly used pharmaceuticals in effluent, freshwater and groundwater at several locations in North America, Europe and Asia.²² The concentrations varied but are comparable to those found in the Great Lakes basin in several cases (see Appendix C).

4.3 Sources and Pathways

Pharmaceutical discharges can be classified under two main groups: point source and diffuse. Point source discharges come from readily identifiable sources, such as municipal WWTPs and effluents released by healthcare facilities and pharmaceutical manufacturing plants. Point source discharges can be modeled mathematically and are easier to study than diffuse discharges, which come from larger-scale geographic areas, such as agricultural/aquaculture operations and landfill leachate leakage (Li, 2014).²³ Figure 2 shows the major sources of pharmaceuticals and their environmental fate, which is described in more detail in the following subchapters.

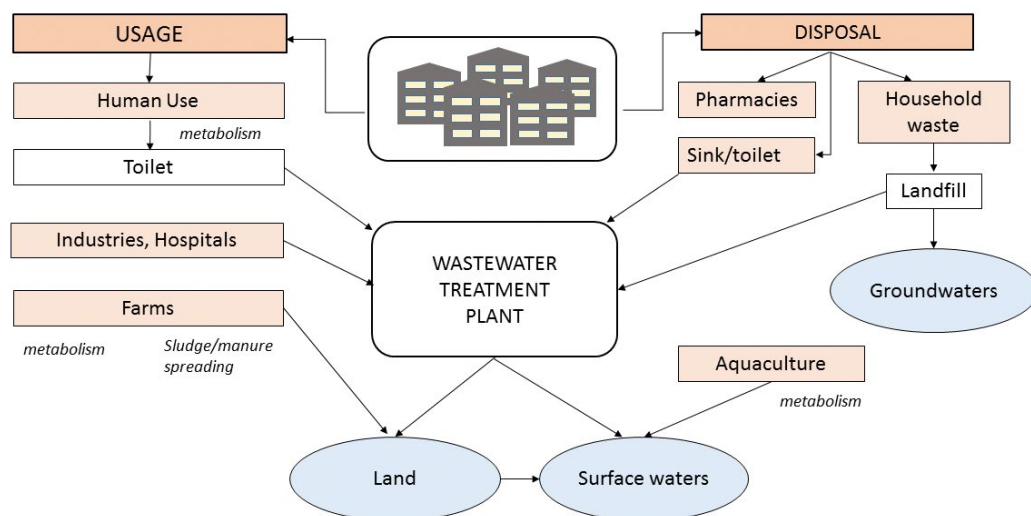


Figure 2. Sources and fate of pharmaceutical substances in the environment.

(Adapted from Nikolaou et al., 2007).²⁴

²⁰ Bay Area Restoration Council. (n.d.) *Hamilton Harbour. About the Bay*. http://hamiltonharbour.ca/about_the_bay

²¹ aus der Beek, T.; Weber, F.A.; Bergmann, A. (2015). *Pharmaceuticals in the Environment: Global Occurrence and Potential Cooperative Action under the Strategic Approach to International Chemicals*

²² Li, W. (2014). Occurrence, Sources, and Fate of Pharmaceuticals in Aquatic Environment and Soil. *Environmental Pollution*, 187, 193–201. <https://doi.org/10.1016/j.envpol.2014.01.015>

²³ Ibid.

²⁴ Nikolaou, A., Meric S., and Fatta, D. (2007). Occurrence Patterns of Pharmaceuticals in Water and Wastewater Environments. *Analytical and Bioanalytical Chemistry*, 387:1225–1234. <https://www.ncbi.nlm.nih.gov/pubmed/17205270>



4.3.1 Municipal Wastewater Systems

Highlights:

- Wastewater effluent is the main pathway of pharmaceutical discharges entering the lakes.
- High rates of effluent discharge from WWTPs mean that even pharmaceuticals with relatively high degradability can accumulate to become chronic pollutants.
- Treatment technologies vary in effectiveness, and a more widespread use of ozone would decrease API concentrations in the Great Lakes
- There is a lack of Canadian research that assesses the relative contributions from human excretion versus the disposal of pharmaceuticals to the Great Lakes from unused or expired medications.
- It is challenging to differentiate between drugs that have passed through a person versus drugs that are directly discharged to the lakes.
- Research from jurisdictions other than Ontario suggests that waste pharmaceuticals could contribute as much as 50% of the total volume of pharmaceuticals entering WWTPs.

The information analyzed during this study identified WWTPs as the main pathway for pharmaceutical contamination of the Great Lakes. More than a thousand municipal WWTPs discharge treated effluent directly into the Great Lakes or via rivers that flow into the lakes. Most of the plants in Ontario provide secondary treatment, and they remove some but not all the pharmaceuticals (see Section 4.5.3). The result is that pharmaceuticals are continuously released into the lakes.

According to Arvai et al. (2014), 18 billion liters per day of treated effluent is discharged to the Great Lakes basin from a total of 1,448 municipal wastewater treatment plants in Ontario and the United States.²⁵ In Ontario, 470 municipal wastewater treatment plants discharge into the basin, of which 212 (45%) are secondary/activated sludge plants, and 68 (15%) are tertiary/advanced treatment facilities. Eight (2%) treatment facilities provide only primary treatment. There are also 175 (37%) lagoon treatment systems, which serve smaller communities and provide a lower rate of secondary treatment.

With respect to the total wastewater flow, only about 15% of the municipal wastewater discharged into the basin in Ontario receives tertiary (advanced) treatment. The remaining wastewater is processed predominantly by secondary treatment facilities, which are less effective in

²⁵ Arvai, A.; Klecka, G.; Jasim, S.; Melcer, H.; Laitta, M. T. (2014). Protecting our Great Lakes: Assessing the Effectiveness of Wastewater Treatments for the Removal of Chemicals of Emerging Concern. *Water Quality Research Journal of Canada*, 49 (1), 23. <https://doi.org/10.2166/wqjrc.2013.104>

removing pharmaceuticals (see Section 4.5.3). In contrast, 978 municipal WWTPs discharge effluent into the basin in the US, 58% of which have advanced treatment, and which process 96% of the total wastewater flow.²⁶ A detailed distribution of Ontario and US wastewater treatment plants by type in the Great Lakes basin is provided in Appendix D.

Several of the studies examined indicated that the highest concentrations of pharmaceuticals in the Great Lakes are found in waters near WWTP discharge points located close to large population centres (see Appendix C).

Evidence from other jurisdictions supports the finding that municipal WWTPs are a major source of pharmaceuticals discharged into the water environment. A study by Sim et al. (2011) investigated the presence of pharmaceuticals in wastewater from municipal, livestock, hospital and pharmaceutical manufacturing WWTPs located near major river basins in Korea.²⁷ The municipal treatment plants had the highest daily “influent” loads of pharmaceuticals (0.404–1201 kg/d), but the effluent loads (0.101–23.0 kg/d) were relatively low compared to the influents. Nevertheless, municipal effluent loads were higher than the livestock and hospital loads. This suggests that while municipal WWTPs have relatively higher removal efficiencies for pharmaceuticals, they remain the principal source of pharmaceuticals in the water environment.²⁸

According to one study participant, the large volumes of effluent released from WWTPs means that even pharmaceuticals with a higher degree of degradability can become pseudo-persistent pollutants. Their rate of replacement is so great that the pharmaceuticals are virtually persistent, even though they do not meet the traditional definition of persistence. They are considered

as “pseudo-persistent,” which means they enter the environment continuously and thus become a permanent presence (Li, 2014).²⁹

Preponderance of Waste Pharmaceuticals

Pharmaceuticals typically enter wastewater systems via human excretion or through improper disposal of unused and expired medications. Research done for this report shows that analysts are unable to determine how to differentiate between API discharges from these sources.^{30,31} Studies in jurisdictions outside of Canada offer a range of estimates for the relative contributions in their geographical areas. A 2012 Product Stewardship Institute study³² indicated that waste pharmaceuticals represented between 10% and 43% of total pharmaceuticals in the United States, while a 2009 NRDC study³³ suggested upper limits of 45% for over-the-counter medications and 52% for prescription medications. According to the European Federation of Pharmaceutical Industries and Associations (EFPIA), unused medicinal products destined for humans represent 3 to 8% of the medicinal products sold.³⁴ Other estimates from the EU project known as KNAPPE (Knowledge and Need Assessment on Pharmaceutical Products in Environmental Waters) are much higher, with the proportion of medicinal products sold unused ranging from 5% in Sweden to 50% in France and the UK.³⁵

²⁶ Of these, 311 and 563 achieve secondary and advanced treatment, respectively. The remaining facilities likely achieve at least secondary treatment performance, which is the minimum standard in the US. The 311 facilities that meet the secondary treatment performance requirement receive about 4% of the total flow. Collectively the combined group of secondary, advanced, and tertiary plants treats 98% of the total wastewater flow discharged into the basin.

²⁷ Sim, W. J.; Lee, J. W.; Lee, E. S.; Shin, S. K.; Hwang, S. R.; Oh, J. E. (2011). Occurrence and Distribution of Pharmaceuticals in Wastewater from Households, Livestock Farms, Hospitals and Pharmaceutical Manufactures. *Chemosphere*, 82 (2), 179–186. <https://doi.org/10.1016/j.chemosphere.2010.10.026>

²⁸ Note: It is not clear from the study what types of wastewater treatment technologies were used at different facilities.

²⁹ Li, W. (2014). Occurrence, Sources, and Fate of Pharmaceuticals in Aquatic Environment and Soil. *Environmental Pollution*, 187, 193–201. <https://doi.org/10.1016/j.envpol.2014.01.015>

³⁰ Glucuronidation. (n.d.). Science Direct. <https://www.sciencedirect.com/topics/neuroscience/glucuronidation>

³¹ This is because drugs undergo glucuronidation but can undergo opposite process via bacteria once in wastewater. Glucuronidation (a common drug excretion step) is the process of attaching a glucuronic acid molecule to a drug molecule to make it more water soluble which makes it easier to excrete. One could look for drug metabolites in their glucuronidated forms within WWTP effluent. However, it is possible for micro-organisms to further modify drug metabolites into other forms. Also, glucuronidation is not the only method of making drug molecules more water soluble. It would be necessary to determine the amount of drug metabolites (excreted from body) in wastewater and then correct the measured concentration based on the rate of metabolite conversion by bacteria. Attempting to distinguish between the amounts of drugs that passed through a person versus the number of drugs that were directly flushed would be nearly impossible. Source: <https://www.sciencedirect.com/topics/neuroscience/glucuronidation>

³² Product Stewardship Institute. (n.d.). Safety Hazards. <http://www.productstewardship.us/?1015>

³³ Natural Resource Defense Council. (2010). Dosed Without Prescription: Preventing Pharmaceutical Contamination of Our Nation's Drinking Water. <https://www.nrdc.org/sites/default/files/dosed4pgr.pdf>

³⁴ European Environmental Bureau. (n.d.). The Environmental and Health Impacts Caused by Emissions of APIs to the Environment. <http://eeb.org/publications/31/chemicals/89561/briefing-on-the-environmental-and-health-impacts-of-active-pharmaceuticals-ingredients.pdf>

³⁵ Ibid.

4.3.2 Animal/Agricultural Industry

Highlights:

- Limited data are available on agricultural pharmaceutical volumes and pathways in the Great Lakes.
- One main pathway is from runoff containing manure/biosolids contaminated with APIs.
- Information on the use and disposal of veterinary drugs from small animal practices is lacking.
- Seasonal and spatial variations in veterinary pharmaceutical concentrations are additional data gaps.

The agricultural industry, particularly animal husbandry, has been identified as an important contributor to pharmaceuticals entering the Great Lakes.

Agriculture is a vital component of the Great Lakes basin economy, producing more than \$15 billion in crops and livestock each year.³⁶ Approximately one-third of the basin's area is used for agricultural production and produces a diversity of products, including grains and oilseeds, corn, fruit, vegetables, dairy and livestock such as cattle and hogs. About 7% of American farm production,³⁷ nearly 25% of Canada's agricultural production, and virtually all of Ontario's agricultural industry, occur in the Great Lakes region.^{38,39} More specifically, there are about 49,600 farms covering a total area of 12,348,463 acres of land in Ontario. The province has a significant livestock industry, which includes 1,623,710 cows, 3,534,104 pigs and 50,759,994 chickens.⁴⁰

The veterinary industry also plays a significant role in the basin. There are approximately 4,600 veterinarians and 2,200 veterinary facilities in Ontario.⁴¹ No information on

the use or disposal of drugs from small animal, equine and other types of veterinary practices was found by this study.

Pharmaceuticals are widely used for agricultural and veterinary purposes. For example, approximately one million kilograms of medically important antimicrobials were distributed for sale and use in animals in Canada in 2016.⁴² Approximately 80% of medically important antimicrobials sold in Canada are used in livestock.⁴³ Antibiotics are used in agriculture to treat infections and promote growth (as feed additives). The main pathway of veterinary pharmaceuticals to waterways is via excretion in feces and urine. Estimates in the US suggest that between 25-75% of antibiotics are excreted unchanged and can persist in the soil after land application.⁴⁴ Pharmaceuticals can enter the environment from agricultural systems through the application of manure on farmlands and the resulting farm runoff (Gaw et al., 2014).⁴⁵

Confined animal feeding operations (CAFOs) are of particular concern, including large-scale producers of hogs, poultry, beef cattle, and dairy cows – typically housing from thousands to tens of thousands or more animals. These facilities produce substantial amounts of waste, which is usually spread on the surrounding crop fields as



³⁶ Centre for Water Policy. (n.d.) Climate Change Impacts on Agriculture in the Great Lakes Basin. http://uwmm.edu/centerforwaterpolicy/wp-content/uploads/sites/170/2013/10/Great-Lakes_Agriculture_Final.pdf

³⁷ US Environmental Protection Agency. (n.d.). Great Lakes Facts and Figures. <https://www.epa.gov/greatlakes/great-lakes-facts-and-figures>

³⁸ Great Lakes Coastal Resilience. (2013). *Great Lakes Coastal Resilience Planning Guide: People in the Great Lakes*. <http://www.greatlakesresilience.org/climate-environment/people-great-lakes>

³⁹ International Joint Commission. (n.d.). *An International Treasure Worth Protecting: Great Facts about the Great Lakes*. http://www.ijc.org/en/activitiesX/consultations/glwqa/guide_stat.htm

⁴⁰ Ontario Ministry of Agriculture, Food and Rural Affairs. (2018). Ontario Farm Data, Census of Agriculture, 1996, 2001, 2006, 2011 and 2016. <http://www.omafr.gov.on.ca/english/stats/census/summary.htm>

⁴¹ College of Veterinarians of Ontario. (n.d.). About the College of Veterinarians of Ontario. <https://cvo.org/>

⁴² Health Canada. (2018). Canadian Antimicrobial Resistance Surveillance System 2017 Report. <https://www.canada.ca/en/public-health/services/publications/drugs-health-products/canadian-antimicrobial-resistance-surveillance-system-2017-report-executive-summary.html>

⁴³ Government of Canada. (2017). *Regulations Amending the Food and Drug Regulations (Veterinary Drugs – Antimicrobial Resistance)*. <http://www.gazette.gc.ca/rp-pr/p2/2017/2017-05-17/html/sor-dors76-eng.html>

⁴⁴ Natural Resources Defense Council. Dosed without Prescription: Preventing Pharmaceutical Contamination of our Nation's Drinking Water. (2009) https://www.nrdc.org/sites/default/files/hea_10012001a.pdf

⁴⁵ Gaw, S., Thomas, K. V., and Hutchinson, T. H. (2014). Sources, Impacts and Trends of Pharmaceuticals in the Marine and Coastal Environment. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 369(1656): 20130572. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4213585/>

a fertilizer. These “spray fields” can introduce antibiotics, hormones and other pharmaceutical contaminants into the waterways.⁴⁶

In addition, APIs can be present in sewage sludge originating from WWTPs. The application of municipal biosolids on farmlands to fertilize crops could also lead to pharmaceutical pollution in water. Ontario generates approximately 300,000 dry tonnes of municipal sewage biosolids per year, of which about 40% is applied to land, 40% goes to landfills and 20% is incinerated.⁴⁷

Limited information is available on API discharges to the Great Lakes from animal/agricultural sources. A study by Wu et al. (2009) examined the occurrence of 18 commonly used pharmaceuticals in an agricultural area on the coastline of Maumee Bay within the western Lake Erie basin.⁴⁸ Caffeine, carbamazepine, ibuprofen and paraxanthine were detected in surface water, but none of these compounds were detected in sediment samples. In a field that was receiving biosolids application, pharmaceuticals were detected in the tile drainage but not in the soil.

CAFOs were found to be a source of pharmaceutical contamination in the US,⁴⁹ but no data for Ontario were found in this study.

Evidence from other jurisdictions than Ontario indicates that the presence of veterinary pharmaceuticals in aquatic environments varies spatially and temporally and is influenced by several factors, including agricultural practices and climatic conditions. A French study by Jaffrézic et al. (2017) analyzed the presence of veterinary pharmaceuticals in agricultural watersheds that form a part of the Haute Rance watershed in northwestern France.⁵⁰ Animal-specific and mixed-use pharmaceuticals were detected at all seven sampling points and at concentrations higher than those of human-specific pharmaceuticals.

Animal-specific pharmaceuticals were detected in runoff and during periods of manure spreading.

This suggests that the contribution of various sources (human-specific versus animal-specific versus mixed-use) and seasonal variations in pharmaceutical concentrations at different locations are important data gaps from agriculture operations in the Great Lakes basin.

4.3.3 Aquaculture

Highlights:

- 75% of Canada’s salmonid production occurs in northern Lake Huron.
- Aquaculture operations discharge pharmaceuticals directly into the Great Lakes.
- There is a lack of data on the amount of APIs released from aquaculture operations into the Great Lakes.

Aquaculture has been identified as a stressor to Great Lakes water quality. The northern channel of Lake Huron as well as Georgian Bay are home to about 75% of Ontario’s farmed salmonid production, such as rainbow trout.⁵¹ These operations are performed in open water cages. Pharmaceuticals, including antibiotics, are released directly into the water. Studies in other jurisdictions suggest that up to 75% of the administered dietary dose of a veterinary medicine to farmed fish species can be lost to the surrounding environment (Gaw et al., 2014).⁵² Antibacterial drugs used in aquaculture have been shown to persist in water and sediment in the vicinity of fish farms (Grigorakis and Rigos, 2011).⁵³ However, no data were found in this study on the levels of APIs released to the Great Lakes from these operations.

A range of products are registered for use as antibiotics in the finfish aquaculture industry in Canada.⁵⁴ Approximately

⁴⁶ Ibid.

⁴⁷ Canadian Institute for Environmental Law and Policy. (2009). CIELAP Brief on Biosolids Management in Ontario. http://www.cielap.org/pdf/Brief_Biosolids.pdf

⁴⁸ Wu, C., Witter, J. D., Spongberg, A. L., Czajkowski, K. P. (2009). Occurrence of Selected Pharmaceuticals in an Agricultural Landscape, Western Lake Erie Basin. *Water Research*, 43 (14), 3407–3416. <https://doi.org/10.1016/j.watres.2009.05.014>

⁴⁹ Lincocmycin, a veterinary antibiotic, was found in Sugar Creek in Indiana near a CAFO at a mean concentration of 5.5ng/L in 57% of samples taken (Bernot et al., 2013).

⁵⁰ Jaffrézic, A., Jardé, E., Soulier, A., Carrera, L., Marengue, E., Cailleau, A., Bot, B. L. (2017). Veterinary Pharmaceutical Contamination in Mixed Land Use Watersheds: from Agricultural Headwater to Water Monitoring watershed. *Science of the Total Environment*, 609, 992–1000. <https://doi.org/10.1016/j.scitotenv.2017.07.206>

⁵¹ Great Lakes Environmental Assessment and Mapping Project. (n.d.). Aquaculture. http://www.greatlakesmapping.org/great_lake_stressors/3/aquaculture

⁵² Gaw, S., Thomas, K. V., and Hutchinson, T. H. (2014). Sources, Impacts and Trends of Pharmaceuticals in the Marine and Coastal Environment. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 369(1656): 20130572. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4213585/>

⁵³ Grigorakis K, Rigos G. (2011). Aquaculture effects on environmental and public welfare—the case of Mediterranean mariculture. *Chemosphere*, 85, 899–919. <https://www.ncbi.nlm.nih.gov/pubmed/21821276>

⁵⁴ Oxytetracycline (OTC), trimethoprim80%/sulphadiazine20% (Tribrissen), sulfadimethoxine 80%/ormetoprim 20% (Romet 30), and Florfenicol. The most common in-feed treatments have involved the use of ivermectin, emamectin benzoate (EB) and teflubenzuron (registered as Calicide) (Burridge et al., 2010)

20,000 kilograms of antibiotics were used by this industry in 2007 (Burrige et al., 2010).^{55,56} This medication was emitted either directly or by passing through fish. This is true for all open-water pen-type operations. Land-based tank operations have better control over their medication discharges.

Production in inland waters in Canada accounts for approximately 4% of the national volume of aquaculture, with a dollar value of \$32.6 million.⁵⁷

4.3.4 Landfill Leachate

Highlights:

- A portion of pharmaceuticals disposed of in landfills may end up in leachate.
- Leachate is treated at WWTPs where facilities exist, but treatment does not remove all APIs.
- There are major knowledge gaps on discharge volumes.

Leachate from landfills may be a source of pharmaceuticals in the Great Lakes. There are 32 large landfills in Ontario, 28 of which are situated in the Great Lakes drainage basin.⁵⁸ There are 2,375 small landfills in Ontario, with an unknown number in the Great Lakes basin.⁵⁹ Leachate from large landfills is collected and treated at WWTPs. Some API content will remain after treatment and will be released into the lakes. If landfills are not properly lined or the liners fail, then API-containing leachate can discharge directly to groundwater.

Data on landfill leachate as a source of API discharges is not available for any of the Great Lakes. Study participants suggest that pharmaceutical products in landfill leachate would likely contain APIs. In addition, landfills accepting sewage sludge could contribute leachate-carrying

pharmaceutical products. About 40% of municipal sewage biosolids that are produced in Ontario each year are disposed of in landfills.⁶⁰

Research in other jurisdictions indicates that landfill leachate could be a significant source of APIs.⁶¹ A Taiwanese study by Lu et al. (2016) examined the distribution of 26 pharmaceuticals among four municipal landfill leachates.⁶² The study looked at monitoring wells upstream and downstream from the landfill and concluded that there were significantly higher concentrations of APIs downstream due to leaking leachate.

4.3.5 Pharmaceutical Manufacturing Industry

Highlights:

- Pharmaceutical manufacturing is not likely a significant contributor of overall API discharges to the Great Lakes, but it could be an important localized source.
- There is a lack of transparency in how manufacturers manage their process water.

This study found a lack of transparency and conflicting information about the contribution of the pharmaceutical manufacturing industry to API discharges.

Pharmaceutical manufacturing is a significant industry in Ontario, with provincial exports valued at more than \$7 billion annually.⁶³ There are 21 pharmaceutical companies operating in Ontario and 24 research hospitals that support them.⁶⁴ The pharmaceutical manufacturing activity in the province is concentrated around the western end of Lake Ontario, between Oshawa and Niagara Falls.⁶⁵ In

⁵⁵ Fisheries and Oceans Canada. (2017). Pathway of Effects of Chemical Inputs from the Aquaculture Activities in Canada. http://www.dfo-mpo.gc.ca/csas-sccs/Publications/ResDocs-DocRech/2010/2010_017-eng.html

⁵⁶ Burrige, L. E., Doe, K. G., Ernst, W. (2010). Pathway of Effects of Chemical Inputs from the Aquaculture Activities in Canada. Canadian Science Advisory Secretariat. Research Document 2010/017.

⁵⁷ Fisheries and Oceans Canada. (2012). Aquaculture in Canada 2012: A Report on Aquaculture Sustainability. http://www.dfo-mpo.gc.ca/aquaculture/lib-bis/abi-irida/pdf/DFO_2012_SRI_AQUACULTURE_ENG.pdf

⁵⁸ Government of Ontario. (n.d.). Map of large landfills in Ontario. <https://www.ontario.ca/environment-and-energy/map-large-landfill-sites?region=Ontario>

⁵⁹ Government of Ontario. (n.d.). Small landfill sites list. <https://www.ontario.ca/environment-and-energy/small-landfill-sites-list>

⁶⁰ Canadian Institute for Environmental Law and Policy. (2009). CIELAP Brief on Biosolids Management in Ontario. http://www.cielap.org/pdf/Brief_Biosolids.pdf

⁶¹ Gaw, S., Thomas, K. V., and Hutchinson, T. H. (2014). Sources, Impacts and Trends of Pharmaceuticals in the Marine and Coastal Environment. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 369(1656): 20130572. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4213585/>

⁶² Lu, M.-C.; Chen, Y. Y.; Chiou, M.-R.; Chen, M. Y.; Fan, H.-J. (2016). Occurrence and treatment efficiency of pharmaceuticals in landfill leachates. *Waste Management*, 55, 257–264. <https://doi.org/10.1016/j.wasman.2016.03.029>

⁶³ Ontario Investment Office. (2018). Introduction. <https://www.investinontario.com/pharmaceuticals#intro>

⁶⁴ Ontario Investment Office. (2018). Pharmaceuticals. <https://www.investinontario.com/pharmaceuticals#pharma-in-ontario>

⁶⁵ Pharmaceutical Companies in Ontario. (2018) https://www.google.ca/search?rlz=1C1CHBF_enCA722CA722&q=pharmaceutical+manufacturers+in+Ontario&psic=0&rflfq=1&rlha=0&rlag=43468374.-79475485,38444&tbm=cl&ved=0ahUKewjGnfj9_fZAhWF7YMKHT4VDncQtgMIMg&tbs=lr:f:2m4!1e17!4m2!17m1!1e2!2m1!1e2!2m1!1e3!3s!AE!f:1,lf_ui:2&rdoc=1#rfl=hd::si::mv:1!m3!1d2782342.6219412573!2d-75.49689397109375!3d43.74667651678435!3m2!1!1325!2!724!4f13.1

addition, there are approximately 1,900 life science firms in Ontario.⁶⁶

Several pharmaceutical company websites were reviewed as part of this study, and no information was found on the treatment of their process water and associated environmental impacts.

Kleywegt et al. (2019) examined discharges into sewers in Ontario of APIs during processing from five manufacturing facilities. None of the facilities had on-site treatment of APIs prior to their discharge. The study found that pharmaceutical facilities could be a major source of API loadings to sewers. The researchers detected elevated concentrations of several antidepressants, mood stabilizers, antibiotics, analgesics, cardiovascular drugs and blood pressure control drugs in the effluents as well as downstream of the sites. The study suggests that several kilograms of lost products could be directly discharged into the sewers every day during the manufacturing of pharmaceuticals.⁶⁷

Study participants suggested that pharmaceutical manufacturers are not a significant contributor of API discharges into the Great Lakes. One study participant noted that pharmaceutical manufacturers are required by pharmacopeia standards to remove all APIs and precursors from their wastewater. It was also mentioned that pharmaceutical manufacturers' wastewater treatment technology is superior to most municipal WWTP technology. However, another study participant stated that some pharmaceutical manufacturers were performing at higher levels than others.

Study participant comments contradict studies that indicate that municipal WWTPs have greater removal efficiencies than pharmaceutical manufacturing treatment plants. Sim et al. (2010) investigated the occurrence of pharmaceuticals in wastewater from municipal, livestock, hospital and pharmaceutical manufacturer WWTPs near major river basins in Korea.⁶⁸ The researchers found that

pharmaceutical manufacturers' treatment plants had the second highest concentrations of pharmaceuticals in their influents, while municipal influents showed the highest daily loads of pharmaceuticals. The study found that all source types showed similar loads of pharmaceuticals in their effluents, indicating that while municipal treatment plants had high removal rates of pharmaceuticals, the removal rates in pharmaceutical treatment plants were relatively poor.⁶⁹ A study by Sanchez et al. (2011) found evidence of fish (wild gudgeon) exposure to various pollutants downstream from pharmaceutical manufacturers in the Dore River (Puy de Dôme, France).⁷⁰

The research for this study suggests that the manufacturing industry may be a significant source of pharmaceutical pollution in the aquatic environment. Further investigation, including systematic monitoring of effluents, is required.

4.3.6 Hospital and Healthcare Institutions

Highlights:

- Hospitals could be a source of pharmaceuticals not commonly found in municipal settings (e.g., cancer drugs).
- Hospitals discharge to municipal WWTPs, so they have not been considered by governments as a major concern.
- Data are lacking on the volumes and toxicity of APIs discharged from hospitals and healthcare institutions.

There are 463 hospitals⁷¹ and 625 long-term care facilities⁷² in Ontario. These could be primary dischargers of certain drugs, such as cancer-fighting medications, in wastewater.

This study did not find data suggesting that acutely toxic APIs have been identified in WWTP effluent or in surface waters in the Great Lakes. However, several study

⁶⁶ Ontario Investment Office. (2018). Pharmaceuticals. <https://www.investinontario.com/pharmaceuticals#pharma-in-ontario>

⁶⁷ Kleywegt, S., Payne M., Ngb, F., and Fletcher T. (2019). Environmental Loadings of Active Pharmaceutical Ingredients from Manufacturing Facilities in Canada. *Science of the Total Environment*. 646:257-264. <https://www.ncbi.nlm.nih.gov/pubmed/30055488>

⁶⁸ Sim, W. J.; Lee, J. W.; Lee, E. S.; Shin, S. K.; Hwang, S. R.; Oh, J. E. (2011). Occurrence and Distribution of Pharmaceuticals in Wastewater from Households, Livestock Farms, Hospitals and Pharmaceutical Manufactures. *Chemosphere*, 82 (2), 179–186. <https://doi.org/10.1016/j.chemosphere.2010.10.026>

⁶⁹ It is not clear from the study what types of wastewater treatment technologies were used at different facilities.

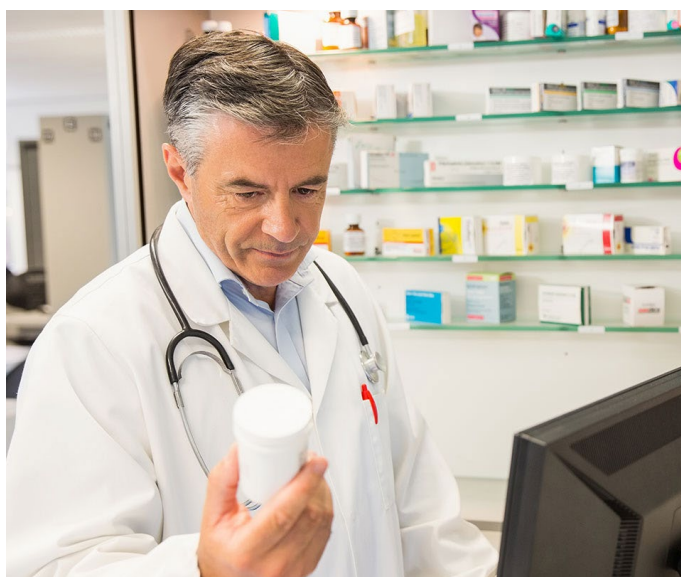
⁷⁰ Sanchez, W.; Sremski, W.; Piccini, B.; Palluel, O.; Maillot-Maréchal, E.; Betoulle, S.; Jaffal, A.; Aït-Aïssa, S.; Brion, F.; Thybaud, E.; Hinfray, N.; Porcher, J.M. (2011). Adverse Effects in Wild Fish Living Downstream from Pharmaceutical Manufacture Discharges. *Environment International*, 37:1342-1348. <https://doi.org/10.1016/j.envint.2011.06.002>

⁷¹ Statista. (n.d.) Number of Hospital Establishments in Canada as of 2015, by Province. <https://www.statista.com/statistics/440923/total-number-of-hospital-establishments-in-canada-by-province/>

⁷² Ontario Long Term Care Association. (2017). About Long-term Care in Ontario: Facts and Figures. [https://www.oltpca.com/oltpca/OLTPCA/LongTermCare/OLTPCA/Public/LongTermCare/FactsFigures.aspx#Ontario's%20long-term%20care%20homes%20\(June%202017\)](https://www.oltpca.com/oltpca/OLTPCA/LongTermCare/OLTPCA/Public/LongTermCare/FactsFigures.aspx#Ontario's%20long-term%20care%20homes%20(June%202017))

participants suggested that healthcare facilities, such as hospitals and retirement homes, can be significant point sources of pharmaceuticals in the lakes, due to the use of a variety of pharmaceuticals, including more toxic drugs, which can end up in their wastewater.

A Spanish study examined pharmaceuticals in wastewater from a medium-size hospital in the Valencia Region. Twenty-four compounds at levels ranging from 5 ng/L to 2 mg/L were found.⁷³ The highest concentrations were recorded for iodinated contrast media (ICM) iomeprol (424 - 2093 µg/L), the analgesic acetaminophen (15–44 µg/L), the diuretic (DIU) furosemide (6–15 µg/L), and the antibiotics ofloxacin and trimethoprim (2–5 µg/L). The researchers conducted a screening level risk assessment study on hospital wastewater and found that eight pharmaceuticals (acetaminophen, diclofenac, ibuprofen, naproxen, clarithromycin, ofloxacin, trimethoprim and propranolol) could pose significant risks to aquatic organisms. However, only ibuprofen was found to pose a moderate risk when the current dilution and degradation processes were taken into account. The study points to the need for a better understanding of the concentrations of pharmaceuticals in hospital effluents, as well as whether pre-treatment of hospital wastewater is required to reduce pharmaceutical discharges to the aquatic environment.



4.4 Impacts on Aquatic Systems and Human Health

4.4.1 Impacts on Aquatic Ecosystems

Highlights:

- Low concentrations of hormones were found to cause intersex (i.e., the presence of both male and female characteristics in a single organism) in multiple species of fish.
- Antidepressants were found to accumulate in fish brains and cause changes in mating behaviour.
- Wastewater effluent was found to increase oxidative stress and reduce survivability of multiple fish species.
- Bacterial colonies close to WWTPs were found to have higher levels of antibiotic resistance.

The literature review and interviews with study participants suggest that endocrine disrupting compounds (such as hormones), antibiotic compounds and psychiatric drugs (e.g., antidepressants) are the main compounds of concern in aquatic ecosystems. Appendix E summarizes the range of impacts observed, including:

- Intersex of males
- Increases in metabolic rates near WWTP effluent
- Reduced predator avoidance
- Bioaccumulation in tissues
- Higher mortality rates
- Changes in reproductive behaviours

More detailed findings

The endocrine disrupting compound 17 α -ethinylestradiol (a common contraceptive drug) has been found to bioaccumulate in shorthead redhorse suckers (Al-Ansari et al., 2010). The same study suggests that this compound would be present in higher concentrations in carnivores and other top predators. More research should be done on possible survival/reproduction effects of estrogen bioaccumulation in carnivores/top predators.

A study by Du et al. (2018) demonstrates that exposure to wastewater effluent reduced survivability in bluegill

⁷³ Mendoza, A., Aceña, J., Pérez, S., Lopez de Alda, M., Barcelo, D., Gil, A., Valcarcel, Y. (2015). Pharmaceuticals and Iodinated Contrast Media in a Hospital Wastewater: A Case Study to Analyse Their Presence and Characterise Their Environmental Risk and Hazard. *Environmental Research*. 140 (10), pp. 225-241. <https://www.sciencedirect.com/science/article/pii/S0013935115001206>

sunfish.⁷⁴ The oxygen consumption of the fish exposed to wastewater effluent was higher than a control group in clean water. It was concluded that exposure to wastewater effluent invokes a metabolic cost that leads to compensatory respiratory improvements in oxygen uptake, delivery and utilization.

Antidepressants have been shown to bioaccumulate in fish brains and cause changes in behaviours such as mating, aggression and predator avoidance. A study by Arnnok et al. (2017) investigated the bioaccumulation potential of antidepressants in the Niagara River. It found that the main metabolite of Sertraline, called Norsertraline, was present in fish brain tissues at concentrations of up to 400,000 ng/kg. This is about 1,000 times greater than the concentration of the parent drug (218ng/L) in the surface water.

The release of antibiotics could contribute to the development of antibiotic resistance in the environment. A study by Ibsen et al. (2017) showed statistically significant differences in aquatic bacterial abundance and antibiotic resistance between down-gradient beach samples and up-gradient coastal wetland samples.⁷⁵ Decaying and free-floating *Cladophora* sampled near the WWTP had the highest bacterial densities overall, including on ampicillin- and vancomycin-treated plates. The presence of bacteria on the antibiotic-treated plates indicates that some level of antibiotic resistance is present. It is not clear whether this was a direct result of exposure to WWTP effluent.

The environmental risk of pharmaceuticals in the Great Lakes has been questioned due to high dilution. Blair et al. (2013a) compared environmental concentrations of pharmaceuticals in Lake Michigan to the predicted no-effect concentrations. The presence of multiple pharmaceuticals was found to be of medium or high ecological risk. The study indicates that dilution alone does not reduce concentrations below their predicted no-effect levels. Nearshore organisms are likely to be the most affected as they are nearest to WWTP outfalls and are therefore exposed to the most concentrated effluent.

Study participants revealed that ecotoxicology data are severely lacking for APIs and mixtures of APIs. This indicates a need for more complete and comprehensive lake-wide monitoring programs.

4.4.2 Impacts on Human Health

Highlights:

- Limited information is available on APIs in drinking water.
- Current understanding is that the human health risk of APIs is low.

Limited information was found in this study on the human health risks of pharmaceutical contamination in the Great Lakes basin. The main exposure pathways of APIs for humans are through the consumption of contaminated drinking water and from eating contaminated foods (e.g., fish tissue). Several study participants stated that due to their low concentration in the lakes, APIs are currently not a human health risk. Human exposure to APIs from lake water occurs at significantly lower doses than would normally illicit a therapeutic effect. However, it is important to consider the potential of mixtures of APIs to have adverse effects on human health, as well as risks related to chronic exposure. One study participant raised concern that certain segments of the population, including children and the elderly, may be more susceptible to exposure than other segments.

More studies on the effects of chronic exposure to mixtures of APIs are needed to better understand the potential for long-term health risks in different population segments.

⁷⁴ Du, S. N. N., McCallum, E. S., Vaseghi-Shanjani, M., Choi, J. A., Warriner, T. R., Balshine, S., Scott, G. R. (2018). Metabolic Costs of Exposure to Wastewater Effluent Lead to Compensatory Adjustments in Respiratory Physiology in Bluegill Sunfish. *Environmental Science & Technology*, 52 (2), pp 801–811. <https://pubs.acs.org/doi/abs/10.1021/acs.est.7b03745>

⁷⁵ Ibsen, M., Fernando, D. M., Kumar, A., Kirkwood, A. E. (2017). Prevalence of Antibiotic Resistance Genes in Bacterial Communities Associated with *Cladophora* Glomerata Mats along the Nearshore of Lake Ontario. *Canadian Journal of Microbiology*, 63: 439–449. <https://www.ncbi.nlm.nih.gov/pubmed/28192677>

4.5 Measures and Actions

This section contains an overview of actions and measures that have been taken to understand the sources and pathways of pharmaceuticals discharged into the Great Lakes, and to assess the effectiveness of mitigation efforts. International examples of leadership on policy implementation, consumer outreach and engagement, and technology development and application are also discussed.

4.5.1 Research, Surveillance and Monitoring Activities

Highlights:

- Research, surveillance and monitoring activities are underway to respond to increasing concerns about pharmaceutical contaminants in the environment, including the Great Lakes.
- These activities are generally disconnected and their impacts are not clear.
- The European Union and the US have better coordinated and more systematic surveillance and monitoring programs than Canada.

Research, surveillance and monitoring have been part of Canada's actions to respond to concerns about pharmaceutical contaminants in the environment. They support the implementation of the federal Chemicals Management Plan (CMP). The efforts are focused on monitoring of chemicals in multiple environmental media, including water, sediment, fish and wildlife, as well as source monitoring (WWTP effluent, and sludge and landfill leachate). The CMP Environmental Monitoring and Surveillance Program complements the human health biomonitoring initiatives conducted by Health Canada. Together, these programs aim to inform risk assessment and management.^{76,77}

From 2008 to 2017, the Pharmaceuticals and Personal Care Products Surveillance Network studied the status of pharmaceuticals and personal care product (PPCP) pollutants in surface waters in Canada. The Network's objectives included: providing baseline data and determining spatial patterns of PPCP pollutants; quantifying exposure levels and generating science-based information necessary to identify risks and inform risk management; and, understanding the environmental fate and behaviour of these chemicals. Several of the Network's monitoring stations were located in the Great Lakes basin and measured substances such as acidic drugs, neutral drugs, and antibiotics. The overarching goal of the Network was to support Environment and Climate Change Canada's freshwater ecosystem approach to watershed management.⁷⁸

The Public Health Agency of Canada leads a multiagency surveillance program, the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS), to keep track of trends in antibiotic resistance in humans and animals, and to report integrated data across species and regions. CIPARS released its latest report in 2017, highlighting antimicrobial resistance (AMR) and antimicrobial use (AMU) surveillance findings in Canada.⁷⁹ This work informs antimicrobial stewardship efforts and helps prevent the spread of AMR in Canada.



⁷⁶ Health Canada. (2017). Monitoring and Surveillance Activities under Canada's Chemicals Management Plan. <https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan/monitoring-surveillance.html>

⁷⁷ Environment and Climate Change Canada. (2012). Environmental Monitoring and Surveillance in Support of the Chemicals Management Plan. <http://www.ec.gc.ca/Publications/default.asp?lang=En&xml=F48952A0-3F54-4D76-BAA6-EA6CF5529590>

⁷⁸ Environment and Climate Change Canada. (2017). Pharmaceuticals and Personal Care Products Surveillance Network. <http://ec.gc.ca/scitech/default.asp?lang=En&n=FDfE3DAA-1>

⁷⁹ Health Canada. (2018). Canadian Antimicrobial Resistance Surveillance System 2017 Report. <https://www.canada.ca/en/public-health/services/publications/drugs-health-products/canadian-antimicrobial-resistance-surveillance-system-2017-report-executive-summary.html>

The Ontario Ministry of the Environment, Conservation and Parks (MECP, formerly the Ontario Ministry of the Environment and Climate Change) has conducted long-term, periodic monitoring of a number of Chemicals of Mutual Concern (CMCs) in the Great Lakes, including some pharmaceuticals. MECP has undertaken collaborative research projects with other ministries and departments to investigate concentrations and pathways of selected pharmaceuticals in various settings, such as river aquatic systems,⁸⁰ groundwater, soil, and subsurface drainage,⁸¹ as well as agricultural areas.^{82,83} The removal efficiency of wastewater treatment plants and drinking water systems for these substances has also been studied.^{84,85}

While Canadian scientists are making significant research contributions through these initiatives, the programs are mostly disconnected efforts, rather than as part of a strategic and systematic research and surveillance effort. A report prepared in 2014 by the federal Standing Senate Committee on Social Affairs, Science and Technology⁸⁶ found that the PPCP Surveillance Network's activities did not constitute a systematic sampling and reporting program. Rather, it was an informal effort by scientists who were involved in other surveillance and research programs. Likewise, the Committee found that access to the data gathered by CIPARS is limited, is not available in a timely and comprehensive manner, and has not been used to its full potential.

A more comprehensive, strategic, coordinated and transparent Canadian approach to the surveillance and monitoring of pharmaceuticals in the environment is needed for the Great Lakes.

Developments in key international jurisdictions

In contrast to Canada, the European Union and the US have longstanding, coordinated and systematic surveillance and monitoring programs.⁸⁷ Under the EU Water Framework Directive (2000/60/EC) as amended, Member States are required to maintain concentrations of these substances below specified levels in water bodies. Several pharmaceuticals have been proposed for inclusion in their list of priority substances; however, none has been added to date. In addition, the European Commission (EC) has established a watch list of substances for which monitoring data are collected across the region for up to four years, to support future prioritisation exercises.⁸⁸ Six pharmaceuticals are currently subject to the watch list monitoring mechanism: diclofenac (anti-inflammatory); 17 alpha-ethinylestradiol (EE2); 17 beta-estradiol (E2) hormones; azithromycin; clarithromycin; and, erythromycin (macrolide antibiotics).

In 1999, the EU created the European Antimicrobial Resistance Surveillance Network, which gathers data from Member Countries, each of which has implemented a surveillance system. Sweden and Denmark were the first European countries to take action against the non-medical use of antibiotics in food-producing animals (i.e., the use of antibiotics as growth promoters). Both countries have implemented a comprehensive cross-sectoral surveillance system, which has led to the withdrawal of antibiotics as growth promoters.⁸⁹

The European Commission (EC) has supported a number of research projects focused on pharmaceuticals in the aquatic environment, under the EU's Research Framework Programmes, which set out the EU's strategic objectives and thematic priorities for research activities and are a principal funding mechanism for research and

⁸⁰ Lishman, L., Smyth, S.A., Sarafin, K., Kleywegt, S., Toito, J., Peart, T., Lee, B., Servos, M., Beland, M., Seto, P. (2006). Occurrence and Reductions of Pharmaceuticals and Personal Care Products and Estrogens by Municipal Wastewater Treatment Plants in Ontario, Canada. *Science of the Total Environment*, 367 (2-3): 544-558.

⁸¹ Gottschall, N., Topp, E., Edwards, M., Payne, M., Kleywegt, S., Russell, P., Lapen, D.R. (2013). Hormones, Sterols, and Fecal Indicator Bacteria in Groundwater, Soil, and Subsurface Drainage Following a High Single Application of Municipal Biosolids to a Field. *Chemosphere*, 91 (3): 275-286.

⁸² Sabourin, L., Beck, A., Duenk, P.W., Kleywegt, S., Lapen, D.R., Li, H., Metcalfe, C.D., Payne, M., Topp, E. (2009). Runoff of Pharmaceuticals and Personal Care Products Following Application of De-watered Municipal Biosolids to an Agricultural Field. *Science of the Total Environment*, 407 (16): 4596-4604.

⁸³ Topp, E., Monteiro, S.C., Beck, A., Coelho, B.B., Boxall, A.B.A., Duenk, P.W., Kleywegt, S., Lapen, D.R., Payne, M., Sabourin, L., Li, H., Metcalfe, C.D. (2008). Runoff of Pharmaceuticals and Personal Care Products Following Application of Biosolids to an Agricultural Field. *Science of the Total Environment*, 396 (1): 52-59.

⁸⁴ Kleywegt, S., Pileggi, V., Yang, P., Hao, C., Zhao, X., Rocks, C., Thach, S., Cheung, P., Whitehead, B. (2011). Pharmaceuticals, Hormones and Bisphenol A in Untreated Source and Finished Drinking Water in Ontario, Canada - Occurrence and Treatment Efficiency. *Science of the Total Environment*, 409 (8): 1481-1488.

⁸⁵ Hicks, K.A., Fuzzen, M.L.M., McCann, E.K., Arlos, M.J., Bragg, L.M., Kleywegt, S., Tetreault, G.R., McMaster, M.E., Servos, M.R. 2017. Reduction of Intersex in a Wild Fish Population in Response to Major Municipal Wastewater Treatment Plant Upgrades. *Environmental Science and Technology*, 51(3): 1811-1819.

⁸⁶ Standing Senate Committee on Social Affairs, Science and Technology. (2013). Prescription Pharmaceuticals in Canada. <https://sencanada.ca/content/sen/Committee/412/soci/rep/rep15oct14-e.pdf>

⁸⁷ Holtz S. (2006). There Is No Away. Pharmaceuticals, Personal Care Products, and Endocrine-Disrupting Substances: Emerging Contaminants Detected in Water, Canadian Institute for Environmental Law and Policy, Toronto, Ontario. <http://www.cielap.org/pdf/NoAway.pdf>

⁸⁸ Carere, M., Polesello, S., Kase, R., Gawlik, B.M. (2015). The Emerging Contaminants in the Context of the EU Water Framework Directive. Emerging Contaminants in River Ecosystems, pp.1-19. DOI: 10.1007/978_2015_5011. https://www.researchgate.net/publication/295551859_The_Emerging_Contaminants_in_the_Context_of_the_EU_Water_Framework_Directive

⁸⁹ Standing Senate Committee on Social Affairs, Science and Technology. (2013). Prescription Pharmaceuticals in Canada. <https://sencanada.ca/content/sen/Committee/412/soci/rep/rep15oct14-e.pdf>

innovation. Examples of multi-year projects focused on pharmaceutical-related issues include: the KNAPPE project, which examined the state of knowledge on pharmaceuticals in the aquatic environment (2007-2008);⁹⁰ the CYTOTHREAT project, which assessed the fate and effects of cytostatic pharmaceuticals in freshwater organisms and in vitro cell lines (2011-2014);⁹¹ and, the PHARMAS project, which evaluated the environmental and health risks associated with antibiotics and anticancer drugs in the environment (2011-2014).⁹²

Since 2005, the EC has funded the network of reference laboratories, research centres and related organisations for monitoring of emerging environmental substances (NORMAN) project to promote a permanent network of reference laboratories and research centers, including academia, industry, standardization bodies and NGOs.⁹³ NORMAN integrates EU-wide activities on chemicals of emerging concern (CECs), including pharmaceuticals, and collects monitoring data on the occurrence, effects and hazardous properties of CECs. This information is used by the NORMAN Prioritisation Working Group to assign substances to priority action categories.⁹⁴ NORMAN also facilitates the provision of transparent information and monitoring data on CECs, as well as the transfer of scientific knowledge to policy makers and regulators.⁹⁵

Notable initiatives in the US include the Great Lakes Fish Monitoring and Surveillance Program (GLFMSP), which was established in the late 1970s and is administered by the US EPA's Great Lakes National Program Office (GLNPO).⁹⁶ The program is designed to monitor contaminant trends in Great Lakes fish and provide information on new

compounds of concern entering the ecosystem.⁹⁷ Since 2009, a key element of GLFMSP has been the Great Lakes Emerging Chemical Surveillance Program. This program aims to determine the presence of Contaminants of Emerging Concern (CECs), including pharmaceuticals, in fish tissue, according to their persistent, bioaccumulative and/or toxic chemical properties.⁹⁸ Information gained from this program is used to guide state and federal monitoring programs.

Since the 1990s, the U.S. Geological Survey (USGS) has conducted numerous national and state level monitoring studies to investigate the sources, distribution, and effects of pharmaceuticals and other emerging contaminants in surface waters and groundwater.^{99,100} USGS's ongoing Toxic Substances Hydrology Program provides scientific information to inform the development of policies and practices that minimize or avoid exposure to toxic substances. The program includes investigations focused on contaminants of emerging concern in the environment, such as pharmaceuticals.

In addition, in 1996, the US established the National Antimicrobial Resistance Monitoring System (NARMS). This is a collaborative program among state and local public health departments and universities, the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC) and the Department of Agriculture (DA).¹⁰¹ The program provides information about emerging bacterial resistance as well as the impact of interventions designed to limit the spread of resistance.

⁹⁰ Community Research and Development Information Service (CORDIS). (2011). Reviewing the Environmental Impact of Pharmaceuticals. KNAPPE – Result In Brief. Project ID: 36864. https://cordis.europa.eu/result/rcn/87817_en.html

⁹¹ Community Research and Development Information Service (CORDIS). (2014). Fate and Effects of Cytostatic Pharmaceuticals in the Environment and the Identification of Biomarkers for and Improved Risk Assessment on Environmental Exposure. CytoThreat. Project ID: 265264. https://cordis.europa.eu/project/rcn/96703_en.html

⁹² Community Research and Development Information Service (CORDIS). (2014). Ecological and Human Health Risk Assessments of Antibiotics and Anti-cancer Drugs Found in the Environment. Pharms. Project ID: 265346. https://cordis.europa.eu/project/rcn/97551_en.html

⁹³ Dulio, V., van Bavel, B., Brorström-Lundén, E., Harmsen, J., Hollender, J., Schlabach, M., Slobodnik, J., Thomas, K. and Koschorreck, J. (2018). Emerging Pollutants in the EU: 10 Years of NORMAN in Support of Environmental Policies and Regulations. *Environmental Sciences Europe*, 30: 5. <https://doi.org/10.1186/s12302-018-0135-3>

⁹⁴ Network of Reference Laboratories, Research Centres and Related Organisations for Monitoring of Emerging Environmental Substances (NORMAN). (n.d.) Why do We Need to Address Emerging Substances? <http://www.norman-network.net/?q=node/19>

⁹⁵ Dulio, V., van Bavel, B., Brorström-Lundén, E., Harmsen, J., Hollender, J., Schlabach, M., Slobodnik, J., Thomas, K. and Koschorreck, J. (2018). Emerging Pollutants in the EU: 10 Years of NORMAN in Support of Environmental Policies and Regulations. *Environmental Sciences Europe*, 30: 5. <https://doi.org/10.1186/s12302-018-0135-3>

⁹⁶ US Environmental Protection Agency. (2017) Great Lakes Fish Monitoring and Surveillance. <https://www.epa.gov/great-lakes-monitoring/great-lakes-fish-monitoring-and-surveillance>

⁹⁷ Murphy, E. (2012) Great Lakes Fish Monitoring and Surveillance Program: Quality Management Plan. https://www.epa.gov/sites/production/files/2016-02/documents/gl_fm_smp_version_2_final_111312_508.pdf

⁹⁸ US Environmental Protection Agency. (2017) Great Lakes Emerging Chemical Surveillance Program. <https://www.epa.gov/great-lakes-monitoring/great-lakes-emerging-chemical-surveillance-program>

⁹⁹ Bright, P., Buxton, H., Balistreri, L., Barber, L., Chapelle, F., Cross, P., David, P. et al. (2013) U.S. Geological Survey Environmental Health Science Strategy— Providing Environmental Health Science for a Changing World. *U.S. Geological Survey*. <https://pubs.usgs.gov/circ/1383e/circ1383-E.pdf>

¹⁰⁰ For example, USGS study led by Kolpin et al. (2002) examined 95 contaminants, including a variety of pharmaceuticals, from industrial, human, and agricultural wastewater sources, in 139 streams in 30 states during 1999–2000. Another nationwide study by Barnes et al. (2008) examined 47 ambient ground-water sites in 18 states and analyzed for 65 contaminants, including pharmaceuticals. In addition, samples were collected from 74 sources of raw, untreated, drinking water in 25 states and Puerto Rico and analyzed for 100 organic wastewater contaminants, including pharmaceuticals. In a study by Benotti et al. (2006), 70 water samples were collected from 61 wells in the upper glacial and Magoghy aquifers during 2002–2005 and analyzed for 24 pharmaceuticals in Suffolk County, New York. For more studies, please see USGS webpage: https://toxics.usgs.gov/regional/emc/environmental_occurrence.html

¹⁰¹ US Food & Drug Administration. (2018). The National Antimicrobial Resistance Monitoring System. <https://www.fda.gov/animalveterinary/safetyhealth/antimicrobialresistance/nationalantimicrobial-resistancemonitoringsystem/>

4.5.2 Treaties, Legislation, Regulations and Policies

Highlights:

- There are no policies or legislation that specifically address the issue of pharmaceuticals in the Great Lakes, including pharmaceuticals entering the lakes through WWTPs.
- Pharmaceuticals fall under shared jurisdiction in Canada, and a variety of laws and regulations exist that can be applied to pharmaceutical pollution in aquatic environments.
- Ontario's Extended Producer Responsibility regulation enables waste take-back through pharmacies in most areas of the province.

Pharmaceuticals in the Great Lakes fall under the authority of two orders of government – federal and provincial. A review by this study of treaties, legislation, regulations and policies that are directly or indirectly related to the Great Lakes environment found no explicit and comprehensive focus on pharmaceutical discharges to the Great Lakes, or to any aquatic environments across Canada. There are no mandatory monitoring requirements or emission limits on pharmaceutical discharges into lakes. Work on pharmaceutical pollution has largely been driven by isolated academic and government research. The activities can be described as fragmented, with a number of disconnected initiatives and a lack of publicly available and up-to-date information.

Other countries and international jurisdictions have made greater progress than Canada and Ontario in addressing the issue of pharmaceuticals in the environment. Europe has taken the lead with its Watch List monitoring mechanism, which targets six pharmaceuticals of concern. Europe is developing a strategic approach to addressing pharmaceuticals in the environment, especially in water. Some European countries have taken steps to limit pharmaceuticals in water and wastewater. In the US, several pharmaceuticals have been included in the Environmental Protection Agency's Contaminant Candidate List (CCL), which is a list of chemicals under consideration for drinking water standards.



The analysis done for this study shows that no mandatory take-back programs for pharmaceuticals exist at the national level in Canada or the US. Such a program has been required in Europe for both human and veterinary pharmaceuticals for about 20 years. Ontario and British Columbia lead Canada with respect to take-back programs for human medicines, as required under Ontario Regulation 298/12 Collection of Pharmaceuticals and Sharps - Responsibility of Producers and the Recycling Regulation of the *Environmental Management Act* (B.C. Reg. 449/2004). Canada and Ontario rely on voluntary programs for animal husbandry with respect to medication training as well as unused medication collection programs. A comprehensive evaluation of these programs is needed to determine if policy changes to move from voluntary to mandatory, widely accessible programs are warranted. This is particularly important considering the large scale and impact of agricultural activities in the Great Lakes Basin.

The following section provides a brief overview of agreements, legislative texts and guidelines. It also identifies gaps and highlights areas for further monitoring and control action.

4.5.2.1 Drugs and Chemicals Management

Drugs are regulated in Canada under the federal *Food and Drugs Act*, which is administered by Health Canada. Under the Act, drugs include any substance for which a health claim has been made, which applies to prescription and non-prescription pharmaceuticals.¹⁰² The *Food and Drug Regulations* set out the requirements for manufacturers to present substantive scientific evidence of a drug's safety, efficacy and quality prior to obtaining approval from Health

¹⁰² Standing Senate Committee on Social Affairs, Science and Technology. (2015). Prescription Pharmaceuticals in Canada. <https://sencanada.ca/content/sen/Committee/412/soci/rep/rep18mar15-e.pdf>

Canada to market the product in Canada.¹⁰³ The *Canadian Environmental Protection Act, 1999* (CEPA) is the key piece of legislation with respect to chemicals management, pollution prevention and the protection of the environment and human health. Under CEPA, ECCC and Health Canada have the authority to regulate the use and release of toxic and harmful substances, and to take measures to prevent and reduce the threats posed by pharmaceuticals that are deemed harmful to human health and the environment.

Pharmaceuticals are covered under the Chemicals Management Plan (CMP) and its Environmental Impact Initiative (EII), whose mandate is to reduce the environmental and indirect human health impacts of substances in products regulated under the *Food and Drugs Act*. The CMP is delivered jointly by Environment and Climate Change Canada and Health Canada. It provides for a proactive, science-based approach that aims to reduce the risks posed by chemicals to human health and the environment through the following actions:

- conducting scientific evaluations to identify potential environmental and health risks from the generation, use and disposal of substances;
- developing risk management actions and promoting compliance with risk management obligations;
- promoting research and monitoring of chemical exposures and their effects on human health and the environment;
- conducting stakeholder and public engagement on the implementation of the plan; and
- collaborating in Canada and internationally on chemicals assessment and management.¹⁰⁴

The Domestic Substances List (DSL) under the CMP provides the basis for distinguishing “existing substances” which were manufactured, imported or used in Canada between January 1, 1984, and December 31, 1986 from

new substances. Through the process of categorization of approximately 23,000 substances on Canada’s DSL, approximately 4,300 substances were identified as requiring further action. The goal of the CMP is to address all 4,300 of those substances by 2020. Since the launch of the CMP in 2006, about 3,200 chemicals identified as priorities for action have been assessed. More than 420 existing substances were found to be harmful to the environment and/or human health, and more than 80 risk management actions have been implemented for these substances.¹⁰⁵ As part of the process, 28 substances used primarily as pharmaceuticals were identified as priorities as they met the categorization criteria of the DSL and/or were associated with a potential concern to the environment or to human health. However, a science-based evaluation (a screening assessment) found that these substances were not entering the environment at levels that are harmful to the environment or human health.¹⁰⁶

The New Substances Program applies to new substances, including pharmaceutical active ingredients, pharmaceutical excipients, veterinary drug active ingredients and veterinary drug excipients. The program aims to ensure that no new substance is introduced into the Canadian marketplace before undergoing ecological and human health assessments.¹⁰⁷ Under the CMP, Health Canada and Environment and Climate Change Canada conduct pre-market assessments of health and environmental effects of approximately 400-500 substances that are new to Canada each year.¹⁰⁸ Health Canada maintains the Drug Product Database (DPD), which contains information on drugs authorized and marketed for use in Canada, including human and veterinary pharmaceuticals, radiopharmaceuticals and disinfectants. The database contains approximately 49,880 products that are currently approved, marketed or cancelled, including 44,043 human drugs and 2,965 veterinary drugs.¹⁰⁹ Of these, approximately 12,034 human drugs and 1,370 veterinary drugs are currently being sold in Canada. The database provides product-specific information about

¹⁰³ Health Canada. (2018). Drug Products. <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products.html>

¹⁰⁴ Government of Canada. (n.d.). Overview of the Chemicals Management Plan. http://chemicalsubstanceschimiques.gc.ca/alt_formats/pdf/fact-fait/overview-vue-eng.pdf

¹⁰⁵ Environment and Climate Change Canada. (2017). Chemicals Management Plan Progress Report. <http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=6044455E-1>

¹⁰⁶ Government of Canada. (2015). Certain Substances on the Domestic Substances List used Primarily as Pharmaceuticals Fact Sheet. <https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/chemicals-glance/substances-domestic-substances-list-used-primarily-pharmaceuticals-fact-sheet.html>

¹⁰⁷ Government of Canada. (2018). New Substances Program of the Chemicals Management Plan. <https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan/initiatives/new-substances.html>

¹⁰⁸ Government of Canada. (2014). Identification of Chemicals and Polymers as Risk Assessment Priorities. <https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan/initiatives/identification-chemicals-polymers-risk-assessment-priorities.html>

¹⁰⁹ Health Canada. (2015). Drug Product Database. <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>

each drug, such as product name, producer, product class, dosage forms, routes of administration and number of active ingredients. However, no detail is provided on the environmental or human health risks of the drugs.

This study concludes that greater transparency is needed with respect to the health and environmental risk assessments of pharmaceuticals that are authorized and marketed for use in Canada. Canadians should have access to easily accessible and transparent information relating to risk assessment decisions, the health and environmental risks of pharmaceuticals (where these have been identified), and the mitigation measures that have been put in place to address these risks. More transparency would help to increase public confidence and participation in decision-making related to the assessment and management of pharmaceuticals in Canada.

Developments in key international jurisdictions

European and the US frameworks for pharmaceuticals and chemicals management share many similarities, but also have striking differences with Canada's framework. As in Canada, European and US regulations covering pharmaceuticals in the aquatic environment are complex and fall under the jurisdiction of different orders of government. However, several policy developments specific to pharmaceuticals are under way in these jurisdictions. The following provides a high-level overview of the key legislative instruments and policy developments on pharmaceuticals and water in Europe and the US, highlighting initiatives that could inform Canada's path forward on this issue.

In Europe, one of the key legislative factors influencing the presence of medicinal products in the environment is the framework for the marketing authorisation (MA) process for medicinal products, which is governed by Directives 2001/83/EC (for human use) and 2001/82/EC94 (for veterinary use), and by Regulation 2004/726. Producers of medicinal products require an MA before the products are allowed into the marketplace. In most cases, the MA application must include an Environmental Risk Assessment (ERA). When the ERA determines that a risk to the environment exists (whether for human or veterinary

medicinal products), risk mitigation measures (RMM) are recommended. However, compliance with RMM has a voluntary character, and the implementation of RMM is not systematically verified. Furthermore, most human medicinal products currently consumed in the EU were authorised prior to 2005, when an ERA became an obligation for human medicinal products. This means the potential risk that older pharmaceuticals that received market authorization prior to 2005 may pose to the environment may not be properly assessed.¹¹⁰

Medicinal products are, for the most part, exempt from the EU's Regulation (EC) 1907/2006 on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), which lays down provisions for the manufacture and sale of chemical substances, with the purpose of improving protection of human health and the environment from the risks of chemicals.

The EU's Water Framework Directive (2000/60/EC) deals with chemical pollution affecting water, but it does not target medicinal products. The contamination of water with pharmaceutical residues has been identified as an emerging environmental concern under Directive 2013/39/EU. The European Commission is currently developing a strategic approach, in consultation with experts and the public, to the pollution of water by pharmaceutical substances. This framework will include proposals to enable more effective consideration of the environmental impacts of medicines heading to market. In addition, the framework will include proposals for measures to address the possible environmental impacts of pharmaceuticals and of reducing discharges of these substances into the aquatic environment.¹¹¹ The strategic approach will aim to address pharmaceuticals in the environment generally, including the water environment.

In the US, the *Federal Food, Drug and Cosmetic Act* (FFDCA) and the *National Environmental Policy Act* (NEPA) establish the legal framework for pharmaceuticals. FFDCA requires that new drugs be shown to be safe before they can be marketed. Under NEPA, the US Food and Drug Administration (FDA) considers the environmental impact of approving drugs.¹¹² It requires a drug

¹¹⁰ BIO Intelligence Service. (2013). *Study on the Environmental Risks of Medicinal Products*, Final Report prepared for Executive Agency for Health and Consumers.

¹¹¹ Directive 2013/39/EU of the European Parliament and of the Council. (2013). Official Journal of the European Union. <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:226:0001:0017:EN:PDF>

¹¹² Roig, B. (2010). *Pharmaceuticals in the Environment: Current Knowledge and Need Assessment*. London; New York: IWA Publishing.

developer to conduct environmental risk assessments of pharmaceuticals for veterinary or human use. If potential adverse environmental impacts are identified, the environmental risk assessment should include a discussion of reasonable alternatives or mitigating actions that lower the environmental risk.

There is no direct or specific policy or legislation related to pharmaceuticals in the aquatic environment in the US. However, a few pharmaceuticals have been included on the Environmental Protection Agency's (USEPA) Contaminant Candidate List (CCL) of chemicals under consideration for drinking water standards.¹¹³ In 2016, the USEPA published CCL 4, which includes a number of compounds used in human and/or veterinary pharmaceuticals, including: 17alpha-estradiol, equilenin, equilin, estriol, ethinyl estradiol (17-alpha ethynyl estradiol, EE2); norethindrone (19-Norethisterone); quinoline (anti-malarial); benzyl chloride, estradiol (17-beta estradiol), estrone, mestranol, nitroglycerin, N-methyl-2-pyrrolidone, o-toluidine and erythromycin.¹¹⁴

4.5.2.2 Sector Specific Policies and Regulations

Municipal wastewater treatment plants

Canada's Wastewater Systems Effluent Regulations under the federal *Fisheries Act* set out national effluent quality standards that are achievable through secondary wastewater treatment. Wastewater systems that do not meet the effluent quality standards must upgrade to secondary treatment.¹¹⁵ The regulations specify monitoring, recording and reporting requirements for wastewater facilities that discharge effluent containing deleterious substances.¹¹⁶ These regulations specifically target the release of carbonaceous biochemical oxygen demanding matter, suspended solids total residual chlorine and un-ionized ammonia. The regulations do not specify emission limits for pharmaceuticals discharged from WWTPs.

The *Fisheries Act* contains key pollution prevention provisions that prohibit the deposit of deleterious



substances into waters frequented by fish. A deleterious substance can be any substance that, if added to any water, would degrade or alter its quality such that it could be harmful to fish, fish habitat or the use of fish by people.¹¹⁷

At the provincial level, the *Environmental Protection Act* (EPA) is Ontario's key environmental legislation that prohibits discharges of contaminants into the aquatic environment. The *Ontario Water Resources Act* regulates water quality and quantity and applies to both groundwater and surface water. The Act prohibits the discharge of polluting material in or near water that may impair the quality of the water, and it prohibits or regulates the discharge of sewage.¹¹⁸ The Act does not contain specific requirements about pharmaceutical pollutants.

In Ontario, almost all wastewater treatment systems are owned and controlled by the municipality in which they are situated. The municipalities can enact by-laws specific to their wastewater operations to establish quality and quantity standards that must be met by local wastewater generators.

This study indicates that several pieces of federal and provincial legislation contain general provisions that could be used to protect the aquatic environment from discharges of pharmaceutical contaminants.

¹¹³ US Environmental Protection Agency. (n.d.). Contaminant Candidate List (CCL) and Regulatory Determination, Contaminant Candidate List 3 - CCL 3. <https://www.epa.gov/ccl/contaminant-candidate-list-3-ccl-3>

¹¹⁴ US Environmental Protection Agency. (n.d.). Contaminant Candidate List (CCL) and Regulatory Determination, Chemical Contaminants - CCL 4. <https://www.epa.gov/ccl/chemical-contaminants-ccl-4>

¹¹⁵ Environment and Climate Change Canada. (2017). Wastewater Systems Effluent Regulations: Frequently Asked Questions. <https://www.canada.ca/en/environment-climate-change/services/pollution-waste-acts-regulations-agreements/wastewater-systems-effluent-frequently-asked-questions.html>

¹¹⁶ Wastewater Systems Effluent Regulations. (2012). <http://laws-lois.justice.gc.ca/eng/regulations/SOR-2012-139/FullText.html>

¹¹⁷ *Fisheries Act*. R.S.C. 1985. c. F-14. 2013. <http://laws-lois.justice.gc.ca/PDF/F-14.pdf>

¹¹⁸ Ontario Water Resources Act, R.S.O. 1990, c. O.40. <https://www.ontario.ca/laws/statute/90o40#BK49>

Developments in key international jurisdictions

As with Canada, EU legislation does not target the issue of medicinal residues in wastewater or require the pre-treatment of wastewater. The Urban Wastewater Treatment Directive (UWWTD, 91/271/EEC) aims to protect the environment from the adverse effects of wastewater discharges. The UWWTD sets out obligations for the treatment of wastewater and discharges from WWTPs to receiving waters. However, there are no provisions in the Directive that require the monitoring or control of residues of medicinal products.¹¹⁹

Some EU Member States are addressing this issue at the national level. Switzerland¹²⁰ is taking the lead in the world on addressing pharmaceuticals in water. It introduced legislation in 2016 requiring wastewater treatment plants to implement an additional treatment process specifically for the removal of micropollutants. A 20-year process to upgrade approximately 100 of the country's 700 wastewater treatment plants is under way. The goal is to achieve an overall reduction of 80% in the micropollutants discharged. The Swiss approach is based on a set of indicator compounds that are of concern in terms of their ecotoxicity in the receiving waters, and that are used widely. They tend to be found to a similar extent at most treatment plants, which facilitates the analysis at the inlet and outlet of the treatment plants. The removal of 11 pharmaceutical compounds is monitored during treatment.¹²¹ Research and pilot projects are under way to assess the effectiveness and costs of promising treatment options, such as the use of ozonation and/or activated carbon in contaminants removal.¹²² A sewage tax based on the polluter pays principle helps fund treatment plant upgrades. This tax finances 75% of the required initial investment, and as soon as a plant is upgraded with the additional purification stage, it is exempted from the tax.¹²³ The Swiss approach offers valuable insights into how pharmaceuticals could be prioritized for monitoring wastewaters in Canada.

US legislation does not target the issue of medicinal residues in wastewater. The USEPA has authority under the *Clean Water Act* (CWA) to regulate the types and amounts of contaminants that may be discharged into surface waters. Under the CWA, the USEPA sets wastewater standards for industry and establishes national water quality criteria recommendations for pollutants in surface waters. The regulations set limits for conventional pollutants, priority toxic pollutants and selected nonconventional pollutants. There are no national water quality criteria under the CWA for most pharmaceuticals. Exceptions include lindane and malathion, which are used to treat lice.¹²⁴ States may use the USEPA's national criteria, modify them to site-specific criteria or adopt other scientifically defensible criteria. Pollution discharges are managed through the National Pollutant Discharge Elimination System (NPDES), a permit system that allows municipal wastewater treatment facilities and other dischargers to release pollutants into water bodies. Since there are no national water quality criteria under the CWA for most of the pharmaceuticals, most of the permits do not contain limitations for them.

California's regulations for groundwater recharge with recycled water require monitoring of recycled water for priority CECs, which include a steroid hormone (17 β -estradiol), antimicrobial (Triclosan) and two pharmaceuticals (Gemfibrozil and Iopromide). The basis for CEC monitoring requirements was an expert-developed framework for prioritizing CECs for recycled water monitoring programs. The monitoring parameters include both health- and performance-based indicators.¹²⁵ The expert panel was reconvened in 2017 to consider additional monitoring for CECs in recycled water applications.

Health care facilities and the pharmaceutical manufacturing industry

In Ontario, pharmaceutical waste is categorized as Waste Class 261, which includes human and veterinary wastes other than biologicals and vaccines, as well

¹¹⁹ BIO Intelligence Service. (2013). *Study on the Environmental Risks of Medicinal Products*. Final Report prepared for Executive Agency for Health and Consumers.

¹²⁰ Note: Switzerland is not part of the political institutions of the EU but it is a member of the European Free Trade Association.

¹²¹ Aqua Strategy. (2016). *Switzerland's Progress on Micropollutants in Sewage*. <https://www.aquastrategy.com/article/switzerlands-progress-micropollutants-sewage>

¹²² Aqua Strategy. (2016). *Expert Insight: Switzerland's Early Lessons on Micropollutants in Wastewater*. <https://www.aquastrategy.com/article/expert-insight-switzerlands-early-lessons-micropollutants-wastewater>

¹²³ Swedish Federal Council. (2015). *100 Water Treatment Plants must be Upgraded – Eawag Info Day 2015*. <https://www.admin.ch/gov/en/start/documentation/media-releases.msg-id-58567.html>

¹²⁴ Eckstein, G. (2015). *Drugs on Tap: Managing Pharmaceuticals in Our Nation's Waters*, *New York University Environmental Law Journal*, pp. 37-91. <https://scholarship.law.tamu.edu/facscholar/690>

¹²⁵ Southern California Coastal Water Research Project (SCCWRP). *Project: Advisory Panel for CECs in Recycled Water*. <http://www.sccwrp.org/ResearchAreas/Contaminants/RecycledWaterAdvisoryPanel.aspx>

as solid residues and liquids from veterinary arsenical compounds.¹²⁶ A few veterinary pharmaceuticals are listed as hazardous chemicals in Schedule 2 of the *Environmental Protection Act*, meaning they require special handling and disposal.

Biomedical waste generated by hospitals, veterinary facilities and other health care facilities is regulated under *EPA Regulation 347*. This regulation prohibits the disposal of untreated hazardous waste in landfills when better treatment or destruction alternatives exist. Hazardous wastes cannot be disposed on land until the waste meets specific land disposal treatment requirements to reduce the mobility or toxicity of its hazardous components.¹²⁷

The Ontario Ministry of the Environment, Conservation and Parks (MOEC), which published *Guideline C-4: The Management of Biomedical Waste in Ontario*, describes best management practices to be followed to minimize the impact of biomedical waste on the environment. It defines biomedical waste as including cytotoxic waste, such as waste consisting of cytotoxic drugs and medicinal chemicals. The Guideline states that biomedical waste should be segregated from all other wastes and deposited into an appropriate reusable container.

There are no provincial or federal regulations that address medicinal residues in hospital sewage water, and no requirements to pre-treat this water.

Municipalities enact by-laws specific to their wastewater operations to establish quality and quantity standards that must be met by local wastewater generators. Municipal sewer-use by-laws reference *Guideline C-4* and impose restrictions on the discharge of sewage containing certain waste categories from industrial and institutional sources, such as hospitals. The restrictions generally apply to biomedical and pathological wastes, as well fuels, oils and grease, polychlorinated biphenyls (PCBs), specified metals and other substances. Industrial and institutional facilities may be required to implement pre-treatment of

wastewater or prepare Pollution Prevention Plans and Best Management Practices.

Industrial wastewater from organic and inorganic chemical manufacturing¹²⁸ is regulated under the *Ontario Water Resources Act*. Site-specific effluent limits and monitoring and reporting requirements are imposed on these facilities.

Developments in key international jurisdictions

As with Canada, EU legislation does not target medicinal residues in hospital sewage water and industrial wastewater or require pre-treatment of such waters. The *Urban Wastewater Treatment Directive* (UWWTD, 91/271/EEC) aims to protect the environment from the adverse effects of discharges from certain industrial sectors. However, the manufacturing of pharmaceutical products or the carrying out of medical activities (such as in hospitals) do not appear in the industrial sectors subject to the Directive.¹²⁹

Some Member States are addressing the issue of medicinal residues in hospital wastewater. In Denmark, hospitals are considered to be point source polluters due to the discharge of pharmaceuticals in wastewater. Limit values have been set for 40 pharmaceuticals, prescribing the maximum acceptable concentrations in wastewater from hospitals that are discharging to public sewers. These values are based on ecotoxicological data as well as removal rates in conventional activated sludge wastewater treatment plants.^{130, 131} The UK has published national guidance for healthcare wastewater discharges. The discharges from hospitals containing non-domestic wastewater constitute “trade effluent” and are regulated by the Sewerage Undertakers. The regulations allow setting conditions and limits for the discharges of hospital non-domestic waste to protect the public and the environment.¹³²

As in the case of Canada and Europe, there are no regulations in the US addressing the issue of medicinal residues in wastewater discharges from pharmaceutical manufacturing and health care facilities. Under the *Clean*

¹²⁶ Government of Ontario. (n.d.) Liquid Industrial and Hazardous Waste Generator Registration Guidance Manual. <https://www.ontario.ca/page/registration-guidance-manual-generators-liquid-industrial-and-hazardous-waste#section-7>

¹²⁷ Government of Ontario. (2017). Land Disposal Restrictions (LDR) Handbook. <https://www.ontario.ca/page/land-disposal-restrictions-ldr-handbook#section-4>

¹²⁸ Government of Ontario. (2018). Rules for Treating Industrial Wastewater. <https://www.ontario.ca/page/rules-treating-industrial-wastewater>

¹²⁹ BIO Intelligence Service. (2013). *Study on the Environmental Risks of Medicinal Products*. Final Report prepared for Executive Agency for Health and Consumers.

¹³⁰ Grundfos Biobooster A/S. (2016). Full Scale Advanced Wastewater Treatment at Herlev Hospital. <https://www.dhigroup.com/-/media/shared%20content/global/news/2016/08/evaluation%20report.pdf>

¹³¹ The Danish Environmental Protection Agency. (2018). Environmentally Friendly Treatment of Highly Potent Pharmaceuticals in Hospital Wastewater - Mermis. <https://www2.mst.dk/Udgiv/publications/2018/03/978-87-93614-81-9.pdf>

¹³² Water UK. (2014). National Guidance for Healthcare Waste Water Discharges. <https://www.dropbox.com/s/mzywcrz3iza9pnr/Water%20UK%20National%20Guidance%20August%202014.pdf?dl=0>

Water Act, the USEPA establishes effluent guidelines and national wastewater discharge standards for various industry categories, including hospitals and pharmaceutical manufacturing facilities.¹³³ The effluent guidelines set limits on the types and amounts of pollutants that can be discharged. The effluent guidelines are incorporated in NPDES permits issued by states and USEPA regional offices. The USEPA's effluent limitation regulations for pharmaceutical manufacturing currently set limitations for conventional pollutants, priority toxic pollutants and selected nonconventional pollutants.¹³⁴ There are no limitations for pharmaceutical constituents in wastewater. Likewise, the USEPA's effluent limitations and guidelines for hospitals¹³⁵ do not set limitations for pharmaceutical constituents in wastewater.

In 2010, the USEPA's Office of Water released a draft guidance document for health care facilities, titled *Best Management Practices for Unused Pharmaceuticals at Health Care Facilities*.¹³⁶ This nonbinding document recommends management practices, including methods to reduce the quantity of unused pharmaceuticals, and explains disposal requirements for hazardous pharmaceuticals. The intent of the document is to help reduce the amount of pharmaceuticals that are discharged to water bodies.

Pharmaceutical wastes are regulated by the USEPA or state environmental agencies if the active ingredient in the pharmaceutical is listed by the *Resource Conservation and Recovery Act* (RCRA) as a hazardous waste, or if the pharmaceutical exhibits a characteristic of hazardous waste. Such waste material must be disposed of in a hazardous waste incinerator or a hazardous waste landfill. The USEPA recommends that health care facilities send the non-hazardous, non-controlled pharmaceuticals to a reverse distributor for credit and proper disposal.¹³⁷ The USEPA has recently developed a proposal for sector-specific regulations pertaining to the management of

hazardous waste pharmaceuticals by healthcare facilities, with the aim of strengthening environmental protection.¹³⁸

Application of sewage biosolids and manure on farms

The land application of sewage biosolids and manure in Ontario is regulated under the *Nutrient Management Act*, 2002, (NMA) and the *Nutrient Management Regulations*. The Regulations aim to ensure that any land-applied biosolids or manure do not degrade the natural environment or pose harm to human or animal health.¹³⁹ Farm operators who apply nutrients from on- and off-farm sources, such as manure and sewage biosolids in their fields, are required to develop nutrient management strategies. Regarding sewage biosolids, the regulation sets out criteria for the concentrations of regulated metals of concern and of pathogen levels,¹⁴⁰ but there are no criteria for pharmaceuticals. The legislation prescribes the following: the amount, method and timing of application; separation distances from sensitive areas such as wells and surface water; and, suitable soil types and topography. However, it is not clear whether these requirements are sufficient to prevent pharmaceutical pollution as there is no obligation to monitor these substances.

Given the significant concentration of agricultural activities in the Great Lakes basin, and the fact that manure and sewage biosolids are frequently used on farmlands in Ontario, monitoring the presence of pharmaceuticals in these substrates would be prudent to help in understanding and evaluating the risks posed by pharmaceutical pollution.

Developments in key international jurisdictions

In Europe, some German federal states (e.g., Bavaria and Nordrhein-Westphalia) have passed legislation restricting the use of sewage sludge in agriculture. One of the drivers of this legislation was the presence of pharmaceuticals in sewage sludge, and the related risk of water contamination.

¹³³ US Environmental Protection Agency. (2018). Industrial Effluent Guidelines. <https://www.epa.gov/eg/industrial-effluent-guidelines>

¹³⁴ US Environmental Protection Agency. (2003). *Code of Federal Regulations, Part 439 – Pharmaceutical Manufacturing Point Source Category*. <https://www.ecfr.gov/cgi-bin/text-idx?SID=890993c-0387972f059839fb345376e90&mc=true&node=pt40.32.439&rgn=div5>

¹³⁵ US Environmental Protection Agency. (1976). *Code of Federal Regulations, Part 460 – Hospital Point Source Category* <https://www.ecfr.gov/cgi-bin/text-idx?SID=9b2ad535d533c8e67ed84ba64ff900de&mc=true&node=pt40.32.460&rgn=div5>

¹³⁶ US Environmental Protection Agency. (2010). Draft Guidance Document: Best Management Practices for Unused Pharmaceuticals at Health Care Facilities. <https://files.nc.gov/ncdeq/Waste%20Management/DWM/SW/Programs%20and%20Planning/MedicalWaste/EPA%20Pharmwaste%20Guidance%20Doc%209-10.pdf>

¹³⁷ US Environmental Protection Agency. (2010). Draft Guidance Document: Best Management Practices for Unused Pharmaceuticals at Health Care Facilities. <https://files.nc.gov/ncdeq/Waste%20Management/DWM/SW/Programs%20and%20Planning/MedicalWaste/EPA%20Pharmwaste%20Guidance%20Doc%209-10.pdf>

¹³⁸ US Environmental Protection Agency. (n.d.). *Proposed Rule: Management Standards for Hazardous Waste Pharmaceuticals*. <https://www.epa.gov/hwgenerators/proposed-rule-management-standards-hazardous-waste-pharmaceuticals>

¹³⁹ Ontario Ministry of Agriculture, Food and Rural Affairs. (2016). *Sewage Biosolids - Managing Urban Nutrients Responsibly for Crop Production*. <http://www.omafra.gov.on.ca/english/nm/nasm/info/brochure.htm>

¹⁴⁰ Government of Ontario. (2002). *Nutrient Management Act, 2002*. Ontario Regulation 267/03. <https://www.ontario.ca/laws/regulation/O30267>

In the US, the *Clean Water Act* and the NPDES set the framework and permit program for sewage sludge (biosolids) use and disposal. The Part 503 Standards for the Use or Disposal of Sewage Sludge establishes pollutant limits, management practices and operational standards for sewage sludge applied to the land. Large Confined Animal Feeding Operations that apply manure on land must meet nutrient planning requirements. Regulations specific to pharmaceuticals that are contained in biosolids or manure do not exist in the US.¹⁴¹

Cage aquaculture operations

In Canada, the deposition of drugs into water by cage aquaculture operations is regulated by the federal *Aquaculture Activities Regulations* under the *Fisheries Act*. The Act stipulates that a drug used in aquaculture operations must be prescribed by an authorized veterinarian. The regulations require that operators take measures to avoid accidental deposits of drugs. Before using drugs, operators must consider alternatives and record them. The onus is on the operator to identify accepted industry standards or practices.¹⁴² The waste generated by cage aquaculture facilities is expected to be assimilated locally by natural water bodies. The Ontario Ministry of the Environment, Conservation and Parks is currently developing water and sediment quality policy objectives for cage aquaculture operations to ensure that any local or lake-wide cumulative effects are minimized.¹⁴³

There is a lack of reporting on the aquaculture industry, particularly on disease outbreaks, the use of chemicals and the impacts on the environment in Canada.¹⁴⁴ Lack of data and transparency makes it difficult to evaluate the amount of pharmaceutical contamination resulting from aquaculture.

More evaluation is needed on pharmaceutical uses in aquaculture in the Great Lakes because medications are mixed with feed and applied to fish in close quarters, so that almost all the medication is dissolved in the water or is excreted by the fish. API discharge concentrations may be too high in parts of Lake Huron, where most of

the aquaculture takes place. Improvements in farming practices, for example, by reductions in fish population densities, may help to reduce the need for pharmaceuticals and thus reduce water pollution. Citizen scientists could assist with evaluating the impacts of fish farms by sampling water quality around these facilities.

Developments in key international jurisdictions

In the EU, *Directive 2006/88/EC (as amended)* introduced a system of authorization for the aquaculture industry, with a focus on disease prevention.¹⁴⁵ Aquaculture facilities have to comply with minimum requirements for the implementation of good hygiene practices and risk-based health surveillance. Member States are required to establish publicly available registers that provide information on each farm, including its health status.

In addition to EU regulations, Member States have adopted their own legislation in the field of aquaculture. The aquaculture industry in Norway, for example, is subject to many laws and regulations at the national, county and municipal levels. All pharmaceuticals that are distributed for use in aquaculture must have prescriptions from veterinarians or authorized fish health biologists. Norway routinely collects and makes public information on a wide range of diseases and parasites affecting cultured fish, including data on the use of pharmaceuticals. Likewise, Scotland maintains a dedicated website that includes a data search tool and an interactive map. A wide range of data is made available, such as industry location, reports on controlled activities, and sea lice infestation treatment residue levels.¹⁴⁶

In the US, the *Clean Water Act* and the NPDES provide a framework and related permitting program for controlling the water quality impacts of aquaculture. The USEPA issued *Effluent Guidelines for Concentrated Aquatic Animal Production* (CAAP) in 2004. The Guidelines apply to facilities that use flow-through, recirculating or net pen systems that directly discharge wastewater and produce at least 100,000 pounds of fish, molluscs or crustaceans

¹⁴¹ US Environmental Protection Agency. (2018). Biosolids Laws and Regulations. <https://www.epa.gov/biosolids/biosolids-laws-and-regulations>

¹⁴² Fisheries and Oceans Canada. (2017) *Aquaculture Activities Regulations Guidance Document*. <http://www.dfo-mpo.gc.ca/aquaculture/management-gestion/aar-aa-gd-eng.htm>

¹⁴³ Ontario Ministry of the Environment and Climate Change. (2016). Provincial Policy Objectives for Managing Effects of Cage Aquaculture Operations on the Quality of Water and Sediment in Ontario's Waters. <http://www.ebr.gov.on.ca/ERS-WEB-External/displaynoticecontent.do?noticeId=MT14MTY0&statusId=MTkzNz11&language=en>

¹⁴⁴ Standing Senate Committee on Fisheries and Oceans. (2015). Volume Two – Aquaculture Industry and Governance in Norway and Scotland. <https://sencanada.ca/content/sen/Committee/412/pofo/rep/rep12jul15Vol2-e.pdf>

¹⁴⁵ European Commission. (2018.) Aquaculture: Introduction. https://ec.europa.eu/food/animals/live_animals/aquaculture_en

¹⁴⁶ Standing Senate Committee on Fisheries and Oceans. (2015). Volume Two – Aquaculture Industry and Governance in Norway and Scotland. <https://sencanada.ca/content/sen/Committee/412/pofo/rep/rep12jul15Vol2-e.pdf>

per year. CAAP facilities are required by regulation to ensure proper storage of drugs and usage in a manner that prevents spills that may result in the discharge of drugs to US waters. Facilities subject to the regulation are required to develop best management practices plans describing how they will achieve these and other requirements.¹⁴⁷

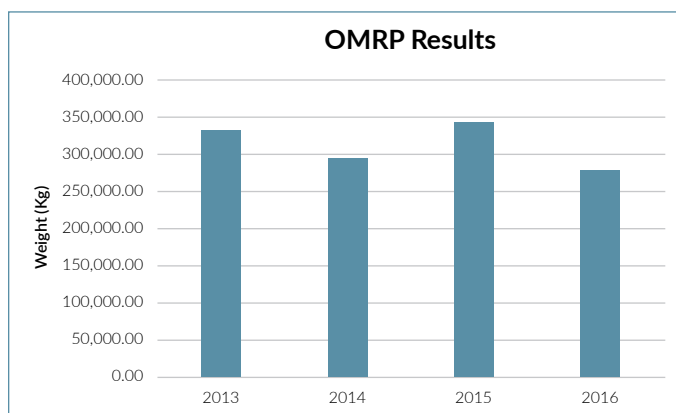
4.5.2.3 Extended Producer Responsibilities for Pharmaceuticals Producers

Several drug return initiatives exist in Canada and are run by public health agencies, industry associations, police services and other organizations. These initiatives include municipal household hazardous waste collection programs, pharmacy take-back programs, private sector programs, drop off programs and others.¹⁴⁸ Health Products Stewardship Association (HPSA)-regulated programs are currently offered in BC, Manitoba, Ontario and PEI. However, there is no national take-back legislation or nationally coordinated collection program for unwanted/waste pharmaceuticals.¹⁴⁹

Ontario is one of the leading jurisdictions in Canada with respect to implementing Extended Producer Responsibility (EPR) for pharmaceutical producers in Canada. *Ontario Regulation 298/12 “Collection of Pharmaceuticals and Sharps – Responsibilities of Producers”* under the *Ontario Environmental Protection Act*, identifies producers of pharmaceuticals and sharps and holds them accountable for the end-of-life management of their products. The regulation obligates producers to have collection locations at 90% of their retail outlets or 90% of their pharmacies, and to have at least one collection location in every municipality that has a retail outlet.¹⁵⁰

The EPR for pharmaceuticals sold for consumer use in Ontario is implemented through the Medications Return Program (OMRP), which is operated by the HPSA. The program aims to reduce the number of pharmaceutical products that end up in the environment and to reduce the risk of user abuse of these substances.¹⁵¹

HPSA’s collection network comprised more than 3,900 pharmacy collection sites in 2017, or about 92% of eligible pharmacies in Ontario.¹⁵² The OMRP allows returns of all prescription medications, over the counter medications, and natural health products to a participating pharmacy. Promotional and educational materials and resources, including a participating retail pharmacy locator tool for consumers, have been developed to increase awareness and use of the program. In 2017, almost 300,000 kilograms of pharmaceuticals were collected and disposed of in Ontario. A consumer survey suggested that awareness and usage of the program increased between 2013 and 2016, as per the summary chart below.¹⁵³ However, more than one third of Ontarians are still not aware of or have not used the program. See section 4.5.5.5 for a comparative summary of take-back quantities of medicinal products collected through different programs in Ontario in 2016.



Year	2013	2016
Awareness of program	57%	63%
Usage (had expired meds)	58%	67%
Know meds can be returned to pharmacy for disposal	54%	67%
Convenient	91%	84%
Number surveyed	505	502

¹⁴⁷ US Environmental Protection Agency. (2004). *Code of Federal Regulations, Part 451—Concentrated Aquatic Animal Production Point Source Category*. <https://www.ecfr.gov/cgi-bin/text-idx?SID=b32f-065c3e56d423dbc1858e2a077818&mc=true&node=pt40.32.451&rqn=div5>

¹⁴⁸ Public Safety Canada. *Prescription Drug Return Initiatives in Canada*. (2018) <https://www.publicsafety.gc.ca/cnt/rsrscs/pblctns/prscptn-drg-rtrn/index-en.aspx>

¹⁴⁹ Health Products Stewardship Association. (2014). *Collection*. <http://www.healthsteward.ca/collection/>

¹⁵⁰ Government of Ontario. (2014). O. Reg. 298/12: *Collection of Pharmaceuticals and Sharps – Responsibilities of Producers*. <https://www.ontario.ca/laws/regulation/120298>

¹⁵¹ Health Products Stewardship Association. (2014). *Returning Unused and Expired Medications in Ontario*. <http://www.healthsteward.ca/returns/ontario>

¹⁵² Health Products Stewardship Association. (2018). *Annual Report on the Ontario Medications Return Program and the Ontario Sharps Collection Program for the period of January 1, 2017 – December 31, 2017*. <http://www.healthsteward.ca/sites/default/files/2017%20Annual%20Report%20to%20Director%20-%20V2.pdf>

¹⁵³ Health Products Stewardship Association. (2017). *Annual Report on the Ontario Medications Return Program and the Ontario Sharps Collection Program for the period of January 1, 2016 – December 31, 2016*. <http://www.healthsteward.ca/sites/default/files/2016%20Annual%20Report%20to%20Director.pdf>

Developments in key international jurisdictions

EU legislation (*Directives 2004/27/EC and 2001/182/EC*) has required collection systems for unused or expired human and veterinary medicinal products since 2004 and 2001, respectively.¹⁵⁴ The packaging of medicinal products must indicate the specific precautions relating to the disposal of unused medicinal products and provide reference to any appropriate collection system in place. Collection is coordinated and/or funded at different jurisdictional levels (federal, regional and municipal) and by various stakeholders (government-owned companies, environmental not-for-profit organizations or industrial stakeholders) in different Member States.

Under the *American Controlled Substances Act*, pharmacies and reverse distributors in the US cannot legally take back controlled substances; they must be disposed of by the US Drug Enforcement Administration (DEA). The DEA operates the National Take-Back Initiative to allow for the disposition of unwanted, unused or expired drugs to the DEA (through the *Secure and Responsible Drug Disposal Act* of 2010). Bi-annual Take-Back Days with DEA-authorized collection sites are set up in communities nationwide, and law enforcement representatives must be present at all take-back locations. The DEA Divisional Offices provide supplies, such as boxes, and are responsible for transportation and destruction of the collected materials at USEPA approved facilities.¹⁵⁵ Many state and local governments have also implemented take-back programs.

4.5.2.4 Other Notable Initiatives

Great Lakes Water Quality Agreement

The Great Lakes Water Quality Agreement (GLWQA) is a commitment between Canada and the United States to restore and protect the waters of the Great Lakes. It provides a framework to identify binational priorities and implement actions that improve water quality. The GLWQA requires the United States and Canada to identify Chemicals of Mutual Concern (CMCs) that are potentially harmful to human health or the environment and that originate from

anthropogenic sources. The International Joint Commission, which measures progress on issues identified in the agreement and advises the governments of Canada and the United States, conducted research on pharmaceuticals in the Great Lakes between 2009 and 2011. The Commission identified pharmaceuticals as chemicals of emerging concern and developed a set of recommendations, including: the implementation of enhanced and ongoing monitoring and research programs to close knowledge gaps; the adoption of enhanced wastewater treatment technologies; and, the development of new policies to address chemicals of emerging concern.¹⁵⁶

The first eight CMCs were identified in 2016, but no pharmaceuticals were included on this list under Annex 3 of the GLWQA.^{157,158} Nor have pharmaceuticals been identified as harmful pollutants under the *Canada-Ontario Agreement (COA) on Great Lakes Water Quality and Ecosystem Health*, which helps Ontario carry out its Great Lakes Strategy and supports Canada in meeting its commitments under the GLWQA.¹⁵⁹

Pan-Canadian Framework for Action on Antimicrobial Resistance and Antimicrobial Use

In 2017, the Public Health Agency of Canada published the Pan-Canadian Framework for Action on Antimicrobial Resistance and Antimicrobial Use. The Framework recognizes bacterial resistance to antibiotics as an issue of the utmost concern that warrants urgent action due to the significant threat it presents to human and animal health. The widespread use of antimicrobials in human and veterinary medicine and in the agricultural industry is considered a key contributing factor to the rapid emergence and spread of antimicrobial-resistant infections.¹⁶⁰ The Framework lays the foundation for collaborative actions to be taken by all sectors to address growing antibiotic resistance and the risk it poses to humans, animals and the environment. The approach focuses on four key components: surveillance, infection prevention and control, stewardship and research and innovation.

¹⁵⁴ Roig, B. (2010). *Pharmaceuticals in the Environment: Current Knowledge and Need Assessment*. London; New York: IWA Publishing.

¹⁵⁵ US Food and Drug Administration. (2018). *Disposal of Unused Medicines: What You Should Know*. <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm186187.htm>

¹⁵⁶ International Joint Commission. (2009). *Work Group Report on Chemicals of Emerging Concern*. <http://www.ijc.org/files/publications/C220.pdf>

¹⁵⁷ Eight CMCs under GLWQA include: Hexabromocyclododecane (HBCD), Long-Chain Perfluorinated carboxylic acids (LC-PFCAs), Mercury, Perfluorooctanoic acid (PFOA), Perfluorooctane sulfonate (PFOS), Polybrominated Diphenyl Ethers (PBDEs), Polychlorinated Biphenyls (PCBs) and Short-Chain Chlorinated Paraffins (SCCPs).

¹⁵⁸ Binational. (2016). *Canada and the United States Designate the First Set of Chemicals of Mutual Concern*. <https://binational.net/2016/05/31/cmcdesig-pcpmdesig/>

¹⁵⁹ Government of Ontario. (2017). *Canada Ontario Great Lakes Agreement*. <https://www.ontario.ca/page/canada-ontario-great-lakes-agreement>

¹⁶⁰ Government of Canada. (2017). *Tackling Antimicrobial Resistance and Antimicrobial Use: A Pan-Canadian Framework for Action*. <https://www.canada.ca/en/health-canada/services/publications/drugs-health-products/tackling-antimicrobial-resistance-use-pan-canadian-framework-action.html>

4.5.3 Waste/Wastewater Management

Highlights:

- Primary wastewater treatment is not effective at removing pharmaceuticals.
- Secondary wastewater treatment involving advanced oxidation significantly increases removal of many, but not all, of the pharmaceuticals.
- Constructed wetlands offer promise for enhanced pharmaceutical removal.

The findings from the literature review and key stakeholder interviews done for this study suggest that conventional wastewater treatment processes are not effective at removing APIs from WWTP effluents. However, the use

of advanced or alternative treatment technologies has significant potential for the improved treatment of trace contamination of pharmaceuticals in the Great Lakes basin.

Existing wastewater treatment technologies vary greatly in terms of the removal efficiency of pharmaceuticals, as per Table 3. Through analysing the information summarized below, this study concludes that chlorination, which is the most commonly used technology for wastewater treatment in the Great Lakes basin, is variable in its effectiveness at removing APIs. The two most effective technologies are ozone and UV light with hydrogen peroxide treatment. Of these two options, ozone is more commonly used. The study concludes that a more widespread use of ozone technology would result in lower discharges of APIs into the Great Lakes.

Table 3: Summary of Wastewater Treatment Technologies in Removing APIs.

Source: Snyder et al., 2007¹⁶¹

Type	Description	Effectiveness in removing APIs
Coagulation, flocculation and chemical softening	Use of Al/Fe salts and CaO/NaOH to precipitate out contaminants, followed by filtration.	Less than 20% for all 27 APIs examined.
Activated carbon adsorption	Carbon with high surface area and micro-pores can sorb contaminants onto the surface of the carbon.	Highly variable, between 1-99%. Efficiency depends greatly on pore size of activated carbon and size/solubility of API.
Chlorination	Chlorine is used to oxidize contaminants. Chlorinated by-products are a concern.	Highly variable, between 1-98%. Efficiency depends on the chemical nature of the contaminant.
Ozonation and ozonation with hydrogen peroxide	Ozone is used to oxidize contaminants. It works faster than chlorine (minutes versus hours). By-products are not a big concern.	58-99%
Ultraviolet and ultraviolet/hydrogen peroxide	UV light can break apart contaminant molecules directly or form highly reactive species in a solution that will react with the contaminants.	56-99% (with hydrogen peroxide) 1-99% (without hydrogen peroxide)
Membranes	Separate contaminants based on size and charge. Multiple types including ultra/nanofiltration (UF/NF) and reverse osmosis (RO).	2-99% (depends on molecular size and charge of contaminant) for UF and NF >80% for RO
Magnetic ion exchange	Ion exchange resin is able to bind charged molecules to its surface, which can later be filtered off.	<50% removal for all APIs except naproxen and diclofenac (painkillers)
Biological processes	Uses non-pathogenic bacteria to consume organic contaminants.	63-99%

¹⁶¹ Snyder, S. A., Wert, E. C., Lei, H., Westerhoff, P., and Yoon, Y. (2007). *Removal of EDCs and Pharmaceuticals in Drinking and Reuse Treatment Processes*. Report prepared for AWWA Research Foundation. <http://s3-us-west-2.amazonaws.com/uclid-nuxeo-ref-media/2b8a1c5f-75dd-419f-be65-517b5263defa>

Rahman et al. (2010) examined the presence of selected pharmaceuticals in Lake Huron water, and their removal using an ozone/hydrogen peroxide-based pre-coagulation, advanced oxidation process (AOP).¹⁶² None of the target chemicals showed significant removals following conventional treatment processes (i.e., coagulation, sedimentation and filtration). The pharmaceuticals studied included diclofenac, ibuprofen and naproxen (all widely used analgesics), carbamazepine (anti-epileptic), fluoxetine (antidepressant), and gemfibrozil and atorvastatin (lipid regulators). For all the target compounds, AOP treatment provided higher removal, compared to conventional treatment. However, pre-coagulation AOP application failed to achieve significant removal of ibuprofen. Carbamazepine and fluoxetine were detected at trace concentrations.

Blair et al. (2013b) examined the removal efficiency of selected pharmaceuticals in a conventional wastewater treatment process.¹⁶³ The study found that the primary treatment and disinfection process had limited impacts on the removal of most APIs. Much of the removal occurred in the secondary treatment process for most of the compounds. Even with secondary treatment, many of the compounds were still present at detectable levels.

Study participants stated that advanced treatment processes can achieve higher rates of removing pharmaceuticals from wastewater than secondary treatment plants. Ozonation, nanofiltration and AOP were suggested as technologies that can effectively remove pharmaceuticals from wastewater. It was also stated that European jurisdictions are more



advanced in their wastewater treatment than Canada, where secondary wastewater treatment is commonly used. Several study participants stated that technology upgrades to WWTPs are needed in Canada to reduce pharmaceutical discharges to the aquatic environment. However, it was noted that most WWTPs have not adopted AOPs due to the prohibitive cost of installation and maintenance, and given the view that pharmaceutical discharges pose a minimal risk to human health. However, the motivation to install AOPs in wastewater facilities could come from the need to address a secondary problem, such as nutrient removal, which would have the co-benefit of removing pharmaceuticals.

4.5.4 Animal Husbandry Practices

Highlights:

- A voluntary medication stewardship program for farmers, offered at no cost every three years, resulted in the collection of more than 12,000 kilograms of material in 2016.
- Training workshops are available for most livestock types.
- Evaluation is needed to determine whether policy changes are warranted to move from voluntary to mandatory programs.
- Aquaculture practices result in the direct application of medication to the Great Lakes, and they should be evaluated.

There is no mandatory training or medication collection program for livestock producers in Ontario. However, Ontario farmers have been participating in several voluntary programs since the 1990s, including participating in workshops on the safe use of livestock medicines, as well as participating in collection pilots that encouraged Ontario farmers to bring unwanted animal health products to designated locations.

A Voluntary Livestock Medicine Education Program is currently available to farmers through the University of Guelph, Ridgetown Campus. The workshop manual discusses proper disposal options for unwanted livestock medicines. This course is designed for practical application

¹⁶² Rahman, M. F., Yanful, E. K., Jasim, S. J., Bragg, L. M., Servos, M. R., Ndongue, S. and Borikar, D. (2010). Advanced Oxidation Treatment of Drinking Water: Part I. Occurrence and Removal of Pharmaceuticals and Endocrine- Disrupting Compounds from Lake Huron Water. *Ozone: Science & Engineering*, 32: 217–229. 10.1080/01919512.2010.489185

¹⁶³ Blair, B.D., Crago, J.P., Hedman, C.J., Magruder, C., Royer, L.S., Treguer, R.F.J., Klaper, R.D. (2013b). Evaluation of a Model for the Removal of Pharmaceuticals, Personal Care Products, and Hormones from Wastewater. *Science of the Total Environment*. 444C, 515–521. <https://www.ncbi.nlm.nih.gov/pubmed/23295178>

for dairy producers and cattle, sheep, goat and equine farms.¹⁶⁴ It promotes the responsible use and safe handling of livestock medicines used on-farm. However, there appears to be a gap in educating poultry farmers.

Starting in 2018, farmers have required a prescription to obtain veterinary antibiotics and medicated feed for their livestock, with the prescription to be issued by a veterinarian who has an active relationship with the farmer. In addition, changes will be made to the labels of what is known as “medically important antimicrobials,” including the removal of growth promotion claims.¹⁶⁵ These changes are being introduced as part of efforts to address antimicrobial resistance in Canada (see Section 4.5.2.5).

Europe is far ahead of Canada in addressing this issue. An EU-wide ban on the use of antibiotics as growth promoters in animal feed has been in effect since 2006.¹⁶⁶

4.5.4.1 Obsolete Pesticide & Livestock Medication Collection Program

Collection of obsolete livestock medications was introduced as a pilot project in Ontario in 2009 and then added to the regular schedule for obsolete pesticide collections. The Obsolete Pesticide & Livestock Medication Collection Program is operated by CleanFARMS Inc., a national, industry-led agricultural waste stewardship organization, in partnership with the Canadian Animal Health Institute (CAHI). The collection program is delivered every three years and comes at no cost to farmers. Between collections, farmers are encouraged to safely store livestock medications until they can properly dispose of them. This is problematic as long-term storage can increase the risk of environmental pollution and the risk to human health. CleanFARMS partners with local agricultural retailers and co-ops to establish collection sites. The unwanted products are transported for disposal at a high-temperature incineration facility.

In 2016, collections took place at 40 participating ag-retail locations throughout the province, from September 20-30, 2016. Ontario farmers returned 12,080 kilograms of livestock and equine medications through the program. The program will be delivered again in the fall of 2019. See section 4.5.5.5 for a comparative summary of take-back quantities of medicinal products collected through different programs in Ontario in 2016.

4.5.4.2 Environmental Farm Plan (EFP) Program

The Environmental Farm Plan (EFP) is a voluntary Ontario program that aims to help farmers minimize potential risks to the environment that may be found on-farm.¹⁶⁷ The program is administered by the Ontario Soil and Crop Improvement Association and funded by the Growing Forward 2 initiative, with the provision of technical information being the responsibility of the Ontario Ministry of Agriculture, Food and Rural Affairs.¹⁶⁸ The EFP process begins with an assessment that is voluntarily prepared by a farmer, focusing on up to 23 environmental aspects. Through the locally-delivered EFP workshops, participants highlight their farms' environmental strengths, identify areas of concern, and set action plans with priority action areas and timelines to improve environmental conditions.¹⁶⁹

As part of the process, a farmer completes an EFP Workbook, which has two parts - the Farm Review and the Action Plan. In the Farm Review section, a farmer assesses the soils on the farm and rates their ability to offset, or increase, potential risks to the environment. The Farm Review includes 23 Worksheets¹⁷⁰ to help rate different situations on a farm, which will inform the development of an Action Plan. Information sheet #6: Disposal of Farm Wastes outlines options to address concerns related to the disposal of farm wastes. The following disposal options are suggested for unwanted animal health care products, such as drugs and medicines:¹⁷¹

¹⁶⁴ Business Development Centre, University of Guelph Ridgetown Campus. (2018). Livestock Medicines Education Program. <https://bdc.ridgetownc.com/takecourse/livestock-courses/livestock-medicine-education-program/>

¹⁶⁵ Draaisma, M. (2017). Farmers Play 'Societal' Role with Tighter Antibiotic Rules in 2018. Canadian Broadcast Corporation. <http://www.cbc.ca/news/canada/kitchener-waterloo/prescription-agricultural-drugs-livestock-federal-changes-2018-john-prescott-1.4472967>

¹⁶⁶ European Commission. (2005). Ban on Antibiotics as Growth Promoters in Animal Feed Enters into Effect. http://europa.eu/rapid/press-release_IP-05-1687_en.htm

¹⁶⁷ Office of the Auditor General of Canada. (2011). 2011 Fall Report of the Auditor General of Canada. http://www.oag-bvg.gc.ca/internet/English/parl_oag_201111_04_e_35936.html#hd5a

¹⁶⁸ Ontario Soil and Crop Improvement Association. (2018). Environmental Farm Plan. <https://www.ontariosoilcrop.org/oscia-programs/workshops-webinars/environmental-farm-plan/>

¹⁶⁹ Ontario Pork. (2016). Ontario's Environmental Farm Plan has driven fundamental change in practices, program delivery. <http://www.ontariopork.on.ca/Communications/Whats-New/ontarios-environmental-farm-plan-has-driven-fundamental-change-in-practices-program-delivery>

¹⁷⁰ Ontario Soil and Crop Improvement Association. (2018). Environmental Farm Plan, Info sheets. <https://www.ontariosoilcrop.org/oscia-programs/workshops-webinars/environmental-farm-plan/infosheets/>

¹⁷¹ Ontario Soil and Crop Improvement Association. (2018). Environmental Farm Plan, Info sheet 6. <http://www.ontariosoilcrop.org/wp-content/uploads/2015/08/EFPInfosheet6.pdf>

- Return to place of purchase – discuss protocols with your veterinarian
- Take to local Hazardous Waste Depot – check with your municipality for details
- Hire a commercial disposal company

The info sheet also states that the accumulation of leftover animal health care products should be avoided, noting that improper storage can pose risks to people, livestock and pets and that an abundance of leftover products increases the potential for medication errors.

Approximately 70% of Ontario's agricultural producers have participated in EFP workshops.¹⁷² However, only 38% of the farms had a formal EFP in 2011. Of these farms, the majority had either fully (38%) or partially (56%) implemented the beneficial management practices recommended in their EFP. The main reason given for not implementing BMPs by all Canadian farms was economic pressures (55%), followed by lack of time (23%).¹⁷³ A 2011 survey of EFP participants found that only 50% of livestock producers (43% of the farms) had identified an activity for info sheet 6 - Disposal of Farm Wastes in their action plan, and 75% of the farmers had completed activities associated with info sheet 6. However, it is not clear whether these activities were specific to pharmaceutical wastes or other types of farm wastes. The high rates of completion in this category may be attributed to the fact that activities associated with the disposal of farm waste were found to have the lowest average cost (\$1,200) as well as one of the lowest average time commitments (seven hours) per farm, when compared to other categories of activities in the plan.¹⁷⁴

The study identified several potential barriers to participation, including insufficient information about EFPs, time constraints, individual farm characteristics and others. A number of mitigation strategies were proposed to address the barriers, such as supplemental workshops/presentations on specific topics or practices, cost-shared programming and research on the motivations of farmers

who have not participated in EFPs.¹⁷⁵ In addition, research is needed to better understand farmer awareness, motivations and activities with respect to pharmaceutical wastes as they relate to EFP implementation, as well as how these could be influenced to ensure that more farmers integrate pharmaceutical waste disposal strategies into their action plans.

Participants in this study suggested that very little to no progress had been made on reducing API discharges from animal husbandry operations. Most agricultural operations have focused on reducing nutrient and pesticide emissions. API emissions do not appear to have been targeted for action. This suggests that more research is needed to better understand the extent to which Ontario farmers have addressed pharmaceutical wastes through EFP program activities.

4.5.5 Stakeholder and Consumer Education and Engagement Programs

Highlights:

- Accurate pharmaceuticals disposal information is not always provided, even by governments.
- Outreach and engagement efforts have significantly increased consumer participation in pharmaceuticals take-back in Ontario.
- Voluntary initiatives exist to help veterinary practices and hospitals reduce the environmental impact of their operations, but there is a lack of information on their effectiveness in reducing pharmaceutical pollution.

General information and resources on the proper disposal of pharmaceuticals is available on government and non-government websites. However, some of the information is inaccurate or misleading. More specifically, Health Canada's webpage states that unused and expired medications can be returned to any pharmacy in Canada on any day of the year.¹⁷⁶ This is incorrect, as only pharmacies participating in take-back programs in some provinces accept unused or expired medications from consumers. Furthermore,

¹⁷² Prairie Research Associates. (2011). Environmental Farm Plans: Measuring Performance, Improving Effectiveness, and Increasing Participation. <https://www.ontariosoilcrop.org/wp-content/uploads/2015/08/Final-Report-EFPs-Measuring-Performance-Improving-Effectiveness-and-Increasing-Participation.pdf>

¹⁷³ Statistics Canada. (2011). Environmental Farm Plan Results. <http://www.statcan.gc.ca/pub/21-023-x/2013001/part-partie1-eng.htm>

¹⁷⁴ Prairie Research Associates. (2011). Environmental Farm Plans: Measuring Performance, Improving Effectiveness, and Increasing Participation. <https://www.ontariosoilcrop.org/wp-content/uploads/2015/08/Final-Report-EFPs-Measuring-Performance-Improving-Effectiveness-and-Increasing-Participation.pdf>

¹⁷⁵ Ibid.

¹⁷⁶ Government of Canada. (2014). *Safe Disposal of Prescription Drugs*. <https://www.canada.ca/en/health-canada/services/safe-disposal-prescription-drugs.html>

Health Canada's webpage outlines steps that should be taken when disposing of medications in household trash. Such advice may lead consumers to believe that garbage disposal is an acceptable method of disposal. This poses a concern as pharmaceuticals in landfill leachate were identified as a possible source of API contamination.

Consumers can return their unused and expired medications to participating pharmacies in Ontario. In addition, some municipalities and local police forces offer take-back programs for unused and expired drugs and health products, including prescription drugs and over-the-counter medications.

Regarding information resources for farmers, the Ontario Ministry of Agriculture, Food and Rural Affairs has published online fact sheets on the safe storage and responsible disposal of medical waste.^{177,178} The fact sheets provide detailed information and guidelines on how and where to store unwanted medicines safely. Returning them to a veterinarian is listed as an appropriate option; however, it is stated that this option may not exist in some areas.

In the US, the FDA website provides information for consumers on the disposal of unused medicines, including National Prescription Drug Take-Back events and take-back programs. As in the case of Canada, the US guidelines on the proper disposal of prescription drugs may be misleading, and in some cases may depend on the type of drug in question.¹⁷⁹ If take-back programs are not readily available, the FDA recommends that certain medicines be flushed down the sink or toilet, or be disposed of in household trash.^{180,181} This recommendation aims to prevent children and young people from gaining access to these drugs and possibly harming themselves. Environmental impact was not taken into account.

The HPSA provides information for both the public and pharmacists on its bilingual web site, with promotional/educational materials downloadable directly to a user's computer or mobile device.¹⁸² The HPSA works with



pharmacies to educate employees in Ontario on how the Ontario Medications Return Program (OMRP) works, and on which materials are acceptable for collection through the program. Promotional material and other resources, including more than 30,000 brochures and bookmarks, have been distributed to participating pharmacies as well as municipalities, doctor's offices/hospitals and other partners for public distribution. The HPSA has a participating retail pharmacy locator tool for consumers that allows visitors to find local collection sites. The web site also contains videos for consumers that were developed through the HPSA's partnership with the Clean Water Foundation (CWF) entitled "I Don't Flush", and a "Teen Takers" commercial developed in partnership with Drug Free Kids Canada (see following information). These videos were created to encourage consumers to properly dispose of their expired and unused medications. Web traffic to the HPSA's website increased by 16% from 2015 to 2016. The website received close to 260 page views per day, with 62% of the users residing in Ontario.¹⁸³

4.5.5.1 I Don't Flush Public Awareness Campaign

The "I Don't Flush" public awareness campaign was launched by the Clean Water Foundation (CWF) and the Ontario Clean Water Agency (OCWA) in 2014 to

¹⁷⁷ Ontario Ministry of Agriculture, Food and Rural Affairs. (2015). Responsible Disposal of Unwanted Medicines and Sharps. <http://www.omafra.gov.on.ca/english/livestock/animalcare/amr/facts/05-051.htm>

¹⁷⁸ Ontario Ministry of Agriculture, Food and Rural Affairs. (2015). Safe On-Farm Storage of Unwanted Medicines and Sharps. <http://www.omafra.gov.on.ca/english/livestock/animalcare/amr/facts/05-053.htm>

¹⁷⁹ Natural Resources Defense Council. (2009). *Dosed without Prescription: Preventing Pharmaceutical Contamination of our Nation's Drinking Water*. https://www.nrdc.org/sites/default/files/hea_10012001a.pdf

¹⁸⁰ US Food and Drug Administration. (2018). Where and How to Dispose of Unused Medicines. <https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm101653.htm>

¹⁸¹ US Food and Drug Administration. (2018). Flushing of Certain Medicines. <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm576167.htm>

¹⁸² Product Stewardship Institution. (n.d.) Got Leftover Medicine? http://c.y.mcdn.com/sites/www.productstewardship.us/resource/resmgr/pharms_reports_factsheets/PSI_Pharms_Disposal_Info_She.pdf

¹⁸³ Health Products Stewardship Association. (2017). Annual Report on the Ontario Medications Return Program and the Ontario Sharps Collection Program for the period of January 1, 2016 – December 31, 2016. <http://www.healthsteward.ca/sites/default/files/2016%20Annual%20Report%20to%20Director.pdf>

encourage the public to take back unused/unwanted medications to the pharmacy, as opposed to flushing them down the toilet or drain or throwing them in the garbage. The campaign was supported by the Region of Peel, the Regional Municipality of York and the HPSA. The campaign used a multi-faceted approach, including a website (www.idontflush.ca) as well as traditional and social media and broadcast/radio public service announcements (PSAs). Notable Ontarians were engaged to promote the program, including Entertainment Tonight Canada's Rick Campanelli and TVOntario's The Water Brothers.

The PSAs aired more than 2,000 times across 20 Canadian television networks and six radio stations, and garnered about 30 million media impressions. The two-month campaign was successful in helping contribute to a 16% increase in pharmaceutical take-back rates in York Region, an almost 10% increase across targeted municipalities in Ontario, and a 6% increase province-wide.¹⁸⁴

4.5.5.2 National Medicine Take-Back Campaign

Since 2013, Drug Free Kids Canada (formerly Partnership for a Drug Free Canada or PDFC), a Canadian registered charity, has run a National Medicine Take-Back Campaign in partnership with pharmacies such as Shoppers Drug Mart and Loblaws DRUGStore Pharmacy. The campaign aims to increase public awareness of the dangers of misuse of unused and expired medications as well as the importance of safe use/disposal practices.¹⁸⁵

The national campaign is supported by a variety of online tools and resources designed to equip Canadians with reliable information about drugs and safe use/disposal practices. Compelling advertising and PSAs on television, radio, print, out-of-home and digital media have been used to encourage Canadians to purge their households of unused and expired prescription drugs and over-the-counter medicine.¹⁸⁶ The theme of the 2016 campaign was

“Teen Takers”, and it dealt with prescription drug misuse by teens.¹⁸⁷ The campaign engaged parents to find out which prescription drugs teens are most likely to abuse, and offered simple actions parents can take to prevent the problem, such as taking unused drugs back to the pharmacy for safe disposal.¹⁸⁸ The campaign titled “Lock Up or Turn in Your Rx Drugs” was rolled out across the country from October 2017 until mid-January 2018.^{189,190}

The National Medicine Take-Back Campaign has been effective in raising awareness and increasing collection and proper disposal of unused prescription drugs. In 2014, 390 tons of medicine were recovered at Shoppers Drug Mart – more than double the amount collected in the previous year. A study commissioned by the PDFC found that more than 80% of Canadian parents were aware that they could return unused or expired medicine to their pharmacy.¹⁹¹

4.5.5.3 Green Veterinary Practice Initiative

The Canadian Veterinary Medical Association (CVMA) launched the Green Veterinary Practice initiative, which provides guidance on how to improve the environmental impact of veterinary practices and infrastructure.¹⁹² The initiative offers a collection of eco-friendly resources, including a booklet with general guidelines for establishing a biomedical waste disposal system and a self-audit tool for evaluating a practice with regard to implementing sustainable environmental initiatives and policies.¹⁹³



¹⁸⁴ Ontario Clean Water Agency. (2016). OCWA Campaign Urges Public to Return Unused Medications. http://www.cwwa.ca/pdf_files/2016-Utility_Awards_OCWA.pdf

¹⁸⁵ Drug Free Kids Canada. (2016) Help Your Teens Before They Help Themselves. <https://www.drugfreekidscanada.org/drug-info/prescription-drugs/>

¹⁸⁶ Shoppers Drug Mart Corporation. (2015). 2015 National Medicine Take-Back Campaign Launched to “Keep Your Drugs off the Streets”. PR Newswire. <https://www.prnewswire.com/news-releases/2015-national-medicine-take-back-campaign-launched-to-keep-your-drugs-off-the-streets-514524501.html>

¹⁸⁷ Drug Free Kids Canada. (n.d.) 5 Ways to Keep Medication in the Right Hands. <https://www.drugfreekidscanada.org/secureyourmeds/>

¹⁸⁸ Singh, H. (2016). Drug Free Kids Takes on ‘Teen Takers’. Strategy Online. <http://strategyonline.ca/2016/07/18/drug-free-kids-targets-teen-takers/>

¹⁸⁹ Cundari News. (2017). Lock Up or Turn in Your Rx Drugs – New Campaign for Drug Free Kids Canada. <https://www.cundari.com/articles/lock-up-or-turn-in-your-rx-drugs-new-campaign-for-drug-free-kids-canada/>

¹⁹⁰ Health Stewardship Products Association. (2017). Lock up or turn in your Rx drugs. <http://www.healthsteward.ca/news/lock-or-turn-your-rx-drugs>

¹⁹¹ Shoppers Drug Mart Corporation. (2015). 2015 National Medicine Take-Back Campaign Launched to “Keep Your Drugs off the Streets”. PR Newswire. <https://www.prnewswire.com/news-releases/2015-national-medicine-take-back-campaign-launched-to-keep-your-drugs-off-the-streets-514524501.html>

¹⁹² Canadian Veterinary Medical Association. (n.d.) *Green Veterinary Practice*. <https://www.canadianveterinarians.net/practice-economics/green-veterinary-practice>

¹⁹³ Canadian Veterinary Medical Association. (n.d.). Green Veterinary Practice Self-Audit Tool. https://www.canadianveterinarians.net/uploads/userfiles/files/cvma_green_self-audit_tool_sept_2013_en.pdf

4.5.5.4 Green Hospital Scorecard

The Green Hospital Scorecard (GHS) is a healthcare benchmarking and recognition tool administered by the Canadian Coalition for Green Health Care.¹⁹⁴ The GHS is targeted at Ontario hospitals (but not at other healthcare institutions) and participation is free. The GHS aims to enable standardized, sector-specific environmental benchmarking and to connect hospitals with information that will assist them in achieving environmental benefits. The Scorecard shows a hospital's environmental performance in five areas: Energy, Water, Waste, Pollution Prevention and Corporate Leadership. Participating hospitals report on their environmental and other sustainability initiatives through the online GHS survey, and they receive a Scorecard summarizing their performance relative to their peers.

While wastewater is not addressed in the Scorecard, hospitals do need to report on the amount of biomedical waste they generate, and they can also report on how much pharmaceutical waste they have diverted under "Other Material Streams".¹⁹⁵ The Pollution Prevention category aims to reduce the downstream impacts caused by managing materials that are considered toxic to human health and the environment, as well as providing information on the appropriate disposal of special and toxic wastes.

Table 4: Returned Medications in 2016

Use of pharmaceuticals	Program	Nature of the program	Number of sites/ participating entities	Mass of medications returned (kg)
Human/ Consumers	Ontario Medications Return Program (OMRP)	Mandatory	3,752 pharmacy collection sites	275,000
Livestock	Obsolete Pesticide & Livestock Medication Collection Program	Voluntary	40 ag-retail locations	12,080
Hospitals	Green Hospital Scorecard	Voluntary	91 Ontario hospital sites submitted data from 55 unique health care organizations	50,700

In 2016, 91 Ontario hospital sites submitted data to the GHS program from 55 unique health care organizations.¹⁹⁶ Based on data from the 2016 GHS program, the participants used 8.7 million cubic metres of water and generated 6,765 tonnes of biomedical waste in 2015.¹⁹⁷ Twenty-five participants measured diverted 50,700 kilograms of pharmaceutical waste from going to landfills.

4.5.5.5 Comparative Summary of Returned Medications in Ontario

Table 4 summarizes the take-back quantities of medicinal products collected through the OMRP and the Obsolete Pesticide & Livestock Medication Collection Program, as well as medications diverted by hospitals through the Green Hospital Scorecard.

The difference in take-back quantities is striking. The mandatory nature of the OMRP for pharmacies, better accessibility for consumers and extensive public and stakeholder education and outreach efforts may have contributed to significantly larger quantities of returned medications by consumers as compared to farmers.

¹⁹⁴ Canadian Coalition for Green Healthcare. (n.d.). Green Hospital Scorecard. <http://greenhealthcare.ca/ghs/>

¹⁹⁵ Canadian Coalition for Green Healthcare. (2017). Green Hospital Scorecard Informational Webinar. <https://drive.google.com/file/d/1qiMPi3Fvi9rCmoObQ7HxcJaHIDrbGH9/view>

¹⁹⁶ Canadian Coalition for Green Healthcare. (2017). Green Hospital Scorecard, Final Project Report. <http://greenhealthcare.ca/wp-content/uploads/2017/07/GHS-Final-Report-Final-July-4.pdf>

¹⁹⁷ Ibid.

4.5.5.6 Citizen Science as a Partial Solution to Pharmaceuticals in the Great Lakes

Study participants stated that enhanced Great Lakes water quality monitoring programs could be a vital step towards gaining a better understanding of pharmaceuticals in the Great Lakes. A study by Miller et al. (2018) investigated whether citizen scientists were able to produce data (via collection and processing of water samples) that had the same quality and usability as data produced by scientists.¹⁹⁸ Volunteers from Ontario's Lake Partner Program produced data that were not statistically different from Ministry of the Environment, Conservation and Parks data. This suggests that volunteers and citizen scientists could play a greater role in supporting large-scale and long-term monitoring programs on the lakes.

4.6 Gap Analysis Summary

The research and analysis done in this study shows that limited data are available on the presence and concentration of APIs throughout the Great Lakes, including in surface water, sediment, fish tissues and drinking water. While some Canadian research, surveillance and monitoring activities have been conducted or are under way, these programs have been and currently remain ad hoc, in contrast to the more coordinated activities in the US and the EU. Lake Ontario is the most studied area in Canada, with Lake Superior being the least studied.

Information is limited on the impacts of pharmaceuticals on aquatic ecosystems, including the cumulative and synergistic impacts of different APIs and API mixtures.

Likewise, more research is needed on human health impacts, including long-term impacts resulting from chronic exposure to low concentrations of pharmaceuticals as well as risks to different segments of the population.

There is a lack of Canadian research on the relative contribution of human excretion versus improper pharmaceutical disposal to the Great Lakes. Information is also lacking on the relative contributions of point and non-point sources of pharmaceuticals, as well as from different sectors (for example, discharges from hospitals and the pharmaceutical manufacturing industry), which makes it challenging to determine the best strategies for reducing discharges to waterways.

In terms of pharmaceuticals disposal in garbage, which ends up in landfills, the resulting leachate is not tested for APIs. As a result, the relative contribution of landfill leachate to overall water contamination is not known. Small landfills are not required to collect and treat leachate, whereas large landfills have to transport leachate to wastewater treatment facilities.

Industrial agricultural operations on land and water are another major source of pharmaceuticals in the Great Lakes basin, for which limited information available on volumes and pathways. Evaluation is needed to determine if policy changes are warranted to move from voluntary to mandatory pharmaceutical training and unused/expired pharmaceutical collection programs. Aquaculture practices need to be evaluated to determine their impact on ecosystems, which may lead to changes in practices.



¹⁹⁸ Millar, E. E.; Hazell, E. C.; Melles, S. J. (2018). The 'Cottage Effect' in Citizen Science? Spatial Bias in Aquatic Monitoring Programs. *International Journal of Geographical Information Science*, 1–21. <https://www.tandfonline.com/doi/abs/10.1080/13658816.2018.1423686>

Conclusions

Findings Include the Following:

1. Pharmaceuticals have been measured throughout the Great Lakes, in all aquatic media (water column, sediment and biota).
2. The main types of pharmaceuticals found include pain killers, hormones and endocrine disrupting compounds, antibiotics and psychiatric drugs. The presence of these pharmaceuticals varies by lake and location.
3. The sources of pharmaceutical pollution in the Great Lakes are multiple and include municipal wastewater (from homes, hospitals and healthcare facilities, landfill leachate and pharmaceutical manufacturers), agriculture and aquaculture.
4. The main pathway for pharmaceuticals entering the Great Lakes is from municipal wastewater treatment plants. Other pathways, such as run-off from agricultural sources are secondary. Agriculture is a major user of antimicrobials and could be an important source of these compounds in the lakes.
5. The consistent use and continuous discharge of pharmaceuticals into the environment implies that some of these products can be considered as pseudo-persistent pollutants.
6. Pharmaceuticals in the Great Lakes are currently not a human health risk and are typically found below environmentally relevant concentrations. The highest concentrations are usually found close to WWTPs. Pharmaceuticals are found at environmentally relevant concentrations in proximity to areas of higher population density and/or intensive agriculture (particularly in Hamilton Harbour)
7. Instances of higher mortality rates and alterations to fish reproductive biology, reproductive behaviour and community behaviour coincide with areas in which environmentally relevant concentrations of pharmaceuticals have been observed.
8. Significant knowledge gaps exist:
 - a. The amount of an ingested pharmaceutical that leaves the human body unaltered or in metabolized form is not well understood.
 - b. Estimates of the relative contribution of excreted pharmaceuticals versus waste pharmaceuticals vary greatly.

THE MAIN PATHWAY FOR PHARMACEUTICALS ENTERING THE GREAT LAKES IS FROM MUNICIPAL WASTEWATER TREATMENT PLANTS. OTHER PATHWAYS, SUCH AS RUN-OFF FROM AGRICULTURAL SOURCES ARE SECONDARY. AGRICULTURE IS A MAJOR USER OF ANTIMICROBIALS AND COULD BE AN IMPORTANT SOURCE OF THESE COMPOUNDS IN THE LAKES.

- c. Ecotoxicology data are severely lacking for active pharmaceutical ingredients (API) and mixtures of APIs.
9. Canadian jurisdictions have a variety of legislative, regulatory and policy tools available to manage pharmaceutical pollution in the Great Lakes.
 10. There is no Canadian strategy to facilitate a coordinated approach to research, analysis and action on pharmaceutical pollution in the Great Lakes.
 11. Information generated through environmental impact assessments and Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARs) is either not publicly available or is not made available in a timely and comprehensive manner.
 12. There is no systematic sampling and reporting program in the Great Lakes that provides timely and publicly accessible information on the presence and impacts of pharmaceuticals.
 13. Federal and Ontario wastewater regulations have no specific requirements pertaining to managing pharmaceutical pollutants.
 14. Government departments and ministries are not providing consistent information on the safe disposal of unused and expired pharmaceuticals.
 15. Ontario's extended producer responsibility regulation for waste pharmaceuticals has achieved measurable diversions of unused and expired pharmaceuticals from going to landfill and municipal wastewater systems.
 16. Outreach and engagement efforts by not-for-profit organizations have increased awareness and participation in pharmaceutical take-back programs and initiatives.



Recommendations

The Following Recommendations are Made For All of the Great Lakes:

1. Develop a list of priority APIs requiring further investigation, based on existing Great Lakes research as well as US and European experience.
2. Implement monitoring programs in waters identified through Great Lakes research as having environmentally relevant concentrations of pharmaceuticals, particularly in embayments surrounded by dense urban populations, and report on changing concentrations of priority substances.
3. Measure and report on concentrations of priority APIs in effluents discharging directly or indirectly to the Great Lakes.
4. Conduct research on the presence and impacts of pharmaceuticals in multiple media, and especially in locations where adverse impacts are more likely to occur (e.g., near high population density areas and large animal husbandry operations).
5. Encourage citizen involvement in basin-wide water quality monitoring to enable a more complete dataset on the presence of pharmaceuticals in Great Lakes water, sediment and biota.
6. Publish the results of pharmaceuticals research in a timely, accessible and understandable form to advance knowledge and facilitate better decision-making.
7. Increase the transparency of health and environmental risk assessments of pharmaceuticals to help Canadians understand potential threats as well as the mitigation measures that are being implemented.
8. Ensure that governments communicate up-to-date information on best practices for the management of unused and expired medications.
9. Conduct feasibility studies on increasing the use of advanced and alternative wastewater treatment technologies in the Great Lakes basin.
10. Monitor discharges from pharmaceutical manufacturers to determine whether they are significant sources of APIs.
11. Monitor wastewaters from healthcare facilities, especially for antimicrobials and cancer-fighting medications, and explore the feasibility of requiring pre-treatment before discharging effluents to WWTPs.

12. Support take-back program outreach and engagement activities to prevent unused and expired pharmaceuticals from entering the Great Lakes.

The Following Lake-Specific Recommendations are Made:

Ontario and Erie:

Given the high population densities and the significant concentration of agricultural operations in these lake basins:

13. Study the costs and benefits of WWTP upgrades to include advanced and alternative treatments.
14. Evaluate the efficacy of voluntary training and unused pharmaceutical collection programs in the agricultural sector, and explore additional actions that may be required.

Huron:

Given the large number of aquaculture operations in Lake Huron:

15. Monitor the concentrations of pharmaceuticals in areas surrounding these operations.
16. Evaluate aquaculture medication application processes to determine if changes are required.

Superior:

Given the lack of data for Lake Superior:

17. Mobilize citizen scientists to collect samples and compile data on pharmaceuticals in water, focusing on priority substances.

Implementing the Recommendations

The recommendations are directed mainly at federal, provincial and municipal governments, as well as at hospitals and healthcare facilities, pharmaceutical manufacturers, pharmacies, agricultural operations and aquaculture. In addition, citizen scientists have a key role to play, as do consumers who can ensure that unused pharmaceuticals are returned to take-back facilities. Not-for-profit organizations can increase public awareness of the adverse impacts of waste pharmaceuticals and thus enhance the effectiveness of take-back programs.



REFERENCES

- Al-Ansari, A.M., Saleem, A, Kimpe, L.E., Sherry, J.P., McMaster, M.E., Trudeau, V.L., Blais, J. M. (2010). Bioaccumulation of the Pharmaceutical 17 α -ethinylestradiol in Shorthead Redhorse Suckers (*Moxostoma macrolepidotum*) from the St. Clair River, Canada. *Environmental Pollution*. 158 (8): 2566-2571. <https://www.sciencedirect.com/science/article/pii/S0269749110002095>
- al Haq, Md. R.; Metcalfe, C.; Li, H.; Parker, W. (2012). Discharge of Pharmaceuticals into Municipal Sewers from Hospitals and Long-term Care Facilities. *Water Quality Research Journal of Canada*, 47.2: 140-151. <https://doi.org/10.2166/wqrjc.2012.015>
- Aqua Strategy. (2016). *Expert insight: Switzerland's Early Lessons on Micropollutants in Wastewater*. <https://www.aquastrategy.com/article/expert-insight-switzerlands-early-lessons-micropollutants-wastewater>
- Aqua Strategy. (2016). *Switzerland's Progress on Micropollutants in Sewage*. <https://www.aquastrategy.com/article/switzerlands-progress-micropollutants-sewage>
- Arnnok, P.; Singh, R. R.; Burakham, R.; Pérez-Fuentetaja, A.; Aga, D. S. Selective Uptake and Bioaccumulation of Antidepressants in Fish from Effluent-Impacted Niagara River. (2017). *Environmental Science & Technology*, 51 (18), 10652–10662. 10.1021/acs.est.7b02912
- Arvai, A.; Klecka, G.; Jasim, S.; Melcer, H.; Laitta, M. T. (2014). Protecting our Great Lakes: Assessing the Effectiveness of Wastewater Treatments for the Removal of Chemicals of Emerging Concern. *Water Quality Research Journal of Canada*, 49 (1), 23. <https://doi.org/10.2166/wqrjc.2013.104>
- aus der Beek, T; Weber, F.A.; Bergmann, A. (2015). *Pharmaceuticals in the Environment: Global Occurrence and Potential Cooperative Action under the Strategic Approach to International Chemicals Management (SAICM)*. IWW Rheinisch-Westfälisches Institut für Wasser Beratungs- und Entwicklungsgesellschaft mbH Moritzstr. http://www.bmub.bund.de/fileadmin/Daten_BMU/Pool/Forschungsdatenbank/fkz_3712_65_408_chemicals_management_bf.pdf
- Barnes, K.K., Kolpin, D.W., Focazio, M.J., Furlong, E.T., Meyer, M.T., Zaugg, S.D., Haack, S.K., Barber, L.B., and Thurman, E.M. (2008). *Water-quality Data for Pharmaceuticals and Other Organic Wastewater Contaminants in Ground Water and in Untreated Drinking Water Sources in the United States, 2000–01*: U.S. Geological Survey Open-File Report 2008–1293, 7 p. plus tables. <https://pubs.usgs.gov/of/2008/1293/>
- Bay Area Restoration Council. (n.d.) *Hamilton Harbour. About the Bay*. http://hamiltonharbour.ca/about_the_bay
- Benotti, M.J., Fisher, S.C., and Terracciano, S.A. (2006). *Occurrence of Pharmaceuticals in Shallow Ground Water of Suffolk County, New York, 2002–2005*: U.S. Geological Survey Open-File Report 2006–1297. <https://pubs.usgs.gov/of/2006/1297/OFR2006-1297.pdf>.
- Bernot M.J., Smith L, Frey J. (2013). Human and Veterinary Pharmaceutical Abundance and Transport in a Rural Central Indiana Stream Influenced by Confined Animal Feeding Operations (CAFOs). *Science of the Total Environment*. <https://www.ncbi.nlm.nih.gov/m/pubmed/23333518/>
- BIO Intelligence Service. (2013). *Study on the Environmental Risks of Medicinal Products*. Final Report prepared for Executive Agency for Health and Consumers. https://ec.europa.eu/health/sites/health/files/files/environment/study_environment.pdf

- Binational. (2016). *Canada and the United States Designate the First Set of Chemicals of Mutual Concern*. <https://binational.net/2016/05/31/cmcdesig-pcpmdesig/>
- Blair, B. D.; Crago, J. P.; Hedman, C. J.; Klaper, R. D. (2013a). Pharmaceuticals and Personal Care Products found in the Great Lakes above Concentrations of Environmental Concern. *Chemosphere*, 93 (9), 2116–2123. <https://doi.org/10.1016/j.chemosphere.2013.07.057>
- Blair, B.D., Crago, J.P., Hedman, C.J., Magruder, C., Royer, L.S., Treguer, R.F.J., Klaper, R.D. (2013b). Evaluation of a Model for the Removal of Pharmaceuticals, Personal Care Products, and Hormones from Wastewater. *Science of the Total Environment*. 444C, 515–521. <https://www.ncbi.nlm.nih.gov/pubmed/23295178>
- Blazer, V. S., Iwanowicz, L. R., Iwanowicz, D. D., Smith, D. R., Young, J. A., Hedrick, J. D., Reeser, S. J. (2007). Intersex (Testicular Oocytes) in Smallmouth Bass from the Potomac River and Selected Nearby Drainages. *Journal of Aquatic Animal Health*, 19(4), 242-253. doi: 10.1577/H07-031.1
- Boxall, A. B, Rudd, M.A., Brooks, B.W., Caldwell, D.J., Choi, K., Hickmann, S., et al. (2012). Pharmaceuticals and Personal Care Products in the Environment: What Are the Big Questions? *Environmental Health Perspectives*, 120:1221–1229; <http://dx.doi.org/10.1289/ehp.1104477>
- Bright, P., Buxton, H., Balistreri, L., Barber, L., Chapelle, F., Cross, P., David, P. et al. (2013.) *U.S. Geological Survey Environmental Health Science Strategy— Providing Environmental Health Science for a Changing World*. U.S. Geological Survey. <https://pubs.usgs.gov/circ/1383e/circ1383-E.pdf>
- Burrige, L. E., Doe, K. G., Ernst, W. (2010). *Pathway of Effects of Chemical Inputs from the Aquaculture Activities in Canada*. Canadian Science Advisory Secretariat. Research Document 2010/017.
- Business Development Centre, University of Guelph Ridgetown Campus. (2018). *Livestock Medicines Education Program*. <https://bdc.ridgetownc.com/takecourse/livestock-courses/livestock-medicine-education-program/>
- Canadian Coalition for Green Healthcare. (n.d.). *Green Hospital Scorecard*. <http://greenhealthcare.ca/ghs/>
- Canadian Coalition for Green Healthcare. (2017). *Green Hospital Scorecard Informational Webinar*. <https://drive.google.com/file/d/1qiMPPI3Fvi9rCmoObQ7HxcJaHIDrbGH9/view>
- Canadian Coalition for Green Healthcare. (2017). *Green Hospital Scorecard, Final Project Report*. <http://greenhealthcare.ca/wp-content/uploads/2017/07/GHS-Final-Report-Final-July-4.pdf>
- Canadian Institute for Environmental Law and Policy. (2009). *CIELAP Brief on Biosolids Management in Ontario*. http://www.cielap.org/pdf/Brief_Biosolids.pdf
- Canadian Veterinary Medical Association. (n.d.). *Green Veterinary Practice*. <https://www.canadianveterinarians.net/practice-economics/green-veterinary-practice>
- Canadian Veterinary Medical Association. (n.d.). *Green Veterinary Practice Self-Audit Tool*. https://www.canadianveterinarians.net/uploads/userfiles/files/cvma_green_self-audit_tool_sept_2013_en.pdf
- Carere, M., Polesello, S., Kase, R., Gawlik, B.M. (2015). *The Emerging Contaminants in the Context of the EU Water Framework Directive. Emerging Contaminants in River Ecosystems*, pp.1-19. DOI: 10.1007/698_2015_5011. https://www.researchgate.net/publication/295551859_The_Emerging_Contaminants_in_the_Context_of_the_EU_Water_Framework_Directive

- Carrara, C., Ptacek, C. J., Robertson W. D., Blowes, D. W., Moncur, M. C., Sverko, E., Backus, S. (2008). Fate of Pharmaceutical and Trace Organic Compounds in Three Septic System Plumes, Ontario, Canada. *Environmental Science & Technology*, 42:2805–2811. <https://pubs.acs.org/doi/abs/10.1021/es070344q>
- Centre for Water Policy. (n.d.). *Climate Change Impacts on Agriculture in the Great Lakes Basin*. http://uwm.edu/centerforwaterpolicy/wp-content/uploads/sites/170/2013/10/Great-Lakes_Agriculture_Final.pdf
- Christensen, V.G., Lee, K.E., Kieta, K.A., and Elliott, S.M. (2012). *Presence of Selected Chemicals of Emerging Concern in Water and Bottom Sediment from the St. Louis River, St. Louis Bay, and Superior Bay, Minnesota and Wisconsin, 2010*. U.S. Geological Survey Scientific Investigations Report 2012–5184, 23 p. with appendixes. <https://pubs.usgs.gov/sir/2012/5184/sir2012-5184.pdf>
- College of Veterinarians of Ontario. (n.d.). *About the College of Veterinarians of Ontario*. <https://cvo.org/>
- Community Research and Development Information Service (CORDIS). (2014). *Ecological and Human Health Risk Assessments of Antibiotics and Anti-cancer Drugs Found in the Environment*. Pharnas. Project ID: 265346. https://cordis.europa.eu/project/rcn/97551_en.html
- Community Research and Development Information Service (CORDIS). (2014). *Fate and Effects of Cytostatic Pharmaceuticals in the Environment and the Identification of Biomarkers for and Improved Risk Assessment on Environmental Exposure*. CytoThreat. Project ID: 265264. https://cordis.europa.eu/project/rcn/96703_en.html
- Community Research and Development Information Service (CORDIS). (2011). *Reviewing the Environmental Impact of Pharmaceuticals*. Knappe – Result In Brief. Project ID: 36864. https://cordis.europa.eu/result/rcn/87817_en.html
- Cundari News. (2017). *Lock Up or Turn In Your Rx Drugs – New Campaign for Drug Free Kids Canada*. <https://www.cundari.com/articles/lock-up-or-turn-in-your-rx-drugs-new-campaign-for-drug-free-kids-canada/>
- Directive 2013/39/EU of the European Parliament and of the Council. (2013). *Official Journal of the European Union*. <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:226:0001:0017:EN:PDF>
- Draaisma, M. (2017). *Farmers Play ‘Societal’ Role with Tighter Antibiotic Rules in 2018*. Canadian Broadcast Corporation. <http://www.cbc.ca/news/canada/kitchener-waterloo/prescription-agricultural-drugs-livestock-federal-changes-2018-john-prescott-1.4472967>
- Drug Free Kids Canada. (n.d.) *5 Ways to Keep Medication in the Right Hands*. <https://www.drugfreekidscanada.org/secureyourmeds/>
- Drug Free Kids Canada. (2016) *Help Your Teens Before They Help Themselves*. <https://www.drugfreekidscanada.org/drug-info/prescription-drugs/>
- Du, S. N. N., McCallum, E. S., Vaseghi-Shanjani, M., Choi, J. A., Warriner, T. R., Balshine, S., Scott, G. R. (2018). Metabolic Costs of Exposure to Wastewater Effluent Lead to Compensatory Adjustments in Respiratory Physiology in Bluegill Sunfish. *Environmental Science & Technology*, 52 (2), pp 801–811. <https://pubs.acs.org/doi/abs/10.1021/acs.est.7b03745>
- Dulio, V., van Bavel, B., Brorström-Lundén, E., Harmsen, J., Hollender, J., Schlabach, M., Slobodnik, J., Thomas, K. and Koschorreck, J. (2018). Emerging Pollutants in the EU: 10 Years of NORMAN in Support of Environmental Policies and Regulations. *Environmental Sciences Europe*, 30: 5. <https://doi.org/10.1186/s12302-018-0135-3>

- Ebelea, A. J., Abdallah, M., A-E., Harrad. S. (2017). Pharmaceuticals and Personal Care Products (PPCPs) in the Freshwater Aquatic Environment, *Emerging Contaminants*, Vol. 3(10), pp. 1-16. <https://www.sciencedirect.com/science/article/pii/S2405665016300488>
- Eckstein, G. (2015). Drugs on Tap: Managing Pharmaceuticals in Our Nation's Waters, *New York University Environmental Law Journal*, pp. 37-91. <https://scholarship.law.tamu.edu/facscholar/690>
- Eggen, T., Moeder, M., and Arukwe, A. (2010). Municipal Landfill Leachates: a Significant Source for New and Emerging Pollutants. *Science of the Total Environment*, 408, 5147–5157. 10.1016/j.scitotenv.2010.07.049
- Elliott, S. M., and VanderMeulen, D. D. (2017). A Regional Assessment of Chemicals of Concern in Surface Waters of Four Midwestern United States National Parks. *Science of the Total Environment*. 579: 1726–1735 <https://www.sciencedirect.com/science/article/pii/S0048969716325682>
- Environment and Climate Change Canada. (2017). *Chemicals management plan progress report*. <http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=6044455E-1>
- Environment and Climate Change Canada. (2012). *Environmental Monitoring and Surveillance in Support of the Chemicals Management Plan*. <http://www.ec.gc.ca/Publications/default.asp?lang=En&xml=F48952A0-3F54-4D76-BAA6-EA6CF5529590>
- Environment and Climate Change Canada. (2017). *Pharmaceuticals and Personal Care Products Surveillance Network*. <http://ec.gc.ca/scitech/default.asp?lang=En&n=FDfE3DAA-1>
- Environment and Climate Change Canada. (2017). *Wastewater Systems Effluent Regulations: frequently asked questions*. <https://www.canada.ca/en/environment-climate-change/services/pollution-waste-acts-regulations-agreements/wastewater-systems-effluent-frequently-asked-questions.html>
- Environment and Climate Change Canada and the U.S. Environmental Protection Agency. (2017). *State of the Great Lakes 2017 Technical Report*. Cat No. En161- 3/1E-PDF. EPA 905-R-17-001. https://binational.net/wp-content/uploads/2017/09/SOGL_2017_Technical_Report-EN.pdf
- European Commission. (2018.) *Aquaculture: Introduction*. https://ec.europa.eu/food/animals/live_animals/aquaculture_en
- European Commission. (2005). *Ban on Antibiotics as Growth Promoters in Animal Feed Enters into Effect*. http://europa.eu/rapid/press-release_IP-05-1687_en.htm
- European Commission. (2016). *Priority Substances and Certain Other Pollutants according to Annex II of Directive 2008/105/EC*. http://ec.europa.eu/environment/water/water-framework/priority_substances.htm
- European Environmental Bureau. *The Environmental and Health Impacts caused by Emissions of APIs to the Environment*. (n.d.) <http://eeb.org/publications/31/chemicals/89561/briefing-on-the-environmental-and-health-impacts-of-active-pharmaceuticals-ingredients.pdf>
- Fisheries Act. R.S.C. 1985. c. F-14. 2013. <http://laws-lois.justice.gc.ca/PDF/F-14.pdf>
- Fisheries and Oceans Canada. (2017) *Aquaculture Activities Regulations Guidance Document*. <http://www.dfo-mpo.gc.ca/aquaculture/management-gestion/aar-raa-gd-eng.htm>
- Fisheries and Oceans Canada. (2012). *Aquaculture in Canada 2012: A Report on Aquaculture Sustainability*. http://www.dfo-mpo.gc.ca/aquaculture/lib-bib/asri-irda/pdf/DFO_2012_SRI_AQUACULTURE_ENG.pdf

- Fisheries and Oceans Canada. (2012). *Pathway of Effects of Chemical Inputs from the Aquaculture Activities in Canada*. http://www.dfo-mpo.gc.ca/csas-sccs/Publications/ResDocs-DocRech/2010/2010_017-eng.html
- Ford, A. T. and Fong, P. P. (2016). The Effects of Antidepressants Appear to be Rapid and at Environmentally Relevant Concentrations. *Environmental Toxicology and Chemistry*, Vol. 35 (4), pp. 794–798. <https://setac.onlinelibrary.wiley.com/doi/epdf/10.1002/etc.3087>
- Gaw, S., Thomas, K. V., and Hutchinson, T. H. (2014). Sources, Impacts and Trends of Pharmaceuticals in the Marine and Coastal Environment. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 369(1656): 20130572. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4213585/>
- Gottschall, N., Topp, E., Edwards, M., Payne, M., Kleywegt, S., Russell, P., Lapen, D.R. (2013). Hormones, Sterols, and Fecal Indicator Bacteria in Groundwater, Soil, and Subsurface Drainage Following a High Single Application of Municipal Biosolids to a Field. *Chemosphere*, 91 (3): 275-286
- Government of Canada. (2015). *Certain Substances on the Domestic Substances List used Primarily as Pharmaceuticals Fact Sheet*. <https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/chemicals-glance/substances-domestic-substances-list-used-primarily-pharmaceuticals-fact-sheet.html>
- Government of Canada. (2014). *Identification of Chemicals and Polymers as Risk Assessment Priorities*. <https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan/initiatives/identification-chemicals-polymers-risk-assessment-priorities.html>
- Government of Canada. (2018). *New Substances Program of the Chemicals Management Plan*. <https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan/initiatives/new-substances.html>
- Government of Canada. (n.d.). *Overview of the Chemicals Management Plan*. http://chemicalsubstanceschimiques.gc.ca/alt_formats/pdf/fact-fait/overview-vue-eng.pdf
- Government of Canada. (2017). *Regulations Amending the Food and Drug Regulations (Veterinary Drugs – Antimicrobial Resistance)*. <http://www.gazette.gc.ca/rp-pr/p2/2017/2017-05-17/html/sor-dors76-eng.html>
- Government of Canada. (2014). *Safe Disposal of Prescription Drugs*. <https://www.canada.ca/en/health-canada/services/safe-disposal-prescription-drugs.html>
- Government of Canada. (2017). *Tackling Antimicrobial Resistance and Antimicrobial Use: A Pan-Canadian Framework for Action*. <https://www.canada.ca/en/health-canada/services/publications/drugs-health-products/tackling-antimicrobial-resistance-use-pan-canadian-framework-action.html>
- Government of Ontario. (2017) *Canada Ontario Great Lakes Agreement*. <https://www.ontario.ca/page/canada-ontario-great-lakes-agreement>
- Government of Ontario. (n.d.) *Hazardous Waste Management*. <https://www.ontario.ca/page/hazardous-waste-management-business-and-industry>
- Government of Ontario. (2017). *Land Disposal Restrictions (LDR) Handbook*. <https://www.ontario.ca/page/land-disposal-restrictions-ldr-handbook#section-4>
- Government of Ontario. (n.d.) *Liquid Industrial and Hazardous Waste Generator Registration Guidance Manual*. <https://www.ontario.ca/page/registration-guidance-manual-generators-liquid-industrial-and-hazardous-waste#section-7>

- Government of Ontario. (n.d.). *Map of large landfills in Ontario*. <https://www.ontario.ca/environment-and-energy/map-large-landfill-sites?region=Ontario>
- Government of Ontario. (2002). *Nutrient Management Act, 2002. Ontario Regulation 267/03*. <https://www.ontario.ca/laws/regulation/030267>
- Government of Ontario. (2014). *O. Reg. 298/12: Collection of Pharmaceuticals and Sharps – Responsibilities of Producers*. <https://www.ontario.ca/laws/regulation/120298>
- Government of Ontario. (n.d.). *Small Landfill Sites List*. <https://www.ontario.ca/environment-and-energy/small-landfill-sites-list>
- Government of Ontario. (2018). *Rules for Treating Industrial Wastewater*. <https://www.ontario.ca/page/rules-treating-industrial-wastewater>
- Great Lakes Coastal Resilience. (2013). *Great Lakes Coastal Resilience Planning Guide: People in the Great Lakes*. <http://www.greatlakesresilience.org/climate-environment/people-great-lakes>
- Great Lakes Environmental Assessment and Mapping Project (GLEAM). (n.d.). *Aquaculture*. http://www.greatlakesmapping.org/great_lake_stressors/3/aquaculture
- Grigorakis K, Rigos G. (2011). Aquaculture Effects on Environmental and Public Welfare—the case of Mediterranean Mariculture. *Chemosphere*, 85, 899–919. <https://www.ncbi.nlm.nih.gov/pubmed/21821276>
- Grundfos Biobooster A/S. (2016). *Full Scale Advanced Wastewater Treatment at Herlev Hospital*. <https://www.dhigroup.com/-/media/shared%20content/global/news/2016/08/evaluation%20report.pdf>
- Hamilton Harbour: What's Good, What's not so Good? (2002). *The Hamilton Spectator* <https://www.thespec.com/news-story/2235878-hamilton-harbour-what-s-good-what-s-not-so-good/>
- Health Canada. (2018). *Canadian Antimicrobial Resistance Surveillance System 2017 Report*. <https://www.canada.ca/en/public-health/services/publications/drugs-health-products/canadian-antimicrobial-resistance-surveillance-system-2017-report-executive-summary.html>
- Health Canada. (2018). *Drug Products*. <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products.html>
- Health Canada. (2015). *Drug Product Database*. <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>
- Health Canada. (2017). *Monitoring and Surveillance Activities under Canada's Chemicals Management Plan*. <https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan/monitoring-surveillance.html>
- Health Products Stewardship Association. (2017). *Annual Report on the Ontario Medications Return Program and the Ontario Sharps Collection Program for the period of January 1, 2016 – December 31, 2016*. <http://www.healthsteward.ca/sites/default/files/2016%20Annual%20Report%20to%20Director.pdf>
- Health Products Stewardship Association. (2018). *Annual Report on the Ontario Medications Return Program and the Ontario Sharps Collection Program for the period of January 1, 2017 – December 31, 2017*. <http://www.healthsteward.ca/sites/default/files/2017%20Annual%20Report%20to%20Director%20-%20V2.pdf>
- Health Products Stewardship Association. (2014). *Collection*. <http://www.healthsteward.ca/collection/>

- Health Products Stewardship Association. (2014). *Returning Unused and Expired Medications in Ontario*. <http://www.healthsteward.ca/returns/ontario>
- Health Stewardship Products Association. (2017). *Lock up or Turn in Your Rx Drugs*. <http://www.healthsteward.ca/news/lock-or-turn-your-rx-drugs>
- Hicks, K.A., Fuzzen, M. L. M., McCann, E. K., Arlos, M. J., Bragg, L. M., Kleywegt, S., Tetreault, G. R., McMaster, M. E., and Servos, M. R. (2017). Reduction of Intersex in a Wild Fish Population in Response to Major Municipal Wastewater Treatment Plant Upgrades. *Environmental Science & Technology*, 51 (3), 1811-1819. <https://pubs.acs.org/doi/abs/10.1021/acs.est.6b05370>
- Holtz S. (2006). *There Is No Away. Pharmaceuticals, Personal Care Products, and Endocrine-Disrupting Substances: Emerging Contaminants Detected in Water*, Canadian Institute for Environmental Law and Policy, Toronto, Ontario, 82 p. <http://www.cielap.org/pdf/NoAway.pdf>
- Hull, R. N., Kleywegt, S., Schroeder, J. (2015). Risk-based Screening of Selected Contaminants in the Great Lakes Basin. *Journal of Great Lakes Research*. 41(1): 238-245. <https://www.sciencedirect.com/science/article/pii/S038013301400238X>
- Ibsen, M., Fernando, D. M., Kumar, A., Kirkwood, A. E. (2017). Prevalence of Antibiotic Resistance Genes in Bacterial Communities Associated with Cladophora Glomerata Mats along the Nearshore of Lake Ontario. *Canadian Journal of Microbiology*, 63: 439-449. <https://www.ncbi.nlm.nih.gov/pubmed/28192677>
- International Joint Commission. (n.d.) *An International Treasure Worth Protecting: Great Facts about the Great Lakes*. http://www.ijc.org/en/activitiesX/consultations/glwqa/guide_stat.htm
- International Joint Commission. (2009). *Work Group Report on Chemicals of Emerging Concern*. <http://www.ijc.org/files/publications/C220.pdf>
- International Union of Pure and Applied Chemistry (IUPAC) (2007). *Glossary of Terms Used in Toxicology*, 2nd Ed. (IUPAC Recommendations 2007). <http://media.iupac.org/publications/pac/2007/pdf/7907x1153.pdf>
- Jaffrézic, A.; Jardé, E.; Soulier, A.; Carrera, L.; Marengue, E.; Cailleau, A.; Bot, B. L. (2017). Veterinary pharmaceutical contamination in mixed land use watersheds: from agricultural headwater to water monitoring watershed. *Science of the Total Environment*, 609, 992–1000. <https://doi.org/10.1016/j.scitotenv.2017.07.206>
- Kleywegt, S., Payne M., Ngb, F., and Fletcher T. (2019). Environmental Loadings of Active Pharmaceutical Ingredients from Manufacturing Facilities in Canada. *Science of the Total Environment*. 646:257-264. <https://www.ncbi.nlm.nih.gov/pubmed/30055488>
- Kleywegt, S., Pileggi, V., Yang, P., Hao, C., Zhao, X., Rocks, C., Thach, S., Cheung, P., Whitehead, B. (2011). Pharmaceuticals, Hormones and Bisphenol A in Untreated Source and Finished Drinking Water in Ontario, Canada - Occurrence and Treatment Efficiency. *Science of the Total Environment*. 409 (8): 1481-1488.
- Kolpin, D. W., Furlong, E. T., Meyer, M. T., Thurman, E. M., Zaugg, S. D., Barber, L. B., and Buxton, H. T. (2002). Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in U.S. Streams, 1999–2000: A National Reconnaissance. *Environmental Science & Technology*, 36 (6), 1202-1211 DOI: 10.1021/es011055j
- Li, H.; Helm, P. A.; Metcalfe, C. D. (2010). Sampling in the Great Lakes for Pharmaceuticals, Personal Care Products, and Endocrine-disrupting Substances Using the Passive Polar Organic Chemical Integrative Sampler. *Environmental Toxicology and Chemistry*, 29 (4), 751–762. <https://doi.org/10.1002/etc.104>

- Li, W. (2014). Occurrence, Sources, and Fate of Pharmaceuticals in Aquatic Environment and Soil. *Environmental Pollution*, 187, 193–201. <https://doi.org/10.1016/j.envpol.2014.01.015>
- Lishman, L., Smyth, S.A., Sarafin, K., Kleywegt, S., Toito, J., Peart, T., Lee, B., Servos, M., Beland, M., Seto, P. (2006). Occurrence and Reductions of Pharmaceuticals and Personal Care Products and Estrogens by Municipal Wastewater Treatment Plants in Ontario, Canada. *Science of the Total Environment*. 367 (2-3): 544-558.
- Lu, M.-C.; Chen, Y. Y.; Chiou, M.-R.; Chen, M. Y.; Fan, H.-J. (2016). Occurrence and Treatment Efficiency of Pharmaceuticals in Landfill Leachates. *Waste Management*, 55, 257–264. <https://doi.org/10.1016/j.wasman.2016.03.029>
- Mendoza, A., Aceña, J., Pérez, S., Lopez de Alda, M., Barcelo, D., Gil, A., Valcarcel, Y. (2015). Pharmaceuticals and Iodinated Contrast Media in a Hospital Wastewater: A Case Study to Analyse Their Presence and Characterise Their Environmental Risk and Hazard. *Environmental Research*. 140 (10), pp. 225-241. <https://www.sciencedirect.com/science/article/pii/S0013935115001206>
- Metcalfe, C. D.; Miao, X.-S.; Koenig, B. G.; Struger, J. (2003). Distribution of Acidic and Neutral Drugs in Surface Waters near Sewage Treatment Plants in the Lower Great Lakes, Canada. *Environmental Toxicology and Chemistry*, 22 (12), 2881. DOI: 10.1897/02-627
- McCallum, E. S., Du S. N. N., Vaseghi-Shanjani, M., Choi, J. A., Warriner, T. R., Sultana, T., Scott, G. R., Balshine, S. (2017). In Situ Exposure to Wastewater Effluent Reduces Survival but has Little Effect on the Behaviour or Physiology of an Invasive Great Lakes Fish. *Aquatic Toxicology*. <https://www.sciencedirect.com/science/article/pii/S0166445X16303757>
- Millar, E. E.; Hazell, E. C.; Melles, S. J. (2018). The 'Cottage Effect' in Citizen Science? Spatial Bias in Aquatic Monitoring Programs. *International Journal of Geographical Information Science*, 1–21. <https://www.tandfonline.com/doi/abs/10.1080/13658816.2018.1423686>
- Monneret, C. (2017). What is an endocrine disruptor? *Comptes Rendus Biologies*, Vol. 340 (9-10), pp. 403-405. <https://www.sciencedirect.com/science/article/pii/S1631069117301257>
- Muir, D.; Simmons, D.; Wang, X.; Peart, T.; Villella, M.; Miller, J.; Sherry, J. (2017). Bioaccumulation of Pharmaceuticals and Personal Care Product Chemicals in Fish Exposed to Wastewater Effluent in an Urban Wetland. *Scientific Reports*, 7 (1). 10.1038/s41598-017-15462-x
- Murphy, E. (2012.) *Great Lakes Fish Monitoring and Surveillance Program: Quality Management Plan*. https://www.epa.gov/sites/production/files/2016-02/documents/glfmsp_qmp_version_2_final_111312_508.pdf
- National Association of Clean Water Agencies (NACWA) and Association of Metropolitan Water Agencies (AMWA). (n.d.). *Pharmaceuticals in the Water Environment*. <https://www.acs.org/content/dam/acsorg/policy/acsonthehill/briefings/pharmaceuticalsinwater/nacwa-paper.pdf>
- National Geographic. (n.d.). *Citizen Science*. <https://www.nationalgeographic.org/encyclopedia/citizen-science/>
- Natural Resources Defense Council. (NRDC). (2010). *Contamination of Our Nation's Drinking Water*. <https://www.nrdc.org/sites/default/files/dosed4pgr.pdf>
- Natural Resources Defense Council (NRDC). (2009). *Dosed without Prescription: Preventing Pharmaceutical Contamination of our Nation's Drinking Water*. https://www.nrdc.org/sites/default/files/hea_10012001a.pdf

- Network of Reference Laboratories, Research Centres and Related Organisations for Monitoring of Emerging Environmental Substances (NORMAN). (n.d.) *Why do We Need to Address Emerging Substances?* <http://www.norman-network.net/?q=node/19>
- Nikolaou, A., Meric S., and Fatta, D. (2007). Occurrence Patterns of Pharmaceuticals in Water and Wastewater Environments. *Analytical and Bioanalytical Chemistry*. 387:1225–1234. <https://www.ncbi.nlm.nih.gov/pubmed/17205270>
- Office of the Auditor General of Canada. (2011). *2011 Fall Report of the Auditor General of Canada*. http://www.oag-bvg.gc.ca/internet/English/parl_oag_201111_04_e_35936.html#hd5a
- Ontario Clean Water Agency. (2016). *OCWA Campaign Urges Public to Return Unused Medications*. http://www.cwwa.ca/pdf_files/2016-Utility_Awards_OCWA.pdf
- Ontario Investment Office. (2018). *Introduction*. <https://www.investinontario.com/pharmaceuticals#intro>
- Ontario Investment Office. (2018). *Pharmaceuticals*. <https://www.investinontario.com/pharmaceuticals#pharma-in-ontario>
- Ontario Long Term Care Association. (2017). *About Long-term Care in Ontario: Facts and Figures*. [https://www.oltca.com/oltca/OLTCA/LongTermCare/OLTCA/Public/LongTermCare/FactsFigures.aspx#Ontario's%20long-term%20care%20homes%20\(June%202017\)](https://www.oltca.com/oltca/OLTCA/LongTermCare/OLTCA/Public/LongTermCare/FactsFigures.aspx#Ontario's%20long-term%20care%20homes%20(June%202017))
- Ontario Ministry of Agriculture, Food and Rural Affairs. (n.d.). *Agriculture in the Great Lakes Basin – Stewardship and Innovation*. http://www.omafra.gov.on.ca/english/environment/facts/gl_basin.htm
- Ontario Ministry of Agriculture, Food and Rural Affairs. (2018). *Ontario Farm Data, Census of Agriculture, 1996, 2001, 2006, 2011 and 2016*. <http://www.omafra.gov.on.ca/english/stats/census/summary.htm>
- Ontario Ministry of Agriculture, Food and Rural Affairs. (2015). *Responsible Disposal of Unwanted Medicines and Sharps*. <http://www.omafra.gov.on.ca/english/livestock/animalcare/amr/facts/05-053.htm>
- Ontario Ministry of Agriculture, Food and Rural Affairs. (2015). *Safe On-Farm Storage of Unwanted Medicines and Sharps*. <http://www.omafra.gov.on.ca/english/livestock/animalcare/amr/facts/05-053.htm>
- Ontario Ministry of Agriculture, Food and Rural Affairs. (2016). *Sewage Biosolids - Managing Urban Nutrients Responsibly for Crop Production*. <http://www.omafra.gov.on.ca/english/nm/nasm/info/brochure.htm>
- Ontario Ministry of the Environment and Climate Change. (2016). *Provincial Policy Objectives for Managing Effects of Cage Aquaculture Operations on the Quality of Water and Sediment in Ontario's Waters*. <http://www.ebr.gov.on.ca/ERS-WEB-External/displaynoticecontent.do?noticeId=MTI4MTY0&statusId=MTkzNzI1&language=en>
- Ontario Pork. (2016). *Ontario's Environmental Farm Plan has Driven Fundamental Change in Practices, Program Delivery*. <http://www.ontariopork.on.ca/Communications/Whats-New/ontarios-environmental-farm-plan-has-driven-fundamental-change-in-practices-program-delivery>
- Ontario Soil and Crop Improvement Association. (2018). *Environmental Farm Plan*. <https://www.ontariosoilcrop.org/oscia-programs/workshops-webinars/environmental-farm-plan/>
- Ontario Soil and Crop Improvement Association. (2018). *Environmental Farm Plan, Info sheets*. <https://www.ontariosoilcrop.org/oscia-programs/workshops-webinars/environmental-farm-plan/infosheets/>

- Ontario Soil and Crop Improvement Association. (2018). *Environmental Farm Plan, Info sheet 6*. <http://www.ontariosoilcrop.org/wp-content/uploads/2015/08/EFPIinfosheet6.pdf>
- Ontario Water Resources Act, R.S.O. 1990, c. O.40. <https://www.ontario.ca/laws/statute/90o40#BK49>
- Parrott, J. L. and Bennie, D. T. (2009). Life-Cycle Exposure of Fathead Minnows to a Mixture of Six Common Pharmaceuticals and Triclosan, *Journal of Toxicology and Environmental Health, Part A*,72:10,633 – 641. 10.1080/15287390902769428
- Parrott, J.L. and Blunt, B.R. (2005). Life-cycle Exposure of Fathead Minnows (*Pimephales Promelas*) to an Ethinylestradiol Concentration below 1 ng/L Reduces Egg Fertilization Success and Demasculinizes Males. *Environmental Toxicology*, 20(2):131-41. <https://www.ncbi.nlm.nih.gov/pubmed/15793829>
- Parrott, J. L. and Metcalfe, C. D. (2017). Assessing the Effects of the Antidepressant Venlafaxine to Fathead Minnows Exposed to Environmentally Relevant Concentrations over a Full Life Cycle. *Environmental Pollution*, 229:403-411. 10.1016/j.envpol.2017.06.009
- Pharmaceutical Companies in Ontario. (2018) https://www.google.ca/search?rlz=1C1CHBF_enCA722CA722&q=pharmaceutical+manufacturers+in+Ontario&npsic=0&rflfq=1&rlha=0&rlag=43468374,-79475485,38444&tbm=lcl&ved=0ahUKewjGnfjJ9_fZAhWF7YMKHT4VDncQtgMIMg&tbs=lr:!2m4!1e17!4m2!17m1!1e2!2m1!1e2!2m1!1e3!3slAE,lf:1,lfui:2&rldoc=1#rfl=hd;;si;;mv:!1m3!1d2782342.6219412573!2d-75.49689397109375!3d43.74667651678435!3m2!1i1325!2i724!4f13.1
- Pollution Probe. (2013). *Great Lakes Fact Sheets*. <http://www.pollutionprobe.org/publications/great-lakes-fact-sheets/>
- Pollution Probe. (2013). *Great Lakes Fact Sheets: Biodiversity*. <http://www.pollutionprobe.org/publications/great-lakes-fact-sheet-8-biodiversity/>
- Pollution Probe. (2013). *Great Lakes Fact Sheets: Harmful Pollutants*. <http://www.pollutionprobe.org/publications/great-lakes-fact-sheet-10-harmful-pollutants/>
- Pollution Probe. (2012). *Primer on Toxic Substances*. <http://www.pollutionprobe.org/publications/primer-on-toxic-substances/>
- Prairie Research Associates. (2011). *Environmental Farm Plans: Measuring Performance, Improving Effectiveness, and Increasing Participation*. <https://www.ontariosoilcrop.org/wp-content/uploads/2015/08/Final-Report-EFPs-Measuring-Performance-Improving-Effectiveness-and-Increasing-Participation.pdf>
- Product Stewardship Institute. (n.d.). *Safety Hazards*. <http://www.productstewardship.us/?1015>
- Product Stewardship Institution. (n.d.). *Got Leftover Medicine?* http://c.ymcdn.com/sites/www.productstewardship.us/resource/resmgr/pharms_reports_factsheets/PSI_Pharms_Disposal_Info_She.pdf
- Public Safety Canada. (2018). *Prescription Drug Return Initiatives in Canada*. <https://www.publicsafety.gc.ca/cnt/rsrscs/pblctns/prscptn-drg-rtrn/index-en.aspx>
- Rahman, M. F., Yanful, E. K., Jasim, S. J., Bragg, L. M., Servos, M. R., Ndiongue, S. and Borikar, D. (2010). Advanced Oxidation Treatment of Drinking Water: Part I. Occurrence and Removal of Pharmaceuticals and Endocrine- Disrupting Compounds from Lake Huron Water. *Ozone: Science & Engineering*, 32: 217–229. 10.1080/01919512.2010.489185

- Roig, B. (2010). *Pharmaceuticals in the Environment: Current Knowledge and Need Assessment*. London; New York: IWA Publishing.
- Saaristo, M., Myers, J., Jacques-Hamilton, R., Allinson, M., Yamamoto, A., Allinson, G., Pettigrove, V., and Wong, B. B. (2014). Altered Reproductive Behaviours in Male Mosquitofish Living Downstream from a Sewage Treatment Plant. *Aquatic Toxicology*, 149: 58–64. [10.1016/j.aquatox.2014.02.001](https://doi.org/10.1016/j.aquatox.2014.02.001)
- Sabourin, L., Beck, A., Duenk, P.W., Kleywegt, S., Lapen, D.R., Li, H., Metcalfe, C.D., Payne, M., Topp, E. (2009). Runoff of Pharmaceuticals and Personal Care Products Following Application of Dewatered Municipal Biosolids to an Agricultural Field. *Science of the Total Environment*, 407 (16): 4596-4604.
- Sanchez, W.; Sremski, W.; Piccini, B.; Palluel, O.; Maillot-Maréchal, E.; Betoulle, S.; Jaffal, A.; Aït-Aïssa, S.; Brion, F.; Thybaud, E.; Hinfrey, N.; Porcher, J.M. (2011). Adverse Effects in Wild Fish Living Downstream from Pharmaceutical Manufacture Discharges. *Environment International*, 37:1342-1348. <https://doi.org/10.1016/j.envint.2011.06.002>
- Sebire, M., Katsiadaki, I., Taylor, N. G., Maack, G., Tyler, C.R. (2011). Short-term Exposure to a Treated Sewage Effluent Alters Reproductive Behaviour in the Three-spined Stickleback (*Gasterosteus Aculeatus*). *Aquatic Toxicology*, 105(1-2):78-88. [10.1016/j.aquatox.2011.05.014](https://doi.org/10.1016/j.aquatox.2011.05.014)
- Shoppers Drug Mart Corporation. (2015). 2015 National Medicine Take-Back Campaign Launched to “Keep Your Drugs off the Streets”. *PR Newswire*. <https://www.prnewswire.com/news-releases/2015-national-medicine-take-back-campaign-launched-to-keep-your-drugs-off-the-streets-514524501.html>
- Sim, W.J.; Lee, J. W.; Lee, E. S.; Shin, S. K.; Hwang, S. R.; Oh, J. E. (2011). Occurrence and Distribution of Pharmaceuticals in Wastewater from Households, Livestock Farms, Hospitals and Pharmaceutical Manufactures. *Chemosphere*, 82 (2), 179–186. <https://doi.org/10.1016/j.chemosphere.2010.10.026>
- Singh, H. (2016). Drug Free Kids Takes on ‘Teen Takers’. *Strategy Online*. <http://strategyonline.ca/2016/07/18/drug-free-kids-targets-teen-takers/>
- Snyder, S. A., Wert, E. C., Lei, H., Westerhoff, P., and Yoon, Y. (2007). *Removal of EDCs and Pharmaceuticals in Drinking and Reuse Treatment Processes*. Report prepared for AWWA Research Foundation. <http://s3-us-west-2.amazonaws.com/uclidc-nuxeo-ref-media/2b8a1c5f-75dd-419f-be65-517b5263defa>
- Southern California Coastal Water Research Project (SCCWRP). *Project: Advisory Panel for CECs in Recycled Water*. <http://www.sccwrp.org/ResearchAreas/Contaminants/RecycledWaterAdvisoryPanel.aspx>
- Spoelstra, J., Senger, N. D., Schiff, S., L. (2017). Artificial Sweeteners Reveal Septic System Effluent in Rural Groundwater. *Journal of Environmental Quality - Groundwater Quality*. 46 (6): 1434-1443. <https://www.ncbi.nlm.nih.gov/pubmed/29293857>
- Standing Senate Committee on Fisheries and Oceans. (2015) *Volume Two – Aquaculture Industry and Governance in Norway and Scotland*. <https://sencanada.ca/content/sen/Committee/412/pofo/rep/rep12jul15Vol2-e.pdf>
- Standing Senate Committee on Social Affairs, Science and Technology. (2013). *Prescription Pharmaceuticals in Canada*. <https://sencanada.ca/content/sen/Committee/412/soci/rep/rep15oct14-e.pdf>
- Standing Senate Committee on Social Affairs, Science and Technology. (2015). *Prescription Pharmaceuticals in Canada*. <https://sencanada.ca/content/sen/Committee/412/soci/rep/rep18mar15-e.pdf>

- Statista. (n.d.). *Number of Hospital Establishments in Canada as of 2015, by Province*. <https://www.statista.com/statistics/440923/total-number-of-hospital-establishments-in-canada-by-province/>
- Statistics Canada. (2011). *Environmental Farm Plan Results*. <http://www.statcan.gc.ca/pub/21-023-x/2013001/part-partie1-eng.htm>
- Swedish Federal Council. (2015). *100 Water Treatment Plants Must be Upgraded – Eawag Info day 2015*. <https://www.admin.ch/gov/en/start/documentation/media-releases.msg-id-58567.html>
- The Danish Environmental Protection Agency. (2018). *Environmentally Friendly Treatment of Highly Potent Pharmaceuticals in Hospital Wastewater - Mermis*. <https://www2.mst.dk/Udgiv/publications/2018/03/978-87-93614-81-9.pdf>
- The Science Advisory Panel. (2015). *Great Lakes Net-Pen Commercial Aquaculture: A Short Summary of the Science*. A Report for the Michigan Quality of Life Group. http://www.michigan.gov/documents/mdard/AquaRprt_504335_7.pdf
- Topp, E., Monteiro, S.C., Beck, A., Coelho, B.B., Boxall, A.B.A., Duenk, P.W., Kleywegt, S., Lapen, D.R., Payne, M., Sabourin, L., Li, H., Metcalfe, C.D. (2008). Runoff of Pharmaceuticals and Personal Care Products Following Application of Biosolids to an Agricultural Field. *Science of the Total Environment*, 396 (1): 52-59.
- US Environmental Protection Agency. (2018). *Biosolids Laws and Regulations*. <https://www.epa.gov/biosolids/biosolids-laws-and-regulations>
- US Environmental Protection Agency. (2003). *Code of Federal Regulations, Part 439 – Pharmaceutical Manufacturing Point Source Category*. <https://www.ecfr.gov/cgi-bin/text-idx?SID=890993c0387972f059839fb345376e90&mc=true&node=pt40.32.439&rgn=div5>
- US Environmental Protection Agency. (1976). *Code of Federal Regulations, Part 460 –Hospital Point Source Category* <https://www.ecfr.gov/cgi-bin/text-idx?SID=9b2ad535d533c8e67ed84ba64ff900de&mc=true&node=pt40.32.460&rgn=div5>
- US Environmental Protection Agency. (2004). *Code of Federal Regulations, Part 451 –Concentrated Aquatic Animal Production Point Source Category*. <https://www.ecfr.gov/cgi-bin/text-idx?SID=b32f065c3e56d423dbc1858e2a077818&mc=true&node=pt40.32.451&rgn=div5>
- US Environmental Protection Agency. (n.d.). *Contaminant Candidate List (CCL) and Regulatory Determination, Contaminant Candidate List 3 - CCL 3*. <https://www.epa.gov/ccl/contaminant-candidate-list-3-ccl-3>
- US Environmental Protection Agency. (n.d.) *Contaminant Candidate List (CCL) and Regulatory Determination, Chemical Contaminants - CCL 4*. <https://www.epa.gov/ccl/chemical-contaminants-ccl-4>
- US Environmental Protection Agency. (2010). *Draft Guidance Document: Best Management Practices for Unused Pharmaceuticals at Health Care Facilities*. <https://files.nc.gov/ncdeq/Waste%20Management/DWM/SW/Programs%20and%20Planning/MedicalWaste/EPA%20Pharmwaste%20Guidance%20Doc%2009-10.pdf>
- US Environmental Protection Agency. (2017) *Great Lakes Emerging Chemical Surveillance Program*. <https://www.epa.gov/great-lakes-monitoring/great-lakes-emerging-chemical-surveillance-program>
- US Environmental Protection Agency. (n.d.). *Great Lakes Facts and Figures*. <https://www.epa.gov/greatlakes/great-lakes-facts-and-figures>
- US Environmental Protection Agency. (2017) *Great Lakes Fish Monitoring and Surveillance*. <https://www.epa.gov/great-lakes-monitoring/great-lakes-fish-monitoring-and-surveillance>

- US Environmental Protection Agency. (2018). *Industrial Effluent Guidelines*. <https://www.epa.gov/eg/industrial-effluent-guidelines>
- US Environmental Protection Agency. (n.d.). *Proposed Rule: Management Standards for Hazardous Waste Pharmaceuticals*. <https://www.epa.gov/hwgenerators/proposed-rule-management-standards-hazardous-waste-pharmaceuticals>
- US Food & Drug Administration. (2018). *The National Antimicrobial Resistance Monitoring System*. <https://www.fda.gov/animalveterinary/safetyhealth/antimicrobialresistance/nationalantimicrobialresistancemonitoringsystem/>
- US Food and Drug Administration. (2018). *Disposal of Unused Medicines: What You Should Know*. <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm186187.htm>
- US Food and Drug Administration. (2018). *Flushing of Certain Medicines*. <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm576167.htm>
- US Food and Drug Administration. (2018). *Where and How to Dispose of Unused Medicines*. <https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm101653.htm>
- US Government Accountability Office. (2011). *Environmental Health. Action Needed to Sustain Agencies' Collaboration on Pharmaceuticals in Drinking Water*. Report to Congressional Requesters. <https://www.gao.gov/new.items/d11346.pdf>
- Uslu, M. O.; Jasim, S.; Arvai, A.; Bewtra, J.; Biswas, N. A. (2013). Survey of Occurrence and Risk Assessment of Pharmaceutical Substances in the Great Lakes Basin. *Ozone: Science & Engineering*, 35 (4), 249–262. <https://doi.org/10.1080/01919512.2013.793595>
- Wastewater Systems Effluent Regulations*. (2012) <http://laws-lois.justice.gc.ca/eng/regulations/SOR-2012-139/FullText.html>
- Water UK. (2014). *National Guidance for Healthcare Waste Water Discharges*. <https://www.dropbox.com/s/mzywcrz3iza9pnv/Water%20UK%20National%20Guidance%20August%202014.pdf?dl=0>
- Webb, S., Ternes, T., Gibert, M., Olejniczak, K. (2003). Indirect Human Exposure to Pharmaceuticals via Drinking Water. *Toxicology Letters*, 142(3), pp. 157-167. [https://doi.org/10.1016/S0378-4274\(03\)00071-7](https://doi.org/10.1016/S0378-4274(03)00071-7)
- Weinberger II. J. and Klaper. R. (2014). Environmental Concentrations of the Selective Serotonin Reuptake Inhibitor Fluoxetine Impact Specific Behaviors Involved in Reproduction, Feeding and Predator Avoidance in the Fish *Pimephales Promelas* (Fathead Minnow). *Aquatic Toxicology*, 151: 77-83. 10.1016/j.aquatox.2013.10.012
- Wu, C.; Witter, J. D.; Spongberg, A. L.; Czajkowski, K. P. (2009). Occurrence of Selected Pharmaceuticals in an Agricultural Landscape, Western Lake Erie Basin. *Water Research*, 43 (14), 3407–3416. <https://doi.org/10.1016/j.watres.2009.05.014>

APPENDIX A: STUDY PARTICIPANTS

Ms. Katherine Balpataky, Water Canada Magazine

Dr. Tom Edge, Environment and Climate Change Canada

Dr. Gail Krantzberg, McMaster University

Mr. Robert Liang, PhD (candidate), University of Waterloo

Dr. Erin McCallum, McMaster University

Mr. Eric Meliton, Toronto Region Conservation Authority

Dr. Chris Metcalfe, Trent University

Dr. Wayne Parker, University of Waterloo

Dr. Joanne Parrott, Environment and Climate Change Canada

Dr. Sebastien Sauvé, University of Montreal

Dr. Mark Servos, University of Waterloo

Dr. Brent Wootton, Centre for Advancement of Water and Wastewater Technologies, Fleming College

APPENDIX B: COMPARATIVE ANALYSIS

Sources, Pathways and Impacts

Occurrence of APIs	Lake Ontario	Lake Erie	Lake Huron	Lake Superior	Lake Michigan	Meta-studies/ overall lakes basin	International jurisdictions
WWTP effluent	Yes	Yes	Yes	No	Yes	Yes	Yes
Surface water (nearshore)	Yes	Yes	No	No	Yes	Yes	Yes
Surface water (offshore)	Yes	Yes	No	No	Yes	Yes	Yes
Drinking water	No	No	No	No	No	Yes	Yes
Fish Tissue	Yes	No	Yes	No	No	Yes	Yes
Sediments	No	No	No	No	Yes	No	Yes
Groundwater	No	No	No	No	No	Yes	Yes

Note: “No” indicates that no evidence was found to support the question/statement, but it is not meant to be interpreted as the question/statement being proven to be untrue

Specific Comments:

- Lake Ontario pharmaceutical concentrations in WWTP effluent and downstream from WWTP ranged from 3.6ng/L to 839ng/L and 0.4ng/L to 742.5ng/L, respectively. The concentrations are highly variable but show a decrease in concentrations as effluent is diluted downstream from outfall point.
- Lake Ontario pharmaceutical concentrations in surface water ranged from 2ng/L to 260ng/L.
- Lake Ontario did not have any studies on pharma concentrations in drinking water.
- Lake Ontario pharmaceutical concentrations in fish tissues ranged from 0.05ng/L to 647ng/L.
- Lake Ontario studies didn't identify any pharma concentrations in soils or groundwater.
- Lake Erie pharmaceutical concentrations in WWTP effluent ranged from 7ng/L to 677ng/L.
- Lake Erie pharmaceutical concentrations in surface water ranged from 2ng/L to 46ng/L.
- Lake Erie did not have any studies regarding drinking water, fish tissues, soils, or groundwater.
- Lake Huron pharmaceutical concentrations in WWTP effluent ranged from 5ng/L to 3500ng/L.
- Lake Huron pharmaceutical concentrations in fish tissues ranged from 1.43-1.6ng/L.
- More than 4,000 pharmaceuticals are currently in use so it would be impossible to experimentally assess the environmentally relevant concentrations of all of these in a timely manner (Boxall et al., 2012). It would be important to look at doing ecotoxicology studies on specific pharmaceuticals that are most often detected in wastewater effluent.
- Lake Superior had very few studies in any category showing a lack of information from this basin
- Many PPCPs, such as the anti-diabetic drug metformin, were detected 3.2 km away from the shore of Lake Michigan near Milwaukee (Blair et al., 2013a) showing that pharma concentrations are still at detectable levels far from shore.

- Hydrophobic compounds were detected in sediment at concentrations up to 510 ng/g (Blair et al., 2013a). Hydrophobic compounds are more likely to be found in sediments instead of water in Lake Michigan which highlights the importance of testing multiple environmental media to locate where all the pharmaceutical detections occur.
- A survey of drinking water from treatment facilities and in tap water from 19 U.S. water utilities found that the occurrence of pharmaceuticals in drinking water is not related to the prescription volume of the drug (Webb et al., 2003).
- The anti-cholesterol drug, Lipitor, is the one of the most frequently prescribed drugs in the United States, but it was found in only three of 19 treatment facilities and none of the finished or tap water samples. Drugs such as carbamazepine (anti-epileptic), gemfibrozil (Lipid regulator), meprobamate (Anti-anxiety), sulfamethoxazole and trimethoprim (anti-biotics), which were not in the top 200 prescribed pharmaceuticals for 2006 or 2007 but were among the most frequently detected in drinking water samples (NRDC, 2009)

General Comments:

- Pharmaceuticals appeared in WWTP effluent in all lakes except Superior (Blair et al., 2013a; Muir et al., 2017; McCallum et al., 2017; Metcalfe et al., 2003).
- Pharmaceuticals were detected nearshore as well as in open waters for all examined areas, except Superior (Metcalfe et al. 2003; Wu et al. 2009; Arnnok et al., 2017; Hull et al., 2015)
- Pharmaceuticals were detected in drinking water in the Great Lakes basin and internationally.
- Pharmaceuticals were present in fish samples from Lake Ontario and Lake Huron as well as internationally (Arnnok et al., 2017; Al-Ansari et al., 2010).
- Pharmaceuticals were present in soils/sediments of Lake Michigan and internationally.
- Surface waters nearshore had higher concentrations of pharmaceuticals than further from shore.
- Drinking water studies were very limited but data showed that concentrations were low enough not to be of significant risk.
- Some hydrophobic (low water solubility) pharmaceuticals were shown to have a higher presence in sediments/soils compared to water column.
- Groundwater had low concentrations of APIs near septic systems.
- Artificial sweeteners were found to be good diagnostic tools to determine the presence of pharmaceutical containing septic tank effluent in groundwater (Spoelstra et al., 2017).
- Prescription information alone is a poor proxy for source water occurrence because it does not take into account the dosage, pharmacokinetics, removal during wastewater treatment, or environmental fate

Table B2: Have sources and pathways been identified lake by lake?

Sources and pathways of APIs	Lake Ontario	Lake Erie	Lake Huron	Lake Superior	Lake Michigan	Meta-studies/ overall lakes basin	International jurisdictions
Municipal WWTPs	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Landfill	No	No	No	No	No	No	Yes
Agricultural	No	Yes	No	No	No	No	Yes
Aquaculture	No	No	Yes	No	No	No	Yes
Pharmaceutical Manufacture	No	No	No	No	No	No	Yes
Hospitals and Healthcare institutions	No	No	No	No	No	No	Yes

Comments:

- International studies from Germany and Taiwan (Eggen et al., 2010; Lu et al., 2016) showed that pharmaceuticals can be present in landfill leachate and that the leachate can have high enough pharmaceutical concentrations to be toxic.
- Aquaculture is a growing industry in inland waters of the Great Lakes basin, but lake-based cage culture of salmonids, which began in the mid to late-1980s, occurs only in Georgian Bay and North Channel of Lake Huron (GLEAM, n.d.).
- Aquaculture is the fastest growing food production sector in the world. In Ontario, aquaculture production was 4500 tonnes in 2005 (GLEAM, n.d.).
- Rainbow trout is the dominant species produced in Canadian aquaculture systems (GLEAM, n.d.).
- Approximately 75% of the production comes from eight freshwater cages located in Georgian Bay and the North Channel of Lake Huron (GLEAM, n.d.).
- As of 2015, Ontario licenses six operations at seven facilities; a request for an additional five licenses is under review. Three other aquaculture operations are conducted by First Nations, which are not licensed by Ontario. Facilities are leased from the province under a land-use permit. Estimated annual production from unlicensed and licensed operations approaches 8,000 metric tons of Rainbow Trout annually; about 3,500 metric tons is produced by the licensed facilities (The Science Advisory Panel, 2015).
- The following products are registered for use as antibiotics in the finfish aquaculture industry Canada: Oxytetracycline (OTC), trimethoprim80%/ sulphadiazine20% (Tribrissen), sulfadimethoxine 80%/ ormetoprim 20% (Romet 30), and Florfenicol (Burrige et al. 2010).
- Oxytetracycline is quite water soluble and is noted as being persistent for more than 100 days on sediments depending on temperature and oxygen availability (Burrige et al. 2010).
- Approximately 20,000 kilograms of antibiotics were used in the finfish aquaculture industry in Canada in 2007. Detailed information on what compounds are used, when they are applied and where they are applied is not easily available to scientists making it impossible to interpret the data collected during field studies (Burrige et al., 2010).
- The most common in-feed treatments have involved the use of ivermectin, emamectin benzoate (EB) and teflubenzuron (registered as Calicide) (Burrige et al.,2010).

Table B3: Have impacts on aquatic ecosystems been found?

Impacts on aquatic systems	Lake Ontario	Lake Erie	Lake Huron	Lake Superior	Lake Michigan	Meta-studies/ overall lakes basin/ lab studies	International jurisdictions
Intersex/reproductive issues	No	Yes	No	No	No	No	Yes
Behavioral changes	Yes	No	No	No	No	Yes	Yes
Survivability	Yes	No	No	No	No	No	No
Bio-accumulation	Yes	Yes	Yes	No	No	Yes	No

Comments:

- Some pharmaceuticals (anti-depressants) were found to bio-accumulate in a variety of fish species including wild gold fish, wild carp (Muir et al., 2017), fathead minnows and hybrid striped bass (Arnnok et al., 2017). This is important because it has led to changes in survivability (Du et al. 2018; McCallum et al. 2017), reproduction and behavior.
- Domestic examples from the Grand River have shown intersex to occur to rainbow darter exposed to WWTP effluent (Hicks et al. 2017)
- International examples from the US have shown intersex in Smallmouth Bass due to exposure to estrogens from WWTP effluent (Blazer et al. 2007). This demonstrates that estrogens in WWTP effluent are having reproductive effects on a multiple fish species in multiple geographic locations.

Table B4: Have impacts on human health been found?

Impacts on human health	Lake Ontario	Lake Erie	Lake Huron	Lake Superior	Lake Michigan	Meta-studies/ overall lakes basin	International jurisdictions
Observed Effects	No	No	No	No	No	No	No

Measures and actions addressing pharmaceuticals in the aquatic environment

Table B5: Are there systematic research, surveillance and monitoring activities on pharmaceuticals in the Great Lakes/aquatic environment?

Canada	International
NO	YES: the US and Europe

Comments:

- Canada – several activities are under way but programs are disconnected with a lack of up-to date, publicly available information.
- US – In the US, numerous long-standing national and regional research, surveillance and monitoring activities have been conducted by the U.S. Geological Survey, EPA, state and municipal agencies to gather data on the occurrence of pharmaceuticals in source water, treated drinking water, and treated wastewater.¹⁹⁹ The antimicrobial resistance surveillance program, NARMS is a collaborative program of US state and local public departments and universities.
- Europe – Numerous long-standing surveillance and monitoring programs exist. Publicly funded European Antimicrobial Resistance Surveillance Network gathers

¹⁹⁹ National Association of Clean Water Agencies (NACWA) and Association of Metropolitan Water Agencies (AMWA). (n.d.). *Pharmaceuticals in the Water Environment*. <https://www.acs.org/content/dam/acsorg/policy/acsonthehill/briefings/pharmaceuticalsinwater/nacwa-paper.pdf>

surveillance data from its member countries and provides comparable, representative and accurate data for policy-makers and the public. Sweden and

Denmark have implemented a comprehensive cross-sectoral surveillance system, which have led to the withdrawal of antibiotics as growth promoters.

Table B6: Is there a legislative authority to address the issue of pharmaceuticals in the Great Lakes/aquatic environment?

Canada	International
YES	YES - US and Europe

Comments:

- Canada – The issue is a shared jurisdiction and a variety of legislative and regulatory texts can apply to different aspects of the issue. Health Canada and ECCC have the authority to regulate pharmaceuticals under legislation, including the *Food and Drugs Act*, *Canadian Environmental Protection Act (CEPA)* and the Chemicals Management Plan. The province of Ontario has the authority to regulate certain aspects of the issue through legislation, such as *Environmental Protection Act*, *Ontario Water Resources Act*, *Nutrient Management Act* and others. Municipalities can enact by-laws specific to their wastewater operation to establish wastewater quality and quantity standards that must be met by local wastewater generators.
- US – The USEPA has authority to regulate pharmaceuticals under several statutes, including the *Federal Food, Drug and Cosmetic Act (FFDCA)* and the *National Environmental Policy Act (NEPA)* establish the legal framework for pharmaceuticals in the US.
- Europe – The EU Directives provide a general framework for managing pharmaceuticals and discharges of pollutants into the environment the adoption of specific regulations and measures is left with the Member States. Directives 2001/83/EC (for human use) and 2001/82/EC94 (for veterinary use) govern marketing authorisation (MA) process for medicinal products. A variety of Directives as well as national level legislation influence the presence of the medicinal products in the aquatic environment.

Table B7: Is there a specific policy or regulation (existing or under development) that directly addresses the issue of pharmaceuticals in the Great Lakes/aquatic environment?

Canada/Ontario	International
NO	Under development in Europe

Comments:

- Canada/Ontario – There is no specific policy that directly addresses pharmaceuticals in the Great Lakes. A range of legislative and regulatory provisions apply to different aspects of the issue.
- Europe – The European Commission is currently developing a strategic approach, in consultation with experts and the public, for the pollution of water by pharmaceutical substances. This framework will include proposals to enable more effective consideration of the environmental impacts of medicines heading to market. In addition, the framework will include proposals for measures that could be taken to address the possible environmental impacts of pharmaceutical substances, with a view to reducing discharges of these substances into the aquatic environment.²⁰⁰ The strategic approach will aim to address pharmaceuticals in the environment generally, including the water environment.
- US – There is no direct or specific policy or legislation related to pharmaceuticals in the aquatic environment. A number of pharmaceuticals have been included on the Environmental Protection Agency's Contaminant Candidate List (CCL), a list of chemicals under consideration for drinking water standards. In 2016, USEPA published a CCL 4 which includes many compounds used in human and/or veterinary pharmaceuticals.

²⁰⁰ Directive 2013/39/EU of the European Parliament and of the Council. (2013). Official Journal of the European Union. <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:226:0001:0017:EN:PDF>

Table B8: Does the existing regulatory framework address pharmaceutical discharges from municipal wastewater treatment facilities?

Canada/Ontario	International
NO	In some EU Member States and in some US States

Comments:

- Canada/Ontario – Existing laws and regulations, such as the *Wastewater Systems Effluent Regulations* under the federal *Fisheries Act* and *Ontario Water Resources Act* (OWRA), provide for general protections of the water environment from pollutants but do not contain any specific discharge limits or monitoring requirements with regard to pharmaceutical pollutants.
- US – The USEPA has authority to regulate contaminants (including pharmaceuticals) in wastewater through the *Clean Water Act* (CWA). Under the CWA, the USEPA establishes criteria that may be adopted by the states as enforceable standards through the National Pollutant Discharge Elimination System (NPDES) program.
- California – California’s regulations for groundwater recharge with recycled water require monitoring of recycled water for priority CEC, which include a steroid hormone (17β-estradiol), antimicrobial (Triclosan) and two pharmaceuticals (Gemfibrozil and Iopromide). The

basis for CEC monitoring requirements was an expert –developed framework for prioritizing and selecting CECs for recycled water monitoring programs. The monitoring parameters include both health- and performance-based indicators.²⁰¹ The expert panel was reconvened in 2017 to incorporate the latest science and update the original recommendations for an expanded scope of recycled water applications.

- Europe – The EU-level legislation does not specifically target the issue of medicinal residues in wastewater.
- Switzerland – Switzerland requires wastewater treatment plants to implement an additional treatment process, specifically for the removal of micropollutants. Approximately 100 of the country’s 700 wastewater treatment plants will be upgraded. The goal is to achieve an overall reduction of 80% in the micropollutants discharged. The Swiss approach is to base the action on micropollutants around a set of indicator compounds. The testing protocol includes 11 pharmaceutical compounds, the removal of which will be monitored during treatment.²⁰²

Table B9: Does the existing regulatory framework address pharmaceutical discharges from healthcare facilities and industry?

Canada	International
To some extent	To some extent

Comments:

- Canada/Ontario – The existing framework provides contains general provisions that protect the aquatic environment from the discharges of contaminants through legislation such as Ontario’s EPA and *Regulation 347*. There are no regulations in Ontario or Canada addressing the issue of medicinal residues in hospital sewage water or requirements for the pre-treatment of hospital sewage water. Municipalities can enact by-laws specific to their wastewater

operation and impose monitoring requirements or discharge limits on industrial and institutional sources of wastewater. Industrial wastewater from organic and inorganic chemical manufacturing²⁰³ is regulated under the *Ontario Water Resources Act*. Site-specific effluent limits and monitoring and reporting requirements are imposed on the operation of such facilities.

- USA – Under the federal *Resource Conservation and Recovery Act* (RCRA), pharmaceutical waste may be deemed hazardous, including specifically being

²⁰¹ Southern California Coastal Water Research Project (SCCWRP). *Project: Advisory Panel for CECs in Recycled Water*. <http://www.sccwrp.org/ResearchAreas/Contaminants/RecycledWaterAdvisoryPanel.aspx>

²⁰² Aqua Strategy. (2016). *Switzerland’s Progress on Micropollutants in Sewage*. <https://www.aquastrategy.com/article/switzerlands-progress-micropollutants-sewage>

²⁰³ Government of Ontario. (2018). *Rules for Treating Industrial Wastewater*. <https://www.ontario.ca/page/rules-treating-industrial-wastewater>

listed by USEPA as a hazardous waste (more than 30 APIs are considered listed hazardous wastes²⁰⁴) or by possessing certain hazardous characteristics (e.g., flammable, corrosive, reactive or toxic). In such cases, health care facilities must comply with RCRA requirements for both management and disposal of hazardous wastes. USEPA recommends that health care facilities send the non-hazardous, non-controlled pharmaceuticals to a reverse distributor for potential credit and proper disposal. The US has recently proposed new regulations targeting healthcare facilities with the aim to simplify management standards for discarded and waste pharmaceutical products and prohibit the disposal of pharmaceutical wastes to sewer. The proposal is projected to prevent the flushing of more than 6,400 tons of hazardous waste pharmaceuticals by healthcare facilities annually.²⁰⁵ There are no regulations in the US addressing the issue of medicinal residues in hospital sewage water or requirements for the pre-treatment of hospital sewage water.

- Europe – The EU-level legislation (e.g., Water Framework Directive) provides a framework to deal with chemical pollution affecting water, but it does not specifically target medicinal products in hospital sewage water or require pre-treatment of wastewater/hospital sewage water.
- Denmark – In Denmark, hospitals require a permit to discharge wastewater to the sewer. This permit regulates the discharges of pharmaceutical substances. Limit values have been set for 40 pharmaceuticals, prescribing the maximum acceptable concentrations in wastewater from a hospital being discharged to public sewers.
- UK – The UK published national guidance for healthcare wastewater discharges. The discharges from hospitals containing non-domestic wastewater constitute “trade effluent” and are regulated by the Sewerage Undertakers. The regulations allow setting conditions and limits for the discharges of hospital non-domestic waste to protect from harm the general public and the environment.²⁰⁶

Table B10: Does the existing regulatory framework address pharmaceutical discharges from agricultural operations?

Canada	International
To some extent	To some extent
<ul style="list-style-type: none"> • Canada/Ontario – Ontario’s <i>Nutrient Management Act, 2002</i>, (NMA) and the <i>Nutrient Management Regulation</i> aim to ensure that any land applied biosolids or manure do not degrade the natural environment or pose any harm to human or animal health. The regulations prescribe the amount, method and timing of application of sewage biosolids and manure and sets out criteria for the concentrations of regulated 	<p>metals of concern and pathogen levels,²⁰⁷ but not pharmaceuticals.</p> <ul style="list-style-type: none"> • Germany – German federal states Bavaria and Nordrhein-Westphalia passed legislation restricting the use of sewage sludge in agriculture to reduce the risks of water contamination associated with the presence of pharmaceuticals in sewage sludge.

Table B11: Does the existing regulatory framework address pharmaceutical discharges from aquaculture operations?

Canada	International
To some extent	To some extent
<ul style="list-style-type: none"> • Canada/Ontario – The federal <i>Fisheries Act</i> and regulations require that operators take measures to avoid accidental deposits of drugs. The Ontario 	<p>Ministry of the Environment and Climate Change (MOECC) is currently developing water and sediment quality policy objectives for cage aquaculture</p>

²⁰⁴ United States Government Accountability Office. (2011). *Environmental Health. Action Needed to Sustain Agencies’ Collaboration on Pharmaceuticals in Drinking Water*. Report to Congressional Requesters. <https://www.gao.gov/new.items/d11346.pdf>

²⁰⁵ US Environmental Protection Agency. (n.d.). *Proposed Rule: Management Standards for Hazardous Waste Pharmaceuticals*. <https://www.epa.gov/hwgenerators/proposed-rule-management-standards-hazardous-waste-pharmaceuticals>

²⁰⁶ Water UK. (2014). *National Guidance for Healthcare Waste Water Discharges*. <https://www.dropbox.com/s/mzywcrz3iza9prv/Water%20UK%20National%20Guidance%20August%202014.pdf?dl=0>

²⁰⁷ Government of Ontario. (2002). *Nutrient Management Act, 2002. Ontario Regulation 267/03*. <https://www.ontario.ca/laws/regulation/O30267>

operations. There is a lack of reporting of information regarding the aquaculture industry, particularly on disease outbreaks, the use of chemicals and the impacts on the environment.

- Norway – The aquaculture industry in Norway is subject to many laws and regulations adopted at the national, county and municipal levels. All pharmaceuticals that are distributed for use in aquaculture must have a prescription from a veterinarian or an authorized fish health biologist,

which are registered by the NFSA. The Norwegian Institute of Public Health publishes data on the use of pharmaceuticals by the aquaculture industry on an annual basis. The 2009 Strategy for an Environmentally Sustainable Norwegian Aquaculture Industry (SESNAI) focuses on five areas where the negative environmental impacts of aquaculture should be mitigated: genetic interaction and escapees; pollution and effluents; diseases, including sea lice; the use of coastal areas; and feed resources.

Table B12: Do information resources, engagement programs and/or initiatives exist to promote proper use/disposal of pharmaceuticals among consumers and key sector stakeholders?

Canada	International
Yes	YES
<ul style="list-style-type: none"> • Canada/Ontario – General information and resources on the proper disposal of pharmaceuticals for consumers, farmers and other stakeholders is available on a dedicated government website or is provided by relevant industry associations. Some information presented is inaccurate or could be misleading. For example, municipal landfills are listed as an appropriate option. • The “I Don’t Flush” public awareness campaign launched by the Clean Water Foundation (CWF) and the Ontario Clean Water Agency (OCWA) encourages the public to take back unused/unwanted medications to the pharmacy as opposed to flushing them down the toilet or drain or throwing them in the garbage. • Drug Free Kids Canada runs an Ontario Medicine Take-Back Campaign in partnership with pharmacies, such as Shoppers Drug Mart and Loblaws Pharmacy. The theme of the 2016 campaign was “Teen Takers” and it dealt with prescription drug misuse by teens. • Voluntary initiatives exist to help farmers, veterinary practices and hospitals to reduce the environmental impact of their operations. • The Environmental Farm Plan (EFP) is a voluntary Ontario program that aims to help farmers to minimize potential risks to the environment that may be found on-farm. As part of the process, farmers assess 	<p>disposal of farm wastes, including unwanted animal health care products, such as drugs and medicines.</p> <ul style="list-style-type: none"> • The Canadian Veterinary Medical Association (CVMA) launched the <i>Green Veterinary Practice</i> initiative that provides guidance to veterinarians on how to improve the environmental impact of their veterinary practice and infrastructure. • The Green Hospital Scorecard (GHS) is a healthcare benchmarking and recognition tool administered by the Canadian Coalition for Green Health Care. While wastewater is not addressed in the Scorecard, hospitals do need to report on the amount of biomedical waste they generate and can also report on how much pharmaceutical waste they have diverted under “Other Material Streams.” • US – The FDA website provides information for consumers on disposal of unused medicines but guidelines may be misleading and in some cases depend on the type of drug in question. • Europe – The EU has a dedicated webpage (http://medsdisposal.eu/) that provides a high-level summary of how medicines disposal is arranged in each member state and a link to national level information. Programming and availability of information varies in different Member States.

Table B14 Do mandatory Medication Take-back Programs exist?

Medication Take-back Programs	Canada	International
Consumer-focused	No – Canada Ontario - Yes	No - US Yes – Europe
Farmer-focused	No – Canada/Ontario	Yes - Europe

- Canada/Ontario – Ontario Regulation 298/12 “Collection of Pharmaceuticals and Sharps – Responsibilities of Producers”, under the Ontario Environmental Protection Act. The regulation clearly identifies producers of pharmaceuticals and sharps and holds them directly accountable for the end of life management of their products.
- There is no mandatory training or medication collections program for livestock producers in Ontario. The Obsolete Pesticide & Livestock Medication Collection Program is a voluntary program that is delivered every three years in Ontario.
- The US – No national take-back legislation or nationally coordinated system for the management of unwanted/waste pharmaceuticals. Many state and local government have implemented take-back legislation and programs. The U.S. Drug Enforcement Administration (DEA) operates National Prescription Drug Take-Back initiative, local law enforcement agencies may also operate medicine take-back programs.
- Europe – EU legislation has required appropriate collection systems for unused or expired human and veterinary medicinal products since 2004 and 2001, respectively.

APPENDIX C: OCCURRENCE OF PHARMACEUTICALS IN THE GREAT LAKES BASINS.

Table C1: Overall pharmaceutical occurrence in Great Lakes							
Overall for Great Lakes							
Compound	Water Quality Guideline (WQG)	No Observed Effect Concentration (NOEC) in ng/L	Lowest Observed Effect Concentration (LOEC) in ng/L	Average Concentration in ng/L	References	Impacts	Comments
Anti-epileptic							
Carbamazepine	N/A	3000	750	749	Hull et al. 2015	N/A	N/A
Anti-inflammatory							
Ibuprofen	N/A	N/A	16000	790	Hull et al. 2015	N/A	N/A
Naproxen	N/A	1700	170	551	Hull et al. 2015	N/A	N/A

Table C2: Pharmaceutical occurrence in Lake Ontario								
Compound	Medium (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Analgesics								
Acetaminophen	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	23.8ng/L (Effluent) 4.5ng/L (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
Anti-biotics								
Erythromycin	Surface water	Niagara River (river)	2-83 ng/L	N/A	WWTP	Arnnok et al. 2017	N/A	N/A
Sulfamethoxazole	Surface water	Niagara River (river)	3-260 ng/L	N/A	WWTP	Arnnok et al. 2017	N/A	N/A
	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	23.8 ng/L (Effluent) 2.5ng/L (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS

Table C2: Pharmaceutical occurrence in Lake Ontario

Compound	Medium (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Trimethoprim	Surface water	Niagara River (river)	3-52 ng/L	N/A	WWTP	Arnnok et al. 2017	N/A	N/A
	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	51.5ng/L (Effluent) 4.7ng/L (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
	WWTP effluent and surface waters near plant	Burlington WWTP and Hamilton Harbour	84ng/L (Effluent) 43ng/L (Surface waters)	N/A	WWTP	Metcalfe et al. 2003	N/A	N/A
Anti-depressants								
Norfluoxetine	Fish tissues	Niagara River (river)	0.2-40 ng/g	N/A	WWTP	Arnnok et al. 2017	N/A	From bio-accumulation
Fluoxetine	WWTP effluent and surface waters near plant	Burlington WWTP and Hamilton Harbour	38ng/L (Effluent) 13ng/L (Surface waters)	N/A	WWTP	Metcalfe et al. 2003	N/A	N/A
Norsertaline	Fish tissues	Niagara River (river)	400 ng/g in brain, 647 ng/g in liver, 44 ng/g in gonad, and 73 ng/g in muscle	N/A	WWTP	Arnnok et al. 2017	N/A	N/A
Sertraline	Surface water	Niagara River (river)	218ng/L	30-60 µg/L (pH 8.5) 120 µg/L (pH 7.5) 250-500 µg/L (pH 6.5)	WWTP	Arnnok et al. 2017	Decreased growth/survival rates of fathead minnow after 7 days exposure	N/A
	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	11.1ng/L (Effluent) 0.4ng/L (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
Bupropion	Surface water	Niagara River (river)	217ng/L	200-2000 ng/L	WWTP	Arnnok et al. 2017	Altered predator avoidance behavior of minnows	N/A
Venlafaxine	Surface water	Niagara River (river)	387ng/L	200 µg/L	WWTP	Arnnok et al. 2017	ERC causes decrease in prey capture ability	N/A
	Fish Tissues	Niagara River (river)	57 ng/g	N/A	WWTP	Arnnok et al. 2017	N/A	From Bio-accumulation
	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	123.4ng/L (Effluent) 50.7ng/L (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS

Table C2: Pharmaceutical occurrence in Lake Ontario

Compound	Medium (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Citalopram	Surface water	Niagara River (river)	168 to 188 ng/L	5 µg/L	WWTP	Arnnok et al. 2017	Decrease cortisol levels in trout. Causes decrease in predator avoidance.	N/A
Anti-diabetics								
Metformin	Surface water	Niagara River (river)	3-20 ng/L	N/A	WWTP	Arnnok et al. 2017	N/A	N/A
Anti-epileptics								
Carbamazepine	Surface water	Niagara River (river)	<3 ng/L	N/A	WWTP	Arnnok et al. 2017	N/A	N/A
	WWTP effluent and downstream	Cootes Paradise Marsh	92.7ng/L (Effluent)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
		Hamilton Harbour	54.9ng/L (Downstream)	N/A	WWTP			
	WWTP effluent and surface waters near plant	Burlington WWTP and Hamilton Harbour	64ng/L (Effluent) 23ng/L (Surface waters)	N/A	WWTP	Metcalfe et al. 2003	N/A	N/A
Dilantin	Surface water	Niagara River (river)	<3 ng/L	N/A	WWTP	Arnnok et al. 2017	N/A	N/A
Anti-histamines								
Diphenhydramine	Surface water	Niagara River (river)	252 ng/L	5.6 µg/L, pH 6.5-8.5 49.1 µg/L, pH 6.5-8.5	WWTP	Arnnok et al. 2017	Affects feeding at conc 1 and growth at conc 2 at 7 days exposure	N/A
	Fish Tissues	Niagara River (river)	0.05-7.3 ng/g	N/A	WWTP	Arnnok et al. 2017	N/A	From Bio-accumulation
Anti-inflammatory								
Ibuprofen	WWTP effluent and downstream	Cootes Paradise Marsh	92.4ng/L (Effluent)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
		Hamilton Harbour	20.3ng/L (Downstream)	N/A	WWTP			
	WWTP effluent and surface waters near plant	Burlington WWTP and Hamilton Harbour	94ng/L (Effluent) 27ng/L (Surface waters)	N/A	WWTP	Metcalfe et al. 2003	N/A	N/A

Table C2: Pharmaceutical occurrence in Lake Ontario								
Compound	Medium (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Naproxen	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	73.4ng/L (Effluent) 30.2ng/L (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
	WWTP effluent and surface waters near plant	Burlington WWTP and Hamilton Harbour	41ng/L (Effluent) 39ng/L (Surface waters)	N/A	WWTP	Metcalfe et al. 2003	N/A	N/A
Fenoprofen	WWTP effluent and surface waters near plant	Burlington WWTP and Hamilton Harbour	62ng/L (Effluent) 142ng/L (Surface waters)	N/A	WWTP	Metcalfe et al. 2003	N/A	N/A
Ketoprofen	WWTP effluent and surface waters near plant	Burlington WWTP and Hamilton Harbour	13ng/L (Effluent) Not determined (Surface waters)	N/A	WWTP	Metcalfe et al. 2003	N/A	N/A
Diclofenac	WWTP effluent and surface waters near plant	Burlington WWTP and Hamilton Harbour	5ng/L (Effluent) 18ng/L (Surface waters)	N/A	WWTP	Metcalfe et al. 2003	N/A	N/A
Beta Blockers								
Atenolol	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	9.0ng/L (Effluent) 10.9ng/L (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
Metoprolol	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	8.7ng/L (Effluent) 5.7ng/L (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
Propranolol	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	59.9ng/L (Effluent) 4.7ng/L (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
Hormones								
Estrone (E1)	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	5.2ng/L (Effluent) <LOQ (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
Estradiol (E2)	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	Not detected	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS

Table C2: Pharmaceutical occurrence in Lake Ontario

Compound	Medium (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Androstenedione	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	3.62ng/L (Effluent) 2.0ng/L (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
Testosterone	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	<LOQ	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS

Lipid regulators

Gemfibrozil	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	6.2ng/L (Effluent) 1.3ng/L (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
	WWTP effluent and surface waters near plant	Burlington WWTP and Hamilton Harbour	5ng/L (Effluent) 38ng/L (Surface waters)	N/A	WWTP	Metcalfe et al. 2003	N/A	N/A
Bezafibrate	WWTP effluent and surface waters near plant	Burlington WWTP and Hamilton Harbour	12ng/L (Effluent) 10ng/L (Surface waters)	N/A	WWTP	Metcalfe et al. 2003	N/A	N/A
Atorvastatin	WWTP effluent and surface waters near plant	Burlington WWTP and Hamilton Harbour	44ng/L (Effluent) 10ng/L (Surface waters)	N/A	WWTP	Metcalfe et al. 2003	N/A	N/A

Stimulants

Caffeine	WWTP effluent and downstream	Cootes Paradise Marsh Hamilton Harbour	839.4ng/L (Effluent) 742.5ng/L (Downstream)	N/A	WWTP	McCallum et al. 2017	N/A	Time weighted concentrations taken with POCIS
	WWTP effluent and surface waters near plant	Burlington WWTP and Hamilton Harbour	22ng/L (Effluent) 33ng/L (Surface waters)	N/A	WWTP	Metcalfe et al. 2003	N/A	N/A

Table C3: Pharmaceutical occurrence in Lake Erie

Compound	Matrix (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Anti-biotics								
Trimethoprim	WWTP effluent and surface waters near plant	West Windsor WWTP and Detroit River	9ng/L (Effluent) Not determined (Surface waters)	Not mentioned	WWTP	Metcalfe et al. 2003	Not mentioned	N/A
Anti-depressants								
Anti-epileptics								
Carbamazepine	WWTP effluent and surface waters near plant	West Windsor WWTP and Detroit River	7ng/L (Effluent) 4ng/L (Surface waters)	Not mentioned	WWTP	Metcalfe et al. 2003	Not mentioned	N/A
Anti-inflammatories								
Diclofenac	WWTP effluent and surface waters near plant	West Windsor WWTP and Detroit River	63ng/L (Effluent) Not determined (Surface waters)	Not mentioned	WWTP	Metcalfe et al. 2003	Not mentioned	N/A
Ibuprofen	WWTP effluent and surface waters near plant	West Windsor WWTP and Detroit River	167ng/L (Effluent) Not determined (Surface waters)	Not mentioned	WWTP	Metcalfe et al. 2003	Not mentioned	N/A
Naproxen	WWTP effluent and surface waters near plant	West Windsor WWTP and Detroit River	168ng/L (Effluent) Not determined (Surface waters)	Not mentioned	WWTP	Metcalfe et al. 2003	Not mentioned	N/A
Lipid regulators								
Bezafibrate	WWTP effluent and surface waters near plant	West Windsor WWTP and Detroit River	65ng/L (Effluent) Not determined (Surface waters)	Not mentioned	WWTP	Metcalfe et al. 2003	Not mentioned	N/A
Gemfibrozil	WWTP effluent and surface waters near plant	West Windsor WWTP and Detroit River	43ng/L (Effluent) 2ng/L (Surface waters)	Not mentioned	WWTP	Metcalfe et al. 2003	Not mentioned	N/A
Stimulants								
Caffeine	WWTP effluent and surface waters near plant	West Windsor WWTP and Detroit River	677ng/L (Effluent) 46ng/L (Surface waters)	Not mentioned	WWTP	Metcalfe et al. 2003	Not mentioned	N/A

Table C4: Pharmaceutical occurrence in Lake Huron

Compound	Medium(What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Anti-epileptic								
Carbamazepine	WWTP effluent	Grand River	Approx. 0.5µg/L	Not mentioned	WWTP	Hicks et al. 2017	Not mentioned	N/A
Anti-inflammatory								
Ibuprofen	WWTP effluent	Grand River	Approx. <0.5-3.5µg/L	Not mentioned	WWTP	Hicks et al. 2017	Not mentioned	N/A
Naproxen	WWTP effluent	Grand River	Approx. <0.5-3.5µg/L	Not mentioned	WWTP	Hicks et al. 2017	Not mentioned	N/A
Hormones								
17α-ethynylestradiol (EE2)	Fish tissues	St. Clair River	averaged 1.6 ± 0.6 ng/g (wet weight) in males and 1.43 ± 0.96 ng/g in females	Not mentioned	WWTP	Al-Ansari et al. 2010	Shorthead Redhorse Suckers had bio-accumulation in multiple tissues	N/A
EE2	WWTP effluent	Grand River	Between 5-20ng/L	Approx. 5ng/L	WWTP	Hicks et al. 2017	Intersex of male rainbow darter	N/A

Table C5: Pharmaceutical occurrence in Lake Superior

Compound	Medium (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Anticonvulsant								
Gabapentin	Surface water	Lake Superior nearshore sampling sites (Apostle Islands National Lakeshore)	13.7ng/L	Not mentioned	Not mentioned	Elliott and VanderMeulen, 2017	Not mentioned	N/A
Carbamazepine	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.06 µg/L	Not mentioned	Not mentioned	Christensen et al., 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	3.3µg/kg	Not mentioned	Not mentioned	Christensen et al., 2012	Not mentioned	N/A
Antimicrobial								
Triclosan	Surface water	Lake Superior nearshore sampling sites (Apostle Islands National Lakeshore)	74.9 ng/L	Not mentioned	Not mentioned	Elliott and VanderMeulen, 2017	Not mentioned	N/A

Table C5: Pharmaceutical occurrence in Lake Superior

Compound	Medium (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Psychoactive central nervous system stimulant								
1,7-Dimethylxanthine (p-Xanthine)	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.1 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	4.1µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Caffeine	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.06 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	2.6 µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Opiate								
Codeine	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.046 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	2.6µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Antianginal and antihypertensive								
Dehydronifedipine	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.08 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A

Table C5: Pharmaceutical occurrence in Lake Superior

Compound	Medium (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Diltiazem	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.06 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	3.0µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Antihistamine								
Diphenhydramine	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.036 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	2.7µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Dehydronifedipine	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	3.4µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Antibiotics								
Sulfamethoxazole	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.16 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	3.2µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Thiabendazole	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.06 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	2.1µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A

Table C5: Pharmaceutical occurrence in Lake Superior

Compound	Medium (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Trimethoprim	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.034 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	3.0µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Azithromycin	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	1.7µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Erythromycin	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	3.3µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Anticoagulant								
Warfarin	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.08 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	2.5µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Pain/fever medicine								
Acetaminophen	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.12 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	1.5µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A

Table C5: Pharmaceutical occurrence in Lake Superior

Compound	Medium (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Respiratory disease medicine								
Albuterol (Salbutamol)	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.08 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	2.2µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Stomach Acid Production Suppressant								
Ranitidine	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	2.2µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Cimetidine	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	1.8µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
OCD, Major Depression, Anxiety Medicine								
Fluvoxamine	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	1.2µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Antifungal								
Miconazole	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	1.9µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A

Table C5: Pharmaceutical occurrence in Lake Superior

Compound	Medium (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Antidepressant								
Cotinine	Filtered surface water	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.6 µg/L	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	2.6µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Buprion	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.25µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Citalopram	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.25µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Duloxetine	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.25µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Fluoxetine	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake superior	4.4µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Norfluoxetine	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	2.5µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Norsertaline	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.5µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A
Paroxetine	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.25µg/kg	Not mentioned	Not mentioned	Christensen <i>et al.</i> , 2012	Not mentioned	N/A

Table C5: Pharmaceutical occurrence in Lake Superior

Compound	Medium (What it was found in)	Location (where it was found)	Concentration (how much)	Environmentally relevant concentration (ERC)	Source (What is the emission source)	References	Impacts	Comments
Sertraline	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.25µg/kg	Not mentioned	Not mentioned	Christensen et al., 2012	Not mentioned	N/A
Venlafaxine	Bottom sediment	Howards Bay, St. Louis River, and Superior Bay at Lake Superior	0.25µg/kg	Not mentioned	Not mentioned	Christensen et al., 2012	Not mentioned	N/A

Table C6: Occurrence of Pharmaceuticals in International Jurisdictions (Source: Li, 2014)

Range of Concentrations (ng/L)										
	North America			Europe			Asia			PNEC (ng/L)
	WWTP effluent	Surface Waters	Groundwater	WWTP effluent	Surface Waters	Groundwater	WWTP effluent	Surface Waters	Groundwater	
Antibiotics										
Trimethoprim	2550	145	18	39	59.9	n/a	2000	1808	n/a	1000
Ciprofloxacin	n/a	77	0.28	499	n/a	n/a	2050	n/a	40	20
Sulfamethoxazole	310	170	458	185	33	38	397	4330	3	20000
Analgesics										
Naproxen	1550	555	n/a	n/a	80.5	n/a	n/a	n/a	n/a	37000
Ibuprofen	11900	203	3.97	8000	468	395	1600	30	n/a	5000
Acetaminophen	n/a	n/a	1890	n/a	40	n/a	n/a	n/a	n/a	9200
Ketoprofen	n/a	16	n/a	940	293	2886	128	620	n/a	15.6x10 ⁶
Diclofenac	4200	n/a	n/a	740	794	24	1760	62	n/a	10000
Salicylic acid	n/a	n/a	n/a	3170	184	n/a	n/a	n/a	n/a	11200
Anti-epileptic										
Carbamazepine	1550	735	420	150	366	3600	21000	120	n/a	25000
Stimulants										
Caffeine	n/a	n/a	290	300	568	4500	3180	n/a	n/a	n/a
Estrogens										
Estriol	590	n/a	n/a	n/a	1.9	0.16	25	n/a	n/a	1520
Estrone	n/a	n/a	n/a	70	0.3-4.6	1.6-3.5	36	5	n/a	100
17β-estradiol	n/a	n/a	n/a	9.2	1.2	0.79	1	n/a	n/a	10
17α-estradiol	180	n/a	n/a	n/a	0.31	0.21-1.6	n/a	n/a	n/a	n/a
17α-ethinylestradiol	n/a	n/a	n/a	n/a	0.33	0.94-3	1.3	n/a	n/a	30

APPENDIX D. DISTRIBUTION OF WASTEWATER TREATMENT PLANTS IN THE GREAT LAKES BASIN

Table D1: Distribution of Ontario wastewater treatment plants in the Great Lakes basin. Source: Arvai et al. (2014)

Facility type	Number of facilities	Percentage of total number of facilities	Total average daily flow (MLD = million liters per day)	Percentage of total average daily flow
Primary	8	1.7%	96.0	1.7%
Community septics (all types)	7	1.5%	1.0	0.0%
Lagoons (all types)	175	37.2%	178.0	3.1%
Secondary	212	45.2%	5038.1	87.3%
Tertiary	68	14.5%	456.8	7.9%
Totals	470	100%	5769.1	100%

Table D2: Distribution of US wastewater treatment plants in the Great Lakes basin. Source: Arvai et al. (2014)

Facility type	Number of facilities	Percentage of total number of facilities	Total average daily flow (MLD = million liters per day)	Percentage of total average daily flow
Secondary	311	31.8%	514.4	4.2%
Advanced treatment	563	57.6%	11780	95.8%
Unknown	104	10.6%	n/a	n/a
Totals	978	100.0%	12294	100.0%

APPENDIX E. IMPACTS OF PHARMACEUTICALS ON SELECTED SPECIES

Table E1: Observed impacts on selected species

Name of Species	Location of Study	Observed Impact	Reference
Rainbow Darters	Grand River	Estrogens in WWTP effluent caused severe intersex of males	Hicks et al. (2017)
Bluegill Sunfish	Cootes Paradise Marsh	Increase in metabolic rate in response to wastewater effluent exposure	Du et al. (2018)
Shorthead Redhorse Suckers	St. Clair River	Bio-accumulation of 17 α -ethinylestradiol (a common contraceptive drug)	Al-Ansari et al. (2010)
Oregon Shore Crab	Lab in Oregon	Reduced predator avoidance behaviour when exposed to fluoxetine (anti-depressant)	Peters et al. (2017)
Smallmouth Bass	Niagara River	Bio-accumulation of variety of pharmaceuticals including anti-depressants (Citalopram, Sertraline, Venlafaxine, Bupropion), anti-histamines (Diphenylhydramine) and anti-depressant metabolites (Norsertaline, Norfluoxetine)	Arnnok et al. (2017)
	Potomac River	Intersex due to exposure to estrogens	Blazer et al. (2007)
Largemouth Bass	Niagara River	Bio-accumulation of variety of pharmaceuticals including anti-depressants (Citalopram, Sertraline, Venlafaxine, Bupropion), anti-histamines (Diphenylhydramine) and anti-depressant metabolites (Norsertaline, Norfluoxetine)	Arnnok et al. (2017)
Rudd	Niagara River	Bio-accumulation of variety of pharmaceuticals including anti-depressants (Citalopram, Sertraline, Venlafaxine, Bupropion), anti-histamines (Diphenylhydramine) and anti-depressant metabolites (Norsertaline, Norfluoxetine)	Arnnok et al. (2017)
Rock Bass	Niagara River	Bio-accumulation of variety of pharmaceuticals including anti-depressants (Citalopram, Sertraline, Venlafaxine, Bupropion), anti-histamines (Diphenylhydramine) and anti-depressant metabolites (Norsertaline, Norfluoxetine)	Arnnok et al. (2017)
White Bass	Niagara River	Bio-accumulation of variety of pharmaceuticals including anti-depressants (Citalopram, Sertraline, Venlafaxine, Bupropion), anti-histamines (Diphenylhydramine) and anti-depressant metabolites (Norsertaline, Norfluoxetine)	Arnnok et al. (2017)

Table E1: Observed impacts on selected species

Name of Species	Location of Study	Observed Impact	Reference
White Perch	Niagara River	Bio-accumulation of variety of pharmaceuticals including anti-depressants (Citalopram, Sertraline, Venlafaxine, Bupropion), anti-histamines (Diphenylhydramine) and anti-depressant metabolites (Norsertaline, Norfluoxetine)	Arnnok et al. (2017)
Walleye	Niagara River	Bio-accumulation of variety of pharmaceuticals including anti-depressants (Citalopram, Sertraline, Venlafaxine, Bupropion), anti-histamines (Diphenylhydramine) and anti-depressant metabolites (Norsertaline, Norfluoxetine)	Arnnok et al. (2017)
Bowfin	Niagara River	Bio-accumulation of variety of pharmaceuticals including anti-depressants (Citalopram, Sertraline, Venlafaxine, Bupropion), anti-histamines (Diphenylhydramine) and anti-depressant metabolites (Norsertaline, Norfluoxetine)	Arnnok et al. (2017)
Steelhead	Niagara River	Bio-accumulation of variety of pharmaceuticals including anti-depressants (Citalopram, Sertraline, Venlafaxine, Bupropion), anti-histamines (Diphenylhydramine) and anti-depressant metabolites (Norsertaline, Norfluoxetine)	Arnnok et al. (2017)
Yellow Perch	Niagara River	Bio-accumulation of variety of pharmaceuticals including anti-depressants (Citalopram, Sertraline, Venlafaxine, Bupropion), anti-histamines (Diphenylhydramine) and anti-depressant metabolites (Norsertaline, Norfluoxetine)	Arnnok et al. (2017)
Wild Goldfish	Cootes Paradise Marsh	Bio-accumulation of pharmaceuticals (particularly the anti-depressant, fluoxetine)	Muir et al. (2017)
Wild Carp	Cootes Paradise Marsh	Bio-accumulation of pharmaceuticals (particularly the anti-anxiety drugs, diazepam and oxazepam)	Muir et al. (2017)
Round Goby	Dundas WWTP (downstream)	Fish caged closer to outfall point experienced higher mortality rate.	McCallum et al. (2017)
Mosquito Fish	Jackson's Creek WWTP in Victoria, Australia	Endocrine disrupting compounds caused an <u>increase</u> in reproductive behaviour	Saaristo et al. (2014)
Three-Spined Stickleback	In lab using WWTP effluent from Devon, United Kingdom	Endocrine disrupting compounds caused a <u>decrease</u> in reproductive behaviour	Sebire et al. (2011)

Table E1: Observed impacts on selected species

Name of Species	Location of Study	Observed Impact	Reference
Fathead Minnow	In lab conditions using fluoxetine (anti-depressant) only	Reduced predator avoidance behaviours, altered mating behaviours, and even increased aggression of males towards females at the highest exposure levels (100 µg/L) to fluoxetine	Weinberger and Klaper (2014)
	In lab conditions using 17a-ethinylestradiol (EE2) only	Decreased egg fertilization and skewed sex ratio toward females both of which were significantly affected at the lowest EE2 concentration tested (<1 ng/L) Note: Life cycle study	Parrott and Blunt (2005)
	In lab conditions	Naproxen, gemfibrozil, diclofenac, ibuprofen, salicylic acid, and acetaminophen at concentrations of 1,000, 300, 100, 30, or 10 ng/L caused no observable effect individually. It was noted that mixtures of the above at concentrations of 100 or 300 ng/L caused an increased occurrence of larval deformities. Note: Life cycle study	Parrott and Bennie (2009)
	In lab conditions using venlafaxine (anti-depressant) only	Exposed fathead minnows over a full lifecycle in a flow-through system to nominal venlafaxine concentrations of 0.88, 8.8, and 88 mg/L. Mean measured venlafaxine concentrations in these treatments were 1.0, 9.3 and 75 mg/L. During the 167-168 day exposure, no significant changes were observed in survival, or the weights and lengths of fathead minnows Note: Life cycle study	Parrott and Metcalfe (2017)

